

Monday, 25 June 2007

Oral Sessions

MONDAY, 25 JUNE 2007, 8:30–10:00

Guimaraes

Experimental studies on arrhythmia mechanisms

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Differential effects of male and female sexual steroids on heart rate and ventricular repolarization

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Aim: There are well known gender-related differences in cardiac repolarization reserve. In this study we aimed to examine the effects testosterone and estrogen on the ECG parameters in male and female dogs and to compare the dofetilide-induced lengthening of QTc interval in castrated and hormone-treated animals. To understand the underlying molecular mechanism, we examined expression of cardiac ion channels.

Methods: ECG records were taken from 10 male and 10 female dogs of sexually active age. Control ECG measurements (in anaesthesia) were followed by dofetilide challenge. To demonstrate the effect of sex-hormones on ECG, the same recording procedure was repeated one month after surgical castration of animals and further one month period of inverted hormone substitution (estrogen to castrated males and testosterone to castrated females). Finally, the hearts were excised and the expression of ion channels in the inversely hormone substituted groups was compared.

Results: We found that heart rate was decreased and PQ interval increased by deprivation of sex hormones in both genders, while inverted hormonal substitution restored control values. The lack of testosterone (orchietomy) significantly increased the duration of QT and QTc intervals, QTc-dispersion and the dofetilide-induced lengthening of QTc, while testosterone treatment of castrated females had opposite effects. Expression of ion channel proteins responsible for mediation of I_{K1} and I_{to} currents (Kir2.1 and Kv4.3, respectively), was significantly higher in the testosterone-treated castrated females than in the estrogen-treated castrated males.

Conclusions: Our data show that myocardium repolarization reserve is significantly enhanced by testosterone, but not estrogen, in both genders. This effect of testosterone may be the result of K⁺-channel protein over-expression, and thus may provide protective effect against arrhythmias via increasing the repolarization reserve.

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Effect of parasympathetic stimulation on heart rate and rhythm in deltaKPQ-SCN5A mice with Long QT Syndrome 3

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Arrhythmias in long QT 3 (LQT3) occur predominantly at rest. Increased vagal tone during sleep has been suggested as an arrhythmogenic trigger in LQT3 but studies in LQT3 patients are scarce.

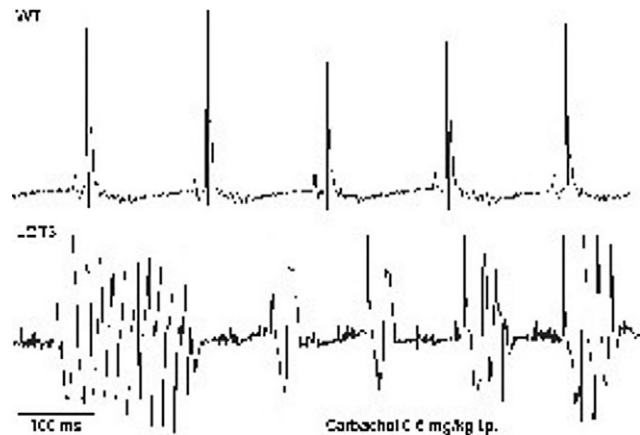
Methods: Telemetry Holter ECGs were recorded in freely roaming adult LQT3 mice with the knock-in deletion Δ KPQ SCN5A and in WT littermates at baseline, during stress protocols, and during administration of carbachol 0.5 mg/kg with or without chronic oral propranolol.

Action potential duration (APD) was measured in isolated, beating hearts in monophasic action potential recorded both at fix RV pacing frequency and during spontaneous rhythm at baseline and during infusion with Carbachol 10–7 to 10–5.

Results: During administration of carbachol, Δ KPQ SCN5A (6/6) but not WT (0/6) developed prolonged ventricular bigemini or runs of ventricular tachycardia in vivo, see figure.

In contrast, arrhythmias were neither documented during physical nor during mental stress tests. Chronic oral propranolol did not protect from carbachol-induced arrhythmias in Δ KPQ SCN5A, $p < 0.05$. Carbachol did not prolong APD at fix pacing frequency, but induced bradycardia and thereby prolonged APD in Δ KPQ LQT3 compared to WT APD and compared to Δ KPQ SCN5A APD at faster heart rate, e.g. carbachol 10–6, APD 90, Δ KPQ SCN5A 87 ± 5 ms, vs. WT 69 ± 8 , $p < 0.05$.

Conclusions: Parasympathetic stimulation is proarrhythmic and β -adrenoreceptor block does not protect from arrhythmias induced by parasympathetic stimulation in the Δ KPQ SCN5A LQT3 mouse model.



Telemetric ECG

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Interventricular Differences on Ventricular Fibrillation Frequencies and Dynamics in Large Mammals

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Background: It remains controversial whether multiple randomly wandering electrical wavelets, a single rotor or multiple spiral-wave breakups maintain VF and if there are intra and/or interventricular clear differences during VF in large hearts.

Objective: We sought to determine in the pig heart whether the robust regional and intraventricular differences in VF dynamics and frequency found in small species such as guinea pig do exist in larger mammals.

Methods: Optical mapping of the anterior and posterior epicardial surfaces of both ventricles (~60–70% of the total surface) was performed in 8 isolated Langendorff-perfused porcine hearts during VF. Sequential epochs (5") were recorded (Di4ANEPPS), randomly focused on left ventricular anterior (LVa), LV posterior (LVp), right ventricle anterior (RVa) and RV posterior (RVp) surfaces. Phase and spectral analyses showed singularity points density (SPd; wavebreaks), maximum dominant frequency (DFmax), percentage of the total filmed area fibrillating at DFmode (ADFmode), standard deviation (SD) of observed DFs, number of DF domains (ND), and mean and maximum regularity index (RImean, RImax).

Results: LV showed significantly higher DFmax than RV (LVa: 14.6 ± 1.1 , LVp: 14.8 ± 0.7 vs RVa: 13.1 ± 0.6 , RVp: 14.3 ± 0.9 Hz; $p = 0.041$;

mean±SE; RM-ANOVA) and lower organization as reflected by: higher values of SPd (36 ± 7 , 44 ± 7 vs 25 ± 5 , 27 ± 9 SP/sec/cm²; $p < 0.001$), SD (1.6 ± 0.3 , 1.7 ± 0.3 vs 1.1 ± 0.2 , 1.3 ± 0.2 Hz; $p = 0.014$) and ND (24.9 ± 3 , 23 ± 3 vs 16.7 ± 1 , 15.6 ± 2 ; $p = 0.004$) and lower ADFmode ($46\pm 5\%$, $47\pm 6\%$ vs $56\pm 4\%$, $60\pm 6\%$; $p = 0.003$), RImean (0.45 ± 0.03 , 0.45 ± 0.03 vs 0.54 ± 0.03 , 0.57 ± 0.03 ; $p < 0.001$) and RImax (0.79 ± 0.02 , 0.78 ± 0.03 vs 0.82 ± 0.02 , 0.83 ± 0.01 ; $p = 0.013$). We found no significant differences in any measured parameters when comparing anterior Vs posterior surfaces of either ventricle.

Conclusions: fibrillatory activity in the LV of large mammals has a higher frequency, and is more irregular and disorganized than the RV. This finding indicates more 1:1 conduction in RV and more fibrillatory conduction where the fibrillation is faster (LV). This is probably secondary to chamber specific differences in ion channel density and electrophysiological properties. Of note, no significant intraventricular differences were found comparing anterior Vs posterior surfaces.

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A new SCN5A mutation (G579R) found in a SIDS case leads to an increased Nav1.5 protein expression without persistent current

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Background: Sudden Infant Death Syndrome (SIDS) is a sudden, unexpected death in infants and it remains unexplained even after appropriate investigation. SIDS is the leading cause of death in infants from 1 month to 1 year old. The index case of this study is a 6 month-old boy found dead in his bed. The post-mortem autopsy was normal, toxicological analyses were negative, and the family history for sudden death is so far unknown. The aim of this study was to screen for mutations in the SCN5A gene of this SIDS case and to examine the mutation-induced alterations in Na_v1.5 function.

Methods: All coding exons of SCN5A, the gene encoding the main cardiac sodium channel Na_v1.5, were screened for mutations. Wild type (WT) and mutant Na_v1.5 channels were expressed in HEK293 cells and sodium currents (I_{Na}) were analyzed using the whole cell patch clamp technique. The level of Na_v1.5 protein expression after transient transfection in HEK293 cells was investigated by Western blot.

Results: A heterozygous missense mutation was identified in the index patient. The G to A substitution at position 1818 resulted in the G579R (GR) mutation located in the first intracellular loop of Na_v1.5. We found a significant 51% increase of the I_{Na} density generated by mutant channels (WT: 255 ± 37 pA/pF n=13 GR: 384 ± 49 pA/pF n=12). The activation properties and the entry into the intermediate inactivation state were unchanged and no tetrodotoxin-sensitive persistent current could be measured. The voltage-dependence of steady-state inactivation of mutant channels showed a small 2 mV positive shift (WT: 80.9 ± 0.5 mV n=7, GR: -78.0 ± 1.1 mV n=9) and the time constant of recovery from inactivation was smaller (8 ms decrease. WT: 5.9 ± 2.1 ms n=11, GR: 24.0 ± 2.7 n=7). However, by themselves, these biophysical alterations cannot explain the increased sodium current. Quantification of the Western blot experiments showed that the G579R mutant Na_v1.5 expression was increased by more than 50%.

Conclusions: This G579R mutation of Na_v1.5 may be the cause of the sudden infant death syndrome by increasing the inward cardiac sodium current. However, the molecular mechanisms underlying this increased expression remain to be further studied.

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Both src tyrosine kinases and PKC mediate inhibitory effects of adrenergic alpha1A receptors on Kir2.x inward rectifier potassium channels

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Purpose: Inhibition of native I_{K1} currents by adrenergic α₁ receptors has been observed in native cardiomyocytes and has been linked to arrhythmogenesis in an animal model. The underlying molecular mechanisms, however, have not been elucidated to date. According to an increasing body of evidence the molecular basis of native I_{K1} current is mainly formed by Kir2.1 (KCNJ2), Kir2.2 (KCNJ12) and Kir2.3 (KCNJ4) channels. We therefore sought to investigate the role of those different Kir2.x channel subunits in this regulation with the use of the Xenopus oocyte expression system.

Methods: Adrenergic α_{1A} receptors (the predominant cardiac isoform) were co-expressed with cloned Kir2.1, Kir2.2 and Kir2.3 channels in Xenopus oocytes and electrophysiological experiments were performed using two-microelectrode voltage clamp.

Results: Activation of co-expressed adrenergic α_{1A} receptors by phenylephrine induced differential effects in Kir2.x channels. No effect was noticed in Kir2.1 channels. However, a marked inhibitory effect was observed in Kir2.2 channels. This regulation could be suppressed by kinase inhibitors staurosporine, genistein and PP2 indicating an essential role of src tyrosine kinase pathways. In contrast, co-application of kinase inhibitors chelerythrine, KN-93 and KT-5720 did not affect the regulation. Furthermore, the same effect as in Kir2.2 wild type channels was also observed in mutated Kir2.2 channels lacking functional phosphorylation sites for PKC and PKA, thereby excluding a functional role of those kinases. Heteromeric Kir2.1/2.2 channels also exhibited an inhibitory regulation by α_{1A} receptors. In Kir2.3 channels, a marked inhibitory effect of α_{1A} receptor activation was observed. This regulation could be attenuated by both staurosporine and chelerythrine but not by genistein, indicating a central role of protein kinase C.

Conclusions: In summary, on the molecular level the inhibitory regulation of I_{K1} currents by adrenergic α_{1A} receptors is probably based on effects on Kir2.2 and Kir2.3 channels. Kir2.2 is regulated via src tyrosine kinase pathways independent of protein kinase C, whereas Kir2.3 is inhibited by protein kinase C dependent pathways. Kir2.1 channels are insensitive to this regulation but may be affected indirectly in Kir2.1/2.2 heteromers. These findings elucidate molecular aspects of the adrenergic regulation of cardiac I_{K1} currents that may contribute to arrhythmogenesis under adrenergic stimulation.

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Functional expression of neuronal and cardiac sodium channels in human heart

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Introduction: Voltage gated sodium channels are responsible for the upstroke of the action potential in cardiac muscle. They are composed of pore-forming α- and auxiliary β-subunits. Different α-isoforms have distinct pharmacological properties and patterns of subcellular expression in the heart. Tetrodotoxin, (TTX) is a specific sodium channel blocker which inhibits different α-isoforms with different affinities. Nav1.5 is blocked by micromolar TTX concentrations whereas neuronal α-isoforms require only nanomolar concentrations. In addition, α-subunits are expressed together with different β-subunits.

Methods: We recorded sodium currents from acutely isolated human atrial cells with the patch-clamp-technique and examined their expression using immunocytochemistry and immuno-blotting.

Results: We show for the first time that neuronal TTX-sensitive isoforms are functionally expressed in human atrial cells, in addition to cardiac TTX-resistant sodium channels. Concentration-response curves for TTX block of sodium currents from atrial myocytes using whole cell patch clamp show that neuronal sodium channel isoforms contribute approximately 15% to the total sodium current whereas TTX-resistant isoforms are responsible for the remaining 85%. The presence of TTX-sensitive neuronal isoforms was confirmed by Western Blot, consistent with our functional data. Using immunocytochemistry, we determined isoform-specific subcellular localization of sodium channel α - and β -subunits. This is also the first demonstration of β -subunit expression in human heart.

Conclusions: We show for the first time that both neuronal and cardiac sodium channels are functionally expressed in human heart. Furthermore, we provide evidence for the existence of all known β -subunits and describe the subcellular co-localization of specific α - and β -subunits.

MONDAY, 25 JUNE 2007, 8:30–10:00

Evora

Epidemiological and clinical aspects of atrial fibrillation

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New onset atrial fibrillation is an independent predictor of in-hospital mortality in patients admitted with heart failure. Results of the Euro Heart Failure Survey

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Background: The prognostic significance of atrial fibrillation (AF) in patients admitted due to heart failure (HF) remains poorly understood.

Objective: To evaluate in what way AF, and its different presentations, affect in-hospital mortality in patients admitted with HF.

Methods: The Euro Heart Failure Survey was conducted to ascertain how hospitalized HF patients are managed in Europe. The survey enrolled 10701 patients over a 6-week period in 115 hospitals from 24 countries. For this analysis patients were divided in 3 groups according to the type of AF; persistent-AF (patients with known history of AF), new onset-AF (no history of AF with AF diagnosed during hospitalization) and no-AF (no history of AF and no AF during hospitalization). Clinical variables, treatment, duration of hospitalization and survival status were assessed and compared among groups.

Results: Table 1 summarises the clinical characteristics and in-hospital evolution of the different groups. In the univariate analysis the type of AF (but not the presence of AF), fast AF (>120 beats/min), age, female gender, ejection fraction (EF), moderate or severe left atrial (LA) dilatation, use of antiarrhythmic drugs (AAD) and inotropic treatment were predictors of mortality. When including these variables in a multivariate model, new onset-AF (not fast AF) remained an independent predictor of mortality (OR 1.5 [CI, 1.1–2.0]).

Conclusion: In patients admitted with HF new onset AF is an independent predictor of in-hospital mortality.

Table 1

	No AF (n = 6027)	Persistent AF (n = 3673)	New Onset AF (n = 1001)	P value
Mean age (SD)	70 (13)	73 (12)	73 (12)	<0.001
Male (%)	54	51	52	0.005
Fast AF (%)	0	27	77	<0.001
EF < 50%	42	43	42	0.012
Mod/Sev LA dilation (%)	13	28	17	<0.001
AAD (%)	7	22	32	<0.001
ACEI/ARB (%)	65	67	61	0.01
Beta blocker (%)	40	33	36	<0.001
Digoxine (%)	21	56	52	<0.001
Days CCU (SD)	1 (3)	1 (3)	2 (4)	<0.001
Mortality (%)	7	7	12	<0.001

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The impact of the sinus rhythm restoration during hospitalization on the long-term mortality in patients with acute myocardial infarction accompanied with atrial fibrillation

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Background: We have previously reported that survivors of acute myocardial infarction with atrial fibrillation (AF) at discharge have higher mortality rate than those without AF. AF can deteriorate hemodynamics in the setting of acute myocardial infarction (AMI), however, it is not fully clarified whether aggressive treatment to restore sinus rhythm during hospitalization benefits long-term mortality.

Aim of the study: In the observational study, we examined AMI patients with AF on admission to determine independent predictors of following sinus recovery and to evaluate the association between the rhythm at discharge and long-term mortality.

Patients and Methods: Among 5,714 patients who had acute myocardial infarction and registered to our database, 324 patients had AF on admission. Eleven patients died during hospitalization and 313 survivors were analyzed in this study. They were divided into two groups according to the heart rhythm at discharge: SR group and AF group. We determined predictors of sinus rhythm restoration during hospitalization using logistic regression model. Furthermore, we compared the mortality after discharge of each group.

Results: Between these two groups, there were no significant differences in age, gender, classical risk factors of AMI. More patients in SR group had reperfusion therapy within 24 hours from the onset (84.6% vs. 75.0%, $p=0.036$) and less heart failure (3.2% vs. 8.6%, $p=0.037$). On the other hand, the size of infarct area evaluated by peak value of creatinine kinase was larger in the SR group. In multivariate analysis using logistic regression model, reperfusion therapy and non-anterior MI were independent predictors of conversion to SR. After discharge, 32 patients died during mean follow-up period of 760 days. There was no significant differences in survival rate between SR group and AF group (89.8% vs. 89.7%, $p=0.87$).

Conclusions: In patients with AMI with AF on admission, conversion to SR during hospitalization had no relation to survival rate after discharge. In such patients AF was highly associated with other predictors of mortality after AMI, so without improving confounding factors the effect of rhythm control on long-term mortality seems to be minimal.

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The significance of acute and chronic atrial fibrillation in post myocardial infarction patients

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Introduction: Atrial fibrillation (AF) is an independent predictor of increased mortality risk and adverse cardiac events in post myocardial infarction patients. The mechanisms behind the increased risk conferred by AF remains unclear. We investigated the significance of acute and chronic AF in the setting of myocardial infarction.

Methods: 500 consecutive patients with a diagnosis of acute myocardial infarction (AMI) were enrolled. 358 male and 142 female patients were identified. Mean age was 68.27 years (Range 28–93 years). The follow up period was 2–4.6 years (Mean = 3.3 years). They were divided into 3 groups – Patients with AF on admission – Chronic AF (n=67), Acute/New Onset AF (n=57) and patients without AF (n=376). Statistical analysis accounted for co-morbid conditions like hypertension, Diabetes mellitus, previous myocardial infarction, smoking and also peak creatine kinase levels, ejection fraction, location of the infarct, family history of ischaemic heart disease, thrombolysis and beta blocker usage.

Results: Patients in the AF group have a significantly higher mortality compared to the Non-AF group (53% vs 23%, $p < 0.001$). Patients in the AF group had a significantly higher incidence of ventricular fibrillation (VF) compared to Non-AF group (12.9% vs 6.38%, $p = 0.03$). The increased risk of VF was confined to the group with AF on admission – ie chronic AF group (16.42%, $p = 0.01$) than New Onset AF group (8.8%, $p = 0.42$). There was no association between AF and ventricular tachycardia ($p = 0.50$).

Univariate analysis demonstrated a significant correlation between VF and ejection fraction ($p = 0.04$), infarct size ($p = 0.043$), peak creatine kinase level ($p = 0.01$) and AF ($p = 0.034$). There was no significant relationship of VF with age ($p = 0.47$), gender ($p = 0.362$), diabetes mellitus ($p = 1.000$), Thrombolysis ($p = 0.624$), beta blocker therapy on admission ($p = 0.18$), previous myocardial infarction ($p = 0.0489$), hypertension ($p = 0.743$) and smokers ($p = 1.000$).

Multi variate analysis showed that only patients with AF on admission ie chronic AF bore a significant independent correlation with VF ($p < 0.001$).

Conclusion: There is a correlation between chronic AF and VF which can account for increased mortality and morbidity in AMI patients. It could be a epiphenomenon or due to irregular stimulation of the vulnerable ventricle with long-short-long sequences as a result of AF. The third mechanism postulated is that chronic AF may alter the ventricular geometry by creating a substrate and the acute myocardial infarction acts as a trigger for arrhythmia provocation.

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The Influence of resting heart rate and diastolic functions on B-type natriuretic peptide levels in patients with atrial fibrillation

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B-type natriuretic peptide (BNP) levels have been found to be elevated in patients with atrial fibrillation (AF). Several mechanisms have been proposed for this elevation but none of them has been established yet. We aimed to investigate the relationship between BNP levels, the average heart rate (HR) and left ventricular (LV) diastolic functions in patients with AF.

Method: Patients with a newly diagnosed persistent AF and normal ejection fraction without underlying significant structural heart disease were included in the study. After transesophageal echocardiography (Echo) they were cardioverted electrically. Before cardioversion (CV), patients rested under HR monitoring for 30 mins. Average HR of last five minutes was recorded as “basal HR”. Blood samples were taken for the measurement of BNP levels just before (“basal”) and 30 minutes after CV. All patients with sinus rhythm were given amiodarone. At 1st month, LV diastolic functions in sinus rhythm were evaluated by Echo and patients were defined to have no/mild and moderate/severe diastolic dysfunction. BNP levels were measured again.

Results: Thirty-one patients (19 female, mean age: 69.2 years) were included. Mean BNP level and basal HR were 241 pg/ml and 104 bpm, respectively. There was a weak but significant correlation between basal HR and BNP values (Pearson, $r = 0.43$, $p = 0.016$). Mean peak E/Em ratio measured by Echo during AF was 7.54, and it has also a weak but significant correlation with basal BNP levels (Pearson, $r = 0.378$, $p = 0.036$). Sinus rhythm was achieved in 28 patients (90.3%). AF recurred in 4 of 28 patients after 1 month. BNP levels at 30 minutes were significantly higher in patients with early AF recurrence (318.5 vs 153.4 pg/ml; $p = 0.05$). BNP levels decreased significantly after CV and went on decreasing at one month with the sinus rhythm maintenance (224.3 vs 153.4 vs 100.4 pg/ml). Patients with moderate-to-severe diastolic dysfunction had higher basal (279.9 vs 146.6 pg/ml, $p = 0.022$), 30 min (194.1 vs 96.6 pg/ml, $p = 0.022$) and 1st month (137.9 vs 47.9 pg/ml, $p = 0.002$) BNP levels comparing those with no or mild dysfunction.

Conclusions: BNP levels are increased in patients with AF and decrease significantly with the restoration of sinus rhythm. Patients resting HR has a positive correlation with the BNP levels. The severity of underlying diastolic dysfunction that could be observed after the restoration of sinus

rhythm seems to influence the elevation of BNP. Our data support the hypothesis that the HR and diastolic function of the patients might have a role in the mechanism of BNP elevation in patients with AF.

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Predictors of arrhythmia recurrence in patients with lone atrial fibrillation

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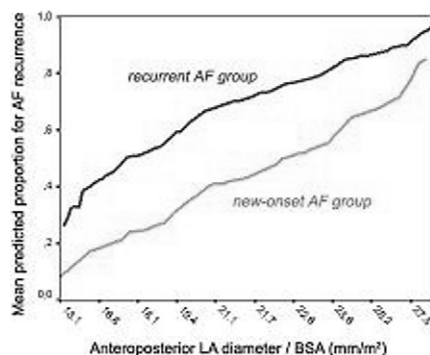
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Background: The need for antiarrhythmic drugs (AAD) after a first episode of atrial fibrillation (AF) is determined by the probability of recurrence.

The aim of this study was to assess the probability of relapse and the predictors of recurrence in patients with idiopathic AF.

Methods and Results: A cohort of 98 consecutive patients (pts) younger than 65 years admitted at the emergency room due to an episode of symptomatic idiopathic (lone) AF were included. On admission, a medical history was taken, an echocardiogram and 24-hour Holter monitoring were performed. Pts were seen at 3 and 6 months after the index episode. There were 35 (35.7%) pts with a new-onset AF episode and 63 (64.3%) with a recurrent AF episode. A majority of them were male (71%), with a mean age of 48 ± 11 years. New-onset AF episodes did not receive AAD. At 6-months follow-up, 57% of all patients suffered at least one symptomatic AF relapse. Pts with AF relapses belong more often to the recurrent group versus new-onset group of AF (65.1% vs. 34.9%, respectively, $p = 0.03$); they had larger LA diameter indexed for body surface area (BSA) (22.6 ± 3.7 mm/m² vs. 19.8 ± 3.2 mm/m², $p = 0.001$), larger left ventricular end-systolic diameter (18.4 ± 3.1 mm/m² vs. 17.2 ± 2.5 mm/m², $p = 0.05$) and a tendency towards a higher proportion of atrial tachycardia runs on Holter (66.7% vs. 50%, $p = 0.09$). Logistic regression analysis showed that the presence of previous episodes of AF (OR: 3.2; CI: 95%; 1.0–8.0, $p = 0.04$) and a larger anteroposterior LA diameter (OR: 1.3; CI: 95%; 1.1–1.6, $p = 0.001$) were independent predictors of AF recurrences at 6 months.

Conclusions: The recurrence rate in lone AF patients is high. The presence of previous episodes and a mildly enlarged anteroposterior LA diameter increase the probability of relapse of idiopathic AF.



AF recurrences

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Prospective validation of a simple point score for initial energy of external rectilinear biphasic cardioversion in patients with persistent atrial fibrillation

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Background: The optimal protocol of rectilinear biphasic cardioversion (Bi-DC) for persistent atrial fibrillation (AF) has not yet been prospectively evaluated. Therefore, it would be valuable to assess clinical utility of recently developed simple scoring system for Bi-DC.

Aims: Prospective validation of REBICAF (REctilinear BIphasic Cardioversion of persistent AF) point score in unselected patients persistent AF.

Methods and Results: Data from 644 procedures of Bi-DC in unselected patients with persistent AF were included into analysis. Data from 302 consecutive patients with AF who underwent step-up protocol (sequential shocks of 50 J-1 J/kg-2 J/kg-200 J) were used for development of REBICAF point score (group A). Additional group of consecutive patients (n=230) who underwent step-up protocol were included as validation group (group B). Finally, 114 patients underwent prospective validation of Bi-DC according to REBICAF-based protocol (group C). REBICAF score spans from 0-4 and adds two points to AF duration >7 months, and one point to previous cardioversion or left atrial >4.5 cm.

In group A and B more than 90% cumulative success rate was achieved by 1 J/kg, 2 J/kg and 200 J Bi-DC shocks in REBICAF score subgroups (0-1, 2 and 3-4 points), respectively. This initial energy settings for REBICAF subgroups (1 J/kg - 0-1 point, 2 J/kg - 2 points, and 200 J - 3-4 points) followed by 2 J/kg and/or 200 J were proposed as REBICAF-based protocol. Step-up protocol and REBICAF-based protocol had similar cumulative success rate (98% vs 90%, p=NS). However, REBICAF-based protocol had significantly higher conversion rate after initial shock (88% vs 35%, p<0.005) and required significantly lower number of shocks (1.03±0.21 vs 1.98±0.94, p<0.005) and mean cumulative energy (126±69 J vs 165±140 J, p<0.005) as compared to step-up protocol.

Conclusion: REBICAF point score seems to be a simple and useful method for prediction of successful initial energy for Bi-DC of persistent AF. Very low number of shocks and mean cumulative energy could be achieved according to REBICAF-based protocol.

MONDAY, 25 JUNE 2007, 8:30-10:00

Guarda

Syncope: Pathophysiology and treatment

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Syncope and C825T polymorphism in the gen encodes the B3 subunit of the human G protein - initial letter

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Recent studies have shown that polymorphisms of genes encoding sympathetic nervous system components could be involved in the predisposition to orthostatic hypotension and blood pressure variation. There are no studies assessing the molecular background in neurocardiogenic syncope. The human G protein is responsible for signal intracellular transduction and participates in cardiovascular reflexes. The aim of the study was evaluation an association of C825T polymorphism in the gen encodes the B3 subunit of G protein (GNB3) with the response to tilting in patients with numerous syncope.

Methods: 45 consecutive patients (men: 9 (20%); mean age: 36.9±18.9 years) tilted in a case of numerous syncope (mean: 17±13.3) recurrent from a long period (mean: 8±11.8 years) were enrolled into the study. All patients had no others diseases. Genomic DNA was extracted from blood using an extraction kit. The C825T polymorphism was diagnosed by restriction of the PCR amplicon with BseDI (MBI Fermentas). This polymorphism leads to a single nucleotide exchange at position 825 in the cDNA of GNB3 which causes the replacement of the amino acid cytosine by thymidine. Analysis of C825T polymorphism manifestation was performed according to the outcome of tilting: positive tilting (vasovagal syncope) n=30 vs negative tilting group n=15. Everyone signed up the voluntary agreement form before enrollment to the study. Used protocol obtained the Local Bioethics Committee's acceptance.

Results: In analyzed groups there was prevalence of genotype CT (60% vs 73%, P>0.05). In vasovagal patients uncommonly was genotype TT vs CT+CC (17% vs 83%, P<0.001) and in patients with negative outcome of tilting genotype CC vs CT+TT (7% vs 93%, P<0.001). The C allele

appeared in 53% vs 43% patients of analyzed groups (P>0.05) and the T allele respectively in 47% vs 57% patients (P>0.05).

Conclusions: Genotype CT is the most popular in patients with syncope. The predisposition to syncope in group of subjects with negative outcome of tilting seems to be associated with the GNB3 825T allele. Further population-based studies are needed to confirm these findings.

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Hemodynamic determinants of the clinical syndrome of Postural Orthostatic Hypotension

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Background: Postural Orthostatic Hypotension (POH) is commonly seen in the elderly because of complex age-related impairment in hemodynamic regulation mechanisms.

Purpose: To describe the hemodynamic pattern of the POH and to evaluate the effect of elastic compression treatment as previously described.

Methods: 8 patients (6 female), mean age 65±15 years, affected by symptomatic POH underwent 2 tilt-test procedures, with and without elastic bandage of the legs (compression pressure 40 to 60 mmHg) and of the abdomen (compression pressure 20 to 30 mmHg) in a randomized crossover fashion. Leg bandage was administered for 10 min and was followed by an additional abdominal bandage for a further 10 min. Non invasive beat to beat recording (Task Force Monitor, Graz, At) of systolic blood pressure (SBP), stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR) was used.

Results: Without treatment, the hemodynamic behavior is shown in the table. Active treatment was able to counteract the decrease in TPR. Indeed, TPR were 1768±474 dyn s m²/cm⁵ at baseline and 1623±321 dyn s m²/cm⁵ after 20 min of treatment. SV (57.1±3 ml baseline and 54±5 ml after 20 min) and CO (4.7±1 l/min baseline and 4.3±1 l/min after 20 min) remained unchanged. As consequence SBP decrease was of less entity, being SBP 134±15 mmHg baseline and 107±35 mmHg after 20 min.

Conclusions: Progressive SBP decrease observed in patients affected by POH is characterized by concomitant progressive decrease in TPR (by 37% in this study) while SV and CO have slight changes. Elastic compression bandage is able to counteract this hemodynamic pattern by avoiding the decrease in TPR.

	SBP (mmHg)	HR (beats/min)	SV (ml)	CO (l/min)	TPR (dyn s m ² /cm ⁵)
Baseline	126±18	77±15	63±18	4±1	1726±329
2 min	105±15*	87±21*	57±20	5±1	1360±226*
10 min	85±26*	83±21	54±10	4±1	1163±579*
20 min	84±25*	81±20	54±10	4±1	1150±544*

Values are given as mean±SD. *p<0.05 vs baseline.

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Differing vasoactive effect of water drinking in patients with vasovagal syncope and healthy controls

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Background: Vasovagal syncope (VVS) is characterized by abnormal vasoactive responses. Water drinking has been proposed as an effective therapy for this syndrome. The aim of this study was to assess the effect of water drinking on peripheral vasodilative responses, as assessed by forearm reactive hyperemia in the supine position.

Methods: We studied 30 pts with recurrent VVS (at least 2 syncopal episodes during the last 6 months), mean aged (±SE) 46.5±3.6 years and a recent positive head-up tilt test. Fifteen asymptomatic, healthy, sex and age-matched subjects served as the control group. Strain-gauge venous occlusion plethysmography was used to assess right forearm blood flow

(FBF) (i) at rest, in the supine position, (ii) during reactive hyperemia. The duration of hyperemia was also assessed, as the time during which FBF was at least 50% of its maximal increase relative to baseline flow. The same measurements were repeated 30 min after drinking 500 ml water. FBF was expressed as ml per min per 100 ml of forearm tissue volume. Data are presented as mean±SE.

Results: Before water drinking, VVS pts had decreased baseline FBF relative to controls (3.9±0.3 vs 5.3±1.1 respectively, $p < 0.05$). Despite this, hyperemic FBF was similar between groups (FBF: 8.2±0.7 vs 10.1±1.0, p : NS). An increased duration of reactive hyperemia was observed in pts (22.9±2.9 vs 11.5±0.4 sec, $p < 0.01$). Following water ingestion, baseline FBF decreased within the pts' group (3.3±0.3 vs 3.9±0.3 at baseline, $p < 0.05$). No significant differences were observed in controls (4.4±0.9 vs 5.3±1.1, p : NS). Hyperemic FBF values remained similar between groups. The duration of hyperemia decreased in pts to values similar to those observed respectively in controls (14.1±1.5 vs 17.8±0.5 sec, p : NS).

Conclusion: Among pts with VVS, water drinking decreases peripheral blood flow at rest, a finding consistent with vasoconstriction. At the same time, the duration of reactive hyperemia is reduced to values similar to those of healthy controls². As a whole, the effect of water ingestion in VVS seems to alter not only arteriolar flow in the supine position but also vasoactive reflexes.

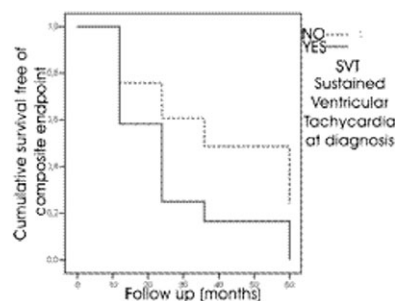
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Non ischaemic dilated cardiomyopathy: syncope as a marker of poor prognosis at appearance and in follow up

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We report a series of 29 (79% male, 59±14 years) consecutive patients referred to Arrhythmia Unit since 2001 for evaluation because of syncope and chronic non-ischemic dilated cardiomyopathy (NIDC): 83% idiopathic. LVEF was 27.7±9.9. Patients received optimal medical therapy. NYHA class were I (21%), II (31%) and III (48%). Syncope was initial symptom for sustained ventricular tachycardia (SVT) in 12 (41%). EP study was performed in 13, with positive induction in 7 (2 bundle branch re-entry). 25 patients (86%) underwent ICD implantation (4 CRT devices). Reasons for not receiving a device were poor medical condition in 1, sudden arrhythmic death (SVT) during in-hospital evaluation in 1, and good functional class with preserved (>35%) LVEF in 2. 64% of ICD recipients suffered appropriate therapies.

In follow up (20.6±17.2 months) 3 deaths occurred: 1 mentioned above sudden arrhythmic death, 1 sudden death during recovery of pneumonia in the patient with poor medical condition and 1 due to progressive cardiac failure. 9 patients (31%) received a cardiac transplant during follow up.



A composite endpoint of events: transplant or death or appropriate ICD therapy was evaluated during follow up. Only 8 patients remained free of events. Analysis of SVT at presentation showed a non-significant trend ($P = 0.14$ Wilcoxon-Gehan) to worse outcome in those with documented spontaneous SVT (figure). Only NYHA class showed a trend to relation with composite endpoint occurrence in multivariate Cox regression analysis.

Conclusion: In our experience syncope in NIDC is a very poor prognosis marker, as long as it is often due to SVT, and those of uncertain origin show quite similar event rates.

Limitations: Referral bias and relatively small sample size must be considered in data interpretation.

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Minor psychiatric disorders and syncope: the role of psychiatric substrate in the expression of vasovagal reflex, and the therapeutic effect of psychiatric treatment

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Although a high prevalence of minor psychiatric disorders (MPDs) has been reported in patients with vasovagal syncope (VVS), the relationship between the psychiatric substrate and syncope remains unclear. In this study, we tested the hypothesis that MPD may predispose to VVS.

Methods: Among 627 patients referred to the Outpatient Psychiatric Department, 82 individuals with recently diagnosed MPDs underwent cardiologic examination, psychiatric evaluation, and quality of life assessment. The response to head-up tilt test (HUTT) and prevalence of syncope were assessed and compared with those in an equal number of matched (i) patients with VVS and (ii) healthy controls. We also assessed the effect of psychiatric treatment on the recurrence of syncope in those patients with MPDs who also reported syncopal episodes.

Results: Fifteen patients refused treatment or follow-up. Among the remaining 67 patients, 39 (58%) had a positive HUTT versus 5% of healthy controls ($p < 0.01$). Thirty patients (45%) had a history of syncope; among them, the rate of positive HUTT was comparable to that observed in the VVS group (83% and 85%, respectively). After psychiatric treatment, (serotonin reuptake inhibitors, benzodiazepines, or both) patients with MPDs and syncope were decreased to 8/67 ($p < 0.01$). Psychiatric symptoms and quality of life were also improved. The number of syncopal spells decreased equally in the MPD and VVS groups.

Conclusion: MPDs are associated with increased excitability of the vasovagal reflex and high incidence of syncope. Improvement in psychiatric status following psychiatric therapy is associated with decrease in syncope recurrence, independently of the drugs being used. This implies that MPDs may contribute in the pathogenesis of VVS. The diagnosis of MPDs (when present) in patients with VVS may be crucial for the effective treatment of their syncopal events.

	Group		
	MPD (n=67)	VVS (n=67)	Control (n=67)
Pts with syncope	30 (45%)*†	67 (100%)*	0 (0%)
Pts with positive HUTT	39 (58%)*†	57 (85%)*	3 (5%)

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Tilt training therapy: a new treatment option in the management of idiopathic autonomic failure

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Autonomic failure is a very disabling disorder which is difficult to treat. In our department tilt training is used as a first line therapy in patients with neurally mediated syncope, with excellent results.

The purpose of the study was to analyse whether patients with idiopathic autonomic failure could also have some benefit from a program of tilt training therapy.

Methods: We report the result of tilt training therapy in a group of 6 patients with severe idiopathic autonomic failure. The patients were

bedridden and were not able to walk independently. The patients underwent a diagnostic tilt test without pharmacological provocation, according to the Westminster protocol: 60° inclination of tilt table. Patients were submitted to daily tilt testing (at 60° inclination) until syncope occurred or until a maximum tilt duration of 45 min. Patients started the tilt training protocol in the hospital and were instructed to continue this therapy at home, by standing every day two 30-min sessions against a wall with the feet 30 cm away from the wall.

The results show an improved orthostatic tolerance during tilt training. The time to achieve a first negative tilt test (= 45 min) was somewhat longer (mean 4 ± 1.6 , median 4) compared to patients with neurally mediated syncope (mean 2.9 ± 1.3 , median 2 sessions) (Ector et al, 2006). In 1 patients the target value of 45 min (= normal value) could not be reached. Before therapy all patients were bedridden or unable to walk independently and after a few days of tilt training all subjects were able to walk independently again.

Conclusion: In patients with severe idiopathic autonomic failure serial tilt testing improved dramatically the orthostatic tolerance and quality of life.

Results of in hospital tilt training

Patient	Age (years)	Gender	Duration diagn T	Duration final T	N° first negative T
1	76	M	19	45	4
2	71	M	11	45	2
3	53	M	20	45	5
4	80	M	12	45	3
5	73	F	24	20	–
6	71	F	6	45	6

(–), no negative tilt test could be obtained; T, tilt test; M, male; F, female; duration is given in minutes.

Monday, 25 June 2007

Poster Session 1

MONDAY, 25 JUNE 2007, 10:00–11:00

Poster Area

Moderated Posters I – Cardiac Pacing

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Quality of life in patients with cardiac pacemaker implantation

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The aim of the study was to evaluate the quality of life in adult pacemaker patients and to investigate difference between them and healthy adults.

Materials and Methods: We conducted a questionnaire survey among 387 patients (186 DDD(R) and 201 VVI(R)), 67.3±13 years and 90 healthy adults, 63.9±10 years. The assesment was based on the questionaire consisted of concrete questions. Follow up period was 98–2185 days.

Results: The significant improvement in overall well-being was found as compared to the time before implantation ($p < 0.05$). The incidence of syncope decreased after implantation ($p < 0.001$). The patients complained of: anxiety for malfunctions of pacemaker (55.3%), pain at the pacemaker place insertion (48.9%), necessity for follow-up visits (35.4%), limitation of arm moving (21%), restriction of sport activity (13.1%), resignation from job (10.1%), limitation of sex activity (11%). There were no significant difference in QOL between patients with VVI(R) and DDD(R) pacemaker ($p < 0.05$). The QOL for patients older than 65 years was similar to that for healthy adults, but for patients of working age was poorer than that for healthy adults.

Conclusion: The questionnaire-based assesment of QOL may be useful in management of pacemaker patients.

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What drives therapy change: VIBRANT Registry final results

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Introduction: The VIBRANT Registry was designed to characterize the utility of diagnostic features in a range of pacemakers (PM), and their impact on clinical decision making in a general pacing population. This analysis evaluates the drivers of medication and programming changes in all 949 patients (pts) enrolled in the registry, receiving Selection AFm (AFm), Clarity, C-Series and T-Series PMs.

Method: VIBRANT was a prospective, multi-center registry. Pts with standard indications for dual chamber devices received one of four PMs. All pts were followed for one year per their physician's standard of care with no pre-specified programming requirements. Therapy changes and the drivers of those changes (pt symptoms only; PM diagnostics only; or a combination of both), were documented during follow-up. In this analysis we compare the results of the devices which include the Therapy Advisor (TA) as part of their advanced diagnostics (C-Series and T-Series), versus those PMs which do not (AFm and Clarity).

Results: In total 273 pts received the AFm; 220 Clarity; 298 C-Series and 158 T-Series PMs. 48% were male, with a mean age of 76 years. Sinus node dysfunction was the most prevalent indication for pacing at 65%. There were 2,784 total follow-up visits with programming and medication changes made at 1,386 and 1,118 follow up visits respectively. Baseline demographics were similar in the two groups. Diagnostics influenced a similar percentage of medication changes in both groups (28% vs 30%). However, the diagnostics of the C/T Series groups influenced the

programming changes 79% of the time compared to 58% in the AFm/Clarity group (Table).

Conclusions: In this general pacing population, medication changes were driven primarily by pt symptoms. The majority of programming changes were driven by the advanced diagnostics of these PMs. This was 21% higher in the C/T Series group, suggesting that Therapy Advisor added incremental information to the advanced diagnostics standard to all four devices.

Table 1: Drivers of Programming Changes

	Diagnostics only	Diagnostics & Symptoms	Symptoms only	Other
C/T-Series	62%	17%	3%	18%
AFm/Clarity	41%	17%	8%	34%

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The occurrence of atrial arrhythmias is not directly related to Ventricular pacing

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Background: Recent studies have demonstrated that frequent right ventricular pacing (VP) is associated with an increased risk of developing atrial fibrillation (AF). The Medtronic EnRhythm™ pacemaker incorporates Managed Ventricular Pacing (MVP™), a new pacing mode that is designed to reduce VP.

Methods: In a prospective, multi-center, randomized, cross-over study, 150 patients were implanted with the EnRhythm device and programmed to one month MVP mode and one month DDDR mode, in random order. Patients were followed for 4 more months with programming at physician discretion. Percent VP, AF Burden and time in sinus rhythm (SR), defined as the proportion of time that the patient was in SR, were calculated from device counters.

Results: Included in this analysis are all 124 patients that completed the cross-over with at least 7 days in both modes, and were not in persistent AF. In the cross-over phase, median percent VP was 1.6% in MVP mode and 90.8% in DDDR mode. Forty-eight patients experienced atrial arrhythmias during the cross-over phase. In these patients, mean AF burden was 8.9% (median 0.02%) in MVP mode and 6.8% (median 1.68%) in DDDR mode (Wilcoxon $p = 0.17$). 109 patients had usable data after month 2, 89 were programmed to MVP mode. Mean AF burden was 4.8% in MVP mode and 0.5% in DDDR mode (Wilcoxon $p = 0.55$). Median time in SR between episodes is 121 sec. It was 124 sec for the first month, 138 sec for the second month and 99 sec for the extended follow-up period. A test for trend is not significant ($p = 0.14$). During the cross-over phase, median time in SR was 131 sec when patients were in MVP mode and 133 sec when patients were in DDDR mode. The difference is not significant ($p = 0.70$).

Conclusion: The successful reduction of ventricular pacing by the MVP feature in the Medtronic EnRhythm pacemaker does not appear to have an immediate effect (during the first 6 months after implantation) on the incidence/occurrence of atrial arrhythmias. This may indicate that frequent ventricular pacing does not trigger AF directly, but rather through remodeling of the atria.

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Prediction of atrial fibrillation in a long-term follow-up:

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Background: Atrial fibrillation (AF) is a very common arrhythmia which often causes the serious complication of a stroke. Attempts to predict AF after coronary bypass grafting or electrical cardioversion were promising with P wave signal averaged ECG (P-SAECG) or chemoreflexsensitivity (CHRS). The consensus of these studies is a longer filtered P wave duration (FPD), a lower root mean square voltage of the last 20 ms of the P wave (RMS 20) and a lower CHRS in patients with a recurrence of AF after electrical cardioversion or a new onset of AF after coronary bypass grafting. Atrial late potentials (ALP) or a pathological CHRS (PCHRS) predicted the onset of AF in these studies.

Object: The aim was to evaluate the utility of pathological chemoreflexsensitivity (PCHRS) and ALP to predict AF in long-term follow-up.

Methods: We investigated a prospective study on the basis of our observation about a PCHRS and ALP in paroxysmal AF. The PCHRS was predefined as a chemoreflexsensitivity below 3.0 ms/mmHg and ALP were predefined as a FPD \geq 120 ms and a RMS 20 \leq 3.5 μ V. A P wave triggered P wave signal averaged ECG and chemoreflexsensitivity was performed on 250 consecutive patients who were divided into four groups. Group I consisted of patients with ALP and PCHRS, patients of group II had only ALP, a PCHRS was only present in group III and patients of group IV had neither ALP nor PCHRS.

Results: During the mean follow-up of 37.8 months AF was observed in 10 patients (4%). The patients of the four groups were similar according to clinical baseline characteristics. The incidence of AF was higher in group I (18% of patients) than in group II (6% of patients, $P=0.229$) and significantly higher than in group III (3% of patients, $P=0.034$) or group IV (1% of patients, $P<0.0001$). Patients with ALP and PCHRS showed a 33-fold risk ($P<0.001$) for the onset of AF.

Conclusions: The results of our study suggest that the probability of AF could be predicted with a P wave signal averaged ECG and an analysis of chemoreflexsensitivity. The predictive power of the combination of ALP and PCHRS might be used for a risk stratification.

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Predictors of successful cardioversion and immediate recurrences in persistent atrial fibrillation patients

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Purpose: Cardioversion of persistent atrial fibrillation (AF) carries a high risk of relapse to AF within a few minutes. The variables associated with successful cardioversion and immediate recurrences of AF (IRAF) after external biphasic direct current shocks are not well characterized.

Methods: 269 patients with persistent AF (66 \pm 8 years, 56% male, mean duration: 13 \pm 22 months) underwent external biphasic cardioversion. Two hundred and forty five patients (91%) were defibrillated successfully. IRAF (recurrent AF after sinus rhythm within 1–20 mins) occurred in 54/388 (14%) cardioversion procedures. Uni- and multivariate analyses were performed on demographic, clinical and echo data, to determine predictors of successful cardioversion and IRAF. Left ventricular ejection fraction followed by left atrial diameter were the most significant independent predictors for conversion to sinus rhythm ($p=0.012$ and $p=0.041$ respectively). Age, sex, left atrial or left ventricular dimensions; ejection fraction, NYHA class and AF duration were not predictive of IRAF. IRAF occurred in patients with lower ventricular rates pre-cardioversion and was also associated with a history of hypertension and valvular heart disease. Pre-treatment with amiodarone was associated with lower IRAF.

Conclusions: External biphasic cardioversion is a very effective method for the restoration of sinus rhythm in patients with persistent AF. The

success rate is associated with higher ejection fraction and smaller left atrial diameter, independent of AF duration. Hypertensive and valvular heart disease are associated with higher IRAF but higher ventricular rates pre-cardioversion and pre-treatment with amiodarone are protective. These findings may be useful for the most appropriate selection of patients for cardioversion.

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Efficacy and safety of ambulatory electric cardioversion of atrial fibrillation with monophasic and biphasic shock

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Background: The aim of this study was to evaluate the safety and efficacy of ambulatory external cardioversion (EC) by means of monophasic and biphasic shock in patients with persistent atrial fibrillation (AF).

Methods: During the period 2002–2005 five hundred and eighty one consecutive patients with AF were submitted to EC, preceded by short general anesthesia with propofol, after pre treatment with oral anticoagulants for at least 4 weeks. In 276 of these patients we used monophasic shock (during the 2002–2003 years) and in 305 patients we used biphasic shock (during the period 2004–2005 years). Our protocol provided for up to 3 shocks delivered at an energy level ranging between 100 and 360J for monophasic and from 70 to 200J for biphasic shock. The patients were discharged after 6 hours of ECG monitoring and following a determination of serum CKMB at the fourth hour.

Results: The mean age of the patients submitted to EC with monophasic and biphasic shock (69 \pm 9 vs 70 \pm 9 years) and the duration of AF (34 \pm 22 vs 32 \pm 25 days) were similar. The efficacy of EC with monophasic shock was 91% and the mean energy delivered was 345 \pm 237J. The efficacy of the EC with biphasic shock was 96% and the mean energy delivered was 121 \pm 80J. The difference between the percentage of efficacy and the number of joules delivered was statistically significant ($p<0.05$). The number of shock was 1.4 \pm 0.7 with monophasic and 1.2 \pm 0.5 with biphasic (ns). The mean value of the CK-MB after 4 hours following delivery of the shock was not significantly different: 2.5 ng/ml for monophasic vs 1.7 ng/ml for biphasic shock (ns).

Conclusions: In our patients, ambulatory EC of persistent AF is safe and feasible; biphasic shock is more efficacious and requires less energy with respect to monophasic shock.

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Clinical implications of reconnection between the left atrium and isolated pulmonary veins provoked by adenosine triphosphate after extensive encircling ipsilateral pulmonary vein isolation

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Background: Dormant pulmonary vein (PV) conduction can be provoked by adenosine triphosphate (ATP) after extensive encircling ipsilateral pulmonary vein isolation (EEPVI). However, the clinical implication of reconnection between the left atrium (LA) and isolated PVs provoked by ATP (ATP-reconnection) remains unknown.

Methods and Results: We studied the clinical consequences of ATP-reconnection during intravenous isoproterenol infusion (ISP-infusion). EEPVI severs conduction between the LA and ipsilateral PVs at their junction. Radiofrequency energy is applied at a distance from the PV ostia guided by double Lasso catheters placed within the ipsilateral superior and inferior PVs. This study comprised 82 patients (67 men, 56 \pm 9 years old) with atrial fibrillation (AF) who underwent injection of ATP during ISP-infusion after successful EEPVI (ATP(+) group). We compared clinical characteristics of 170 patients who underwent earlier EEPVI prior to our use of ATP injection after successful EEPVI (ATP(N/D) group) with those of ATP(+) group patients who underwent one session of EEPVI.

ATP-reconnection occurred in 34 (41%) of 82 ATP(+) group patients. Additional radiofrequency applications were performed to eliminate ATP-reconnection in all ipsilateral PVs. Continuous ATP-reconnection of more than 20 seconds duration occurred in 6 (7.3%) of 82 patients. One hundred two (60%) of 170 patients in the ATP (N/D) group had no recurrence of AF, whereas 60 (73%) of 82 ATP(+) group patients who underwent only one EEPVI session have had no recurrence of AF in a 6.1 ± 3.3 -month follow-up period ($P=0.04$).

Conclusion: Radiofrequency application for provoked ATP-reconnection may reduce clinical AF recurrence.

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A single transeptal puncture for ablation of atrial fibrillation. Retrospective study from a large cohort of patients

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Background: Transeptal puncture is a mainstep maneuver to access the left atrium. The electrophysiologic approach for atrial fibrillation (AF) comprises the positioning of multiple catheters in the left atrial chamber for mapping and ablation; a second transeptal puncture is usually advocated to perform the procedure. Aim To report a retrospective data about success rate, safety and morbidity of a single transeptal puncture for AF ablation in a large cohort of patients (pts).

Methods: Over a period of 5 years, a thousand consecutive patients (mean age 54 ± 8 yrs, 75% men) were recruited in whom left heart catheterisation for ablation of atrial fibrillation was performed. The transeptal puncture was carried out by using a pigtail catheter or a His mapping catheter as anatomic landmark of aorta. Right after crossing the septum a heparin bolus (100 U/Kg) was administered and, afterwards continuous infusion of heparin was provided maintaining ACT value between 250"-300". A guidewire was then anchored in the left superior or inferior pulmonary vein (PV) and the transeptal assembly pull back to the right atrium, while a continuous flushing of the system was provided. Then, an ablation catheter was advanced approaching the septum parallel to the guidewire and guiding the crossing by fluoroscopic left anterior and right anterior views. After the ablation catheter was positioned in the left atrium, the transeptal system was advanced to the left atrium over the guidewire and used for placing a loop-shaped mapping catheter at pulmonary veins ostium.

Results: In only 5/1000 (0.5%) cases a second transeptal puncture was required to position the ablation catheter in the left atrium. Neither complications of the transeptal catheterization such as atrial or aortic perforations, pericardial tamponade, thrombotic formation, air embolism nor complications related to the attempts of crossing the septum with the ablation catheter were reported. In all cases, the ablation catheter was properly maneuvered at each PV ostium.

Conclusions: This retrospective data on a large cohort of pts shows that single transeptal puncture for positioning two catheters in the left atrium for AF ablation is a highly successful and safe maneuver with a very low morbidity in the majority of pts. This can avoid potential complications related to a second transeptal puncture.

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Transcatheter Pulmonary vein isolation in patients with cardiac rheumatic valve disease

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Objectives: The goal of this study was to assess the safety and efficacy of pulmonary vein isolation in patients with rheumatic valve disease(RVD).

Background: Pulmonary vein isolation (PVI) is a widely technique to treat atrial fibrillation (AF) although few data have been published on transcatheter ablation of AF in patients with RVD.

Material and Methods: This is a retrospective study. Continuous variables were compared by the student T test and categorical variables by the chi-square or Fisher exact test. Between September 2004 and January 2005, 35 patients with RVD underwent PVI to treat AF. For each patient with RVD, two control subjects were matched from our database.

Results: The mean duration of fluoroscopy exposure (35 ± 8 vs 37 ± 10 minutes), and radiofrequency delivery (11 ± 1 vs 10 ± 3 minutes), and mean procedural time (175 ± 30 vs 180 ± 23 minutes) were similar in both groups. Complication rate was similar in both groups. No patient developed thromboembolic or cerebrovascular complication. In each group one patient developed mild asymptomatic pulmonary vein stenosis and one patient with RVD and two in the control group had a cardiac perforation during the procedure but only one patient in the control group underwent a surgical repair due to a left appendage perforation. After 6 months, 20 patients (57.1%) in the RVD group vs 50 patients (78.5%) ($p < 0.001$) from our control group are in sinus rhythm without drug therapy after a single procedure. In the RVD group the pattern of recurrence was AF in 7 patients, left or right atrial flutter in 4 and 4 presents both arrhythmias. In the control group the pattern of recurrence was AF in 17 patients, left or right atrial flutter in 2 patients and 1 patient present both arrhythmias.

Conclusion: Ablation of AF is feasibly in patients with RVD. Although with a poor results compared to the control group.

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Intraoperative cooled-tip radiofrequency linear atrial ablation to treat permanent atrial fibrillation

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Atrial fibrillation (AF) surgery has become more engaged in every-day practise of specified cardio-surgical centres. The cut-and-sew technique still remains the gold standard with superior efficacy. Is an intraoperative approach using cooled-tip endocardial radiofrequency energy to induce linear atrial lesions (SICTRA) safe and effective in treating AF?

Methods: 224 patients (mean EuroSCORE 6.4 ± 2.1 , AF duration 8 ± 7 years) presenting with permanent AF (>1 year, 1 failed cardioversion) and the need for cardiac surgery were included. In addition to the cardio-surgical procedure concomitant SICTRA was performed. In 118 patients the ablation pattern was restricted to the left atrium alone. Follow-up constituted of ECG, holter-ECG and Doppler echocardiography.

Results: Cardio-surgical procedures were mitral valve surgery in 95, aortic valve replacement in 29, bypass surgery in 77 including 24 patients with additional mitral valve surgery and combined procedures in 23. During the mean follow-up of 29 months 175 patients (78%) converted to sinusrhythm (SR) without postoperative antiarrhythmic medication. At discharge (0.5 months postoperatively) 30%, at 3 months 62%, at 6 months 76% and after 12 months 75% of patients were in stable SR. Batrial contraction was documented in 82% of patients in SR. In patients with a SICTRA procedure restricted to the left atrium conversion rates were not significantly different compared to a batrial approach (82% versus 74%, $p=0.46$). The type of cardio-surgical procedure did not influence 12-month conversion.

30-day-mortality was found to be 4% (9/222). Histopathology revealed 23% of all lesions to be histologically non-transmural but only 4% of patients developed sustained regular atrial arrhythmia. Overall-mortality was 13.5% (N=30).

Conclusions: SICTRA safely and effectively restores stable sinusrhythm in 78% of patients with permanent AF undergoing open heart surgery. A batrial contraction can be restored in 82% of these patients. Rhythm conversion is not influenced by treatment of the right atrium or the performed cardio-surgical procedure. Sustained regular atrial arrhythmia with the need for invasive treatment strategies occur in 4% although intraoperative ablation lesions are often non-transmural.

MONDAY, 25 JUNE 2007, 10:00–11:00

Poster Area

Atrial Fibrillation: clinical and epidemiological aspects

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Epidemiology. Atrial fibrillation in the Russian north. 25 years follow upE. Serdechnaya¹, B. Tatarkov¹, S. Urieva¹, T. Istomina¹, L. Kulminkaya¹, E. Kazakevich¹¹Arkhangelsk, Russian Federation; ²Almazov Institute of Cardiology, Cardiology, St. Petersburg, Russian Federation; ³Northern Medical University, Cardiology, Arkhangelsk, Russian Federation

Despite being the most common cause of stroke, heart failure and death atrial fibrillation is not well studied in terms of prevalence and incidence, there have been only few major studies dedicated to it.

We aimed to study incidence and prevalence of AF in the European Russian North and to assess concomitant pathology trends in new AF cases during 25 year period.

Cohort retrospective study was conducted at the Northern Medical Center of the Federal Agency on Health. The study included 61 767 persons. Incidence and prevalence were assessed by the admissions to the clinic and annual medicals data. Case studies of 2878 patients (hospitalized from 1980 to 2004) were also analyzed.

It appeared that AF prevalence increased from 0.93/1000 in 1980 to 5.72/1000 in 2004. AF incidence increased from 0.31/1000 to 1.44/1000 accordingly. AF prevalence increases from 0.13 per 1000 in the age group < 40 to 19.7/1000 in the age group of 70–79 years old, and decreases to 10.14/1000 ≥ 80 years old. Incidence standardized by the age was higher in males than in females in all age groups during the whole period of the study, the exception was 70–79 age group. The highest AF incidence was in males of 60–69 years old – 7.08 per 1000 man/year/risk, in females the highest incidence was in 70–79 years old – 7.38 per 1000 man/year/risk. During 10 years period, AF incidence increased in the age group of 50–59 from 1.59 in 1995 year to 2.27/1000 in 2004 and from 3.53 to 5.83/1000 in 60–69 age group.

Prevalence of idiopathic form of newly diagnosed AF increased from 9.5 to 24.4%, arterial hypertension increased from 58.8 to 74.4%, diabetes from 3.4 to 9%.

Conclusion: Our results confirm high AF prevalence and incidence, mostly attributed to the middle age groups input, with the gradual decrease in patients after 80.

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Higher levels of CRP and intensive albuminuria were detected among hypertensive patients with a history of Paroxysmal Atrial Fibrillation (PAF)A. Hatzizianni¹, P. Kyriakou¹, M. Toutouza¹, C. Vasiliadi¹, C. Stefanadis¹, P. Toutouzas¹¹Hippokraton Hospital, Cardiology, Athens, Greece

Introduction: CRP is an inflammatory index increased in atheromatosis which is the main underlying pathology of hypertension. It is also found to be related with AF. On the other hand micro-albuminuria is related to hypertension and well correlated with diastolic dysfunction of LV and the general inflammatory process. It is associated with higher cardiovascular risk, and considered as an early finding in individuals predisposed to hypertension and antecedent hypertension. Combination of inflammation and microalbuminuria are related with diffuse vascular damage.

Aim: We assessed CRP plasma levels and albumin in the urine of hypertensive subjects, and studied the correlation of these markers to the tendency to develop PAF.

Methods: For this purpose, CRP plasma levels and urine albumin levels were measured in 50 hypertensive patients (mean age 58±12 years) with a history of paroxysmal atrial fibrillation (PAF) (group A) and in 50 hypertensive patients (mean age 57.5±10 years) without previous history of PAF (group B). All patients underwent complete echocardiographic study.

Results: There were no differences between the two groups regarding the clinical data (age, gender: males 65% vs 60%, body mass index: 27.57±3.2 vs 27.38±4.4 kg/m², office systolic BP: 147±12 vs 143±11 diastolic 91±7 vs 90±9 mmHg, duration of hypertension: 4.2±2.1 vs 3.9±2.3 years, p=NS for all cases). Patients in group A had increased left ventricular mass index compared to group B (115±27 vs 85±19 gr/m² p<0.001), while left atrial dimension and left ventricular ejection fraction did not differ (3.72±3.64 vs 3.58±3.64 cm, p=0.092 and 65% vs 67%, p=NS). Both CRP plasma levels (21.2±7.7 vs 0.54±0.42 mg/dl, p=0.0005) and albumin urine levels (49.05±35.7 vs 18.3±16.9 mg/l p=0.005) were found to be significantly higher among hypertensive patients with a history of PAF (group A) compared to hypertensive subjects without a history of PAF. There was no difference regarding the incidence of diastolic dysfunction between the two groups (p>0.05). The data were statistically compared using Student t-test analysis.

Conclusion: Hypertensive patients prone to develop PAF present with higher inflammatory indexes as assessed by CRP plasma levels and thereby with intensive albuminuria. Thus AF either increases the inflammatory burden or AF is associated with higher inflammatory burden.

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Hypertensive patients with high BNP or NT-PRO-ANP plasma levels are prone to develop atrial fibrillationA. Hatzizianni¹, P. Kyriakou¹, K. Tsioufis¹, M. Toutouza¹, C. Vasiliadi¹, C. Stefanadis¹, P. Toutouzas¹¹Hippokraton Hospital, Cardiology, Athens, Greece

Introduction: Atrial natriuretic peptide (ANP) levels have been related to increased atrial pressure, alterations of atrial effective refractory period and also correlated with the initiation and duration of atrial fibrillation (AF). However little is known about the role of brain natriuretic peptide (BNP). Hypothesis: We assessed the hypothesis that BNP and NT-pro-ANP plasma levels may be of prognostic value in hypertensive patients predisposed to AF.

Methods: For this purpose, BNP and NT-pro-ANP plasma levels were measured in 50 hypertensive patients with a history of paroxysmal atrial fibrillation (PAF) (group A) and in 30 hypertensive patients without previous history of PAF (group B). In 8 patients from group A, BNP plasma levels were measured during the paroxysm of AF and after the reversion to sinus rhythm. In 12 patients from group A, NT-pro-ANP plasma levels were measured only during PAF. The patients were also assessed with ambulatory ECG and echocardiography.

Results: There were no differences between the two groups, A and B, regarding the clinical data (age: 58±12 vs 57.5±10 years, males: 65% vs 60%, body mass index: 27.57±3.2 vs 27.38±4.4 kg/m², office systolic BP: 147±12 vs 143±11 diastolic 91±7 vs 90±9 mmHg, duration of hypertension: 4.2±2.1 vs 3.9±2.3 years, p=NS for all cases). Patients in group A had increased left ventricular mass index compared to group B (115±27 vs 85±19 gr/m² p<0.001), while the left atrial dimension and the left ventricular ejection fraction did not differ (3.72±3.64 vs 3.58±3.64 cm, p=0.092 and 65% vs 67%, p=NS). BNP plasma levels were significantly higher in group A (49.04±53.8 vs 12.24±14.21 pg/dl, p=0.006). The NT-pro ANP plasma levels were significantly higher and into pathological range in group A compared with group B (3623.87±3186 vs 1945.39±586.88 fmol/ml, p=0.0004). In addition, BNP plasma levels were significantly higher during PAF compared to the levels after reversion to sinus rhythm (142.98±57.71 vs 20.51±26.82 pg/dl, p=0.0003). The NT-pro ANP plasma levels were especially higher during PAF (8155.991±3904.72 fmol/ml, p=0.002). By applying a Student t-test it was revealed that BNP and NT-pro ANP levels were significantly and independently associated with PAF.

Conclusion: BNP and NT-pro-ANP plasma levels are significant and reliable predictive indexes for the detection of hypertensive patients prone to the development of PAF while in sinus rhythm, especially NT-pro-ANP.

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Does the mean heart rate is the ideal parameters of the controlling ventricular rate in atrial fibrillation

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Background: Atrial fibrillation (AF) is the most common form of cardiac arrhythmia. Rate control as the first line therapy for the patients (pts) with AF has been confirmed in many studies. However, the questions which is the correct ventricular rate and what parameters should be estimated, still are opened.

The aim of the study was to evaluate whether the mean heart rate (mHR) in 24 hour ECG Holter monitoring (HM) is a correct parameter for assessment of ventricular rhythm controlling in patients (pts) with AF. Additionally, we try to find out whether other parameters such as: tachy AF episodes, rhythm irregularity and pts symptoms – “palpitations” play an important role in controlling ventricular rate in AF.

Methods: All pts with chronic brady-tachy AF, from 2 to 9 days (mean 5.6 days) after VVI pacemaker (PM) implantation with optimal pharmacotherapy and mean heart rate below 80 bpm were included into this study. Mean HR and coefficient of variations (CV) based on HM and percentage of fast ventricular rates (tachy AF episodes – defined as heart rate >120 bpm) derived from PM memory data were analyzed. During 24 hours, symptoms such as “palpitations” were marked as “+”.

Results: 42 from 48 pts (18M, 24F) with mean age 70.2±8 years were finally included to the study. Mean heart rate in HM ranged from 48bpm to 79bpm, mean 64.8±7.5 bpm. In 21 pts (50%) tachy episodes were noted despite of correct mHR: from 1% to 8%; mean. 2.7±2.02%. Coefficient of variation in HM varied from 0.9 to 0.33; mean = 0.23±0.06. Significant irregularity with CV above 0.2 with correct mHR were found in 73% pts. There were no tachy AF episodes in the majority of pts (10 from 11) with low CV (<0.2). Significant CV (>0.2) was found in 10 from 18 pts (56%) with correct mHR, without tachy AF episodes. In 16 from 21 pts with tachy AF and 9 from 10 without tachy AF episodes with correct mHR heart palpitations were noted. All these pts had significant ventricular rate irregularity with CV > 0.2.

Conclusions: (1) Mean HR derived from HM is not a sufficient parameter for controlling ventricular rate in the majority of pts with brady-tachy AF. (2) It seems that tachy AF episodes, rhythm irregularity and symptoms and not only mHR are necessary for correct controlling of heart rate in pts with AF. (3) Coefficient of variation in pts with correct mHR might be superior to other parameters for estimation of pts with AF.

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Atrial fibrillation and long-term prognosis in non-selected heart failure. A ten years' follow-up study

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Background: Atrial fibrillation (AF) and heart failure (HF) often coexist, but there is conflicting data regarding the association of AF with outcome in HF.

Methods: To examine this further we evaluated the prognostic effect of AF in all confirmed heart failure admissions to our centre during 1996 with follow-up data through 2006.

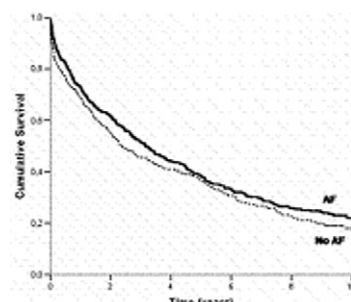
Table

	AF	No AF	p
Age	75.4±11.0	74.1±12.0	0.07
Female gender	331 (63%)	291 (54%)	0.002
Diabetes	131 (25%)	183 (34%)	0.001
Previous MI	60 (12%)	92 (17%)	0.009
LVEF<0.4	114 (33%)	184 (52%)	<0.001
Anticoagulation	178 (36%)	79 (16%)	<0.001
Digoxin	365 (74%)	96 (20%)	<0.001
Diuretics	430 (88%)	385 (80%)	0.001

Clinical profile according to the presence of AF.

Results: A total of 1069 pts were admitted with confirmed HF during 1996. Atrial fibrillation was present in 523 pts (49%). Patients with AF had a different clinical profile than those without (table), and received oral anticoagulation at discharge more frequently, although only 36% received this treatment. Multivariate analysis showed that AF did not influence long-term prognosis (OR 1.00, 95% CI 0.82–1.22, p=0.98).

Conclusion: Atrial fibrillation does not increase long-term mortality in non-selected heart failure.



AF and long-term prognosis

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Can the early analysis of the peak A wave velocity after atrial fibrillation electric cardioversion predict relapse?

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Introduction: auricular stunning (AS), the transient impairment of atrial function, is a frequent event after electrical cardioversion (ECV) of atrial fibrillation (AF) and although its quantification is not well standardized and its physiopathology is not well known, it might be determinant in the thrombo-embolic risk and the arrhythmic relapse.

Target: To know whether the measure of the AS after the ECV of AF using a quantitative method (peak A wave velocity using pulsed doppler) is a good relapse predictor.

Methods: Prospective observational study which included 21 patients with persistent non-valvular AF that underwent ECV. All patients had a transthoracic echocardiography 3 hours, 48 hours, 7 and 30 days after the ECV, defining auricular stunning with peak A wave velocity (<0.5 m/s mitral/<0.3 m/s tricuspid). Clinical evolution was also valued after the first and sixth month of follow-up.

Results: An incidence of 85% of left AS and 66% of right AS was observed just after ECV of AF. There were 10 cases of AF relapse in the first month (Group A) that raised up to 13 after the sixth month. There were no significant differences in age, sex, cardiopathy associated, AF duration, ECV energy administered, body mass index and left atrium volume between both groups (Group A and not relapsed-Group B). A significant increase in the 48-hour medium mitral peak A wave velocity was observed in group B compared to group A (0.34 m/s to 0.46 m/s vs 0.38 m/s to 0.38 m/s; p<0.03). These differences were also observed in the tricuspid peak A wave.

Conclusions: The first 48 hour evolution of the mitral peak A wave velocity after the ECV is an easy and reliable method to predict precocious AF relapse.

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Time of the first episode of atrial fibrillation in overt and concealed Wolf-Parkinson-White syndrome

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Long refractory period of the A-V node is a natural barrier which protects the ventricles from too fast heart rhythm. In WPW syndrome, AF is

particularly dangerous when accessory pathway (AP) has short refractory period. The aim of our study was to analyze the occurrence of AF in dependence on sex, age, property of AP and other factors (CHD, HT).

Methods: 747 pts, mean age 35.5, underwent non-pharmacological treatment of WPW (years 1988–2005). 221 (39.5%) of them (68F, 153M) had documented atrial fibrillation. The results of 12 lead ECG Holter, ECG monitoring, and an echocardiography study were analyzed.

Results: 140 pts (63.3%) have had episode of AF and AVRT, 79 (25.5%) only AF. 20 pts (9%) have documented VF. 18% had HT, 7.3% CHD, 13.7% changes in coronary arteries, 8.7% valvular heart disease. 20% underwent cardioversion. Women had the first episode of AF most frequently at 4 decade (25.5%), men at 3rd (27.6%). The mean age of the first AF episode in men was significantly lower than women (32.4 vs 39.6). More frequently AF occurred in pts with left sided AP (61%) than right-sided (30%). Midseptal occurs seldom (9%). AF occurred most frequently in overt APs: 81.3% (intermittent: 11%; concealed: 7.7%).

Conclusion:

1. Men have had AF episodes 2.2 times more often than women.
2. Men have had first episode of AF earlier than women (32.4 vs 39.6).
3. Pts with avrt have had AF earlier than pts without avrt (36 vs 46).

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External versus oesophageal electrical cardioversion of atrial fibrillation

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Background: Electrical cardioversion (ECV) of atrial fibrillation (AF) is limited by a failure rate of 5–10% and by the need for general anaesthesia. The use of a transoesophageal approach has been proposed as a means of augmenting the success rate of ECV and of avoiding the need for general anaesthesia. We investigated the differences between a transoesophageal and a transthoracic approach in terms of success rate and tolerability using only light sedation.

Methods and Results: We randomly assigned 60 consecutive patients aged 70±10 years attending for ECV of persistent AF of mean duration 11±20 months to a standard transthoracic biphasic ECV or to an approach in which a biphasic shock was delivered via an oesophageal decapolar lead and two precordial patches. Sedation by intravenous bolus injection of midazolam was used in all cases, with a starting dose of 1.5 mg and a maximum of 15 mg. For transoesophageal ECV we used an initial energy setting of 50 J, progressing to 100 J if needed. Transthoracic ECV began with 100 J, progressing to 150 and if necessary a maximum of 200 J. Patients described the level of discomfort caused by the procedure according to a ten point visual analogue scale. Technical success defined as the restoration of sinus rhythm for at least 3 beats was achieved in 29/30 patients (97%) in each group using a mean effective energy of 80±60 J for the transoesophageal and 185±160 J for the transthoracic approach ($p < 0.001$, Mann-Whitney U). No complication occurred and no patient required hospital admission. Mean discomfort score was 0.9±1.3 out of 10 for the transoesophageal ECV and 1.1±1.8 for the transthoracic approach. Sinus rhythm persisted in 90% of patients at 5 minutes after cardioversion, in 67% one week later and in 61% at 1 month, with a similar rate of AF recurrence in both groups.

Conclusion: Outpatient cardioversion of AF may be performed safely and effectively by either a transthoracic or a transoesophageal approach. As transoesophageal ECV shows no clear advantage, transthoracic cardioversion should remain the approach of first choice.

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NT-pro BNP levels during exercise in paroxysmal atrial fibrillation

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Aim: Natriuretic peptides have been used of indexes of increased pressure-stress in cardiac chambers. The aim of our study was to examine

the response of NT-pro brain natriuretic (NT-proBNP) peptides during stress tests in patients with paroxysmal atrial fibrillation.

Methods: Thirteen patients (mean age of 55±7.1, range 42 to 66) with a history of idiopathic paroxysmal atrial fibrillation were included in the study. Eight healthy, asymptomatic adults served as controls. All patients were on antiarrhythmic therapy. They all had a normal left ventricular systolic ejection fraction. All patients underwent a cardiac echocardiography study and a treadmill stress test. The tests were performed in sinus rhythm. Blood samples for the measurement of NT-pro BNP levels were obtained during the stress test, at baseline (1), peak (2) and recovery (3). Statistical analysis: Results are expressed as mean±SD and post hoc analysis was performed with the Fischer test.

Results: In patients with paroxysmal atrial fibrillation baseline NT-pro BNP showed a trend toward higher levels compared with controls (340±108 vs 283±49 fmol/ml) which did not reach levels of statistical significance. However, in 6 of the 13 (46%) pts, NT-proBNP increased significantly during exercise (baseline 356±142, peak 436±153 425±208 fmol/ml, $p < 0.05$ of peak compared to baseline) and their mean left atrial dimensions were 45±6 mm. In the remaining 7 pts, NT-proBNP levels did not change significantly during exercise (baseline 326±78, peak 282±63, recovery 311±113 fmol/ml) whereas their left atrium was slightly increased (41±2 mm). In the control group, left atrial dimensions were normal (35±2 mm) and NT proBNP showed a trend towards lower baseline levels and did not change significantly during exercise (NT-proBNP baseline: 283±50, peak: 296±82 and recovery: 292±62 fmol/ml).

Conclusions: In a significant percentage of patients with paroxysmal atrial fibrillation NT-proBNP levels increase during exercise indicating that increased stress may be implicated in the underlying pathophysiological mechanisms of paroxysmal atrial fibrillation.

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Influence of diabetic autonomic neuropathy on heart rate and recurrence of paroxysmal atrial fibrillation

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Atrial fibrillation (AF) is the commonest sustained arrhythmia. Rate control during AF is important part of the therapy. Diabetic autonomic neuropathy (DAN), a frequent complication of diabetes (DM), is associated with abnormalities in cardio-vascular system.

The aim of this study was to assess the influence of DAN on heart rate and recurrences of AF. We enrolled 45 patients (pts) with paroxysmal AF, which were divided into 3 groups: (1) 18 pts with DM type 2 and DAN established on the basis of Ewing's tests; (2) 15 pts with DM type 2 without DAN; (3) 12 pts without DM we performed Holter ECG in all pts during sinus rhythm and during AF.

We analyzed 24-hours mean heart rate (mHR), day/night mHR, SDNN, rMSSD, pNN50 and coefficient of irregularity (CI) during AF. CI was defined as $CI = SD(mHR)/mHR$, where: $SD(mHR)$ – standard deviation of mHR.

	DM DAN(+)		DM DAN(-)		Without DM	
	sinus	AF	sinus	AF	sinus	AF
mHR (bpm)	79±16	93±24	77±10	94±25	73±7	91±28
day/night mHR	1.23±0.3	1.11±0.1	1.2±0.2	1.18±0.01	1.2±1.2	1.23±0.2
SDNN (ms)	102±32	118±21	123±27	144±26	132±36	146±29
rMSSD (ms)	22±18	96±25	24±14	104±25	26±13	90±23
pNN50 (%)	5±9	54±19	6±9	58±8	10±11	53±15
CI	x	0.14±0.02	x	0.17±0.03	x	0.20±0.05

CI: DM DAN(+) vs. without DM $p < 0.001$; DM DAN(+) vs. DM DAN(-) $p < 0.002$.

SDNN: DM DAN(+) vs. without DM $p < 0.01$; DM DAN(+) vs. DM DAN(-) $p < 0.01$.

HR day/HR night: DM DAN(+) vs. without DM $p < 0.02$.

Results: See the table. The frequency of recurrence of AF were significantly higher in pts with DAN (47 episodes/year) compared to remaining

groups (26 and 22 episodes/year respectively) – $p < 0.01$. We noted significantly higher CI and lower SDNN in pts with DAN compared to pts without DAN or DM.

Conclusions: There were more frequently recurrences of AF in pts with DM and DAN. DM DAN(+) pts had also more stable HR during AF. We do not know how stability of HR observed in DM DAN(+) pts affects the further prognosis.

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Incidence of AF and stroke in children less than 12 years of age with rheumatic heart disease

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Introduction: Rheumatic heart disease (RHD) remains a major public health problem in developing countries. Few studies have reviewed the incidence of atrial fibrillation in children with RHD. We reviewed the incidence of atrial fibrillation and stroke in children ≤ 12 yrs presenting with RHD to a government funded tertiary care centre in India, over four years.

Methods: Hospital records of 500 consecutive children who presented to the Pediatric Cardiology outpatient department of this government funded tertiary care centre from the year 2001 to 2004 were reviewed. Records were scrutinized for clinical information, laboratory parameters and echocardiographic data.

Results: 500 children presenting with RHD, constituting 2.5% of all children seen during this period, were studied. Their age ranged from 2–12 years (mean 9.8 ± 2.2 years) and 320 were males. Only 4 children had atrial fibrillation: their mean age was 11 ± 1.15 yrs. All 4 were males. The mean duration from onset of symptoms to presentation was 13 ± 15.86 months which was comparable to those in sinus rhythm. The mean NYHA symptom status was class II. None had giddiness or syncope. Echocardiographic evidence of left atrial enlargement was seen in only two although all had X-Ray evidence of left atrial enlargement. One patient had a left atrial size of 45 mm. Two patients had severe MR with LAE and cardiomegaly on X-Ray. Another patient had presented with features of acute rheumatic fever, moderate aortic regurgitation and X-Ray features of LAE and cardiomegaly. The fourth patient had severe mitral stenosis and underwent a successful balloon mitral valvotomy. All of them were on rate control with digoxin. None of them were on anticoagulants. None had thromboembolic episodes.

Conclusion: Our data shows that the incidence of atrial fibrillation and thromboembolic episodes in children with rheumatic heart disease is low. This may be due to shorter duration of rheumatic heart disease and as a consequence, absence of chronic, fibrotic changes in the left atrium.

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Relationship between insulin resistance and left atrial spontaneous echo contrast and thrombus in patients with lone atrial fibrillation

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Purpose: Prothrombotic state in atrial fibrillation (AF) is well known. It is clearly known that hyperinsulinemia and insulin resistance (IR) play a prothrombotic role in nondiabetics. In this study, relationship between the IR and left atrial spontaneous echo contrast (SEC) and thrombus on LA or LAA in nondiabetic patients with chronic lone AF was investigated.

Methods and Results: Forty-four lone AF patients were included in the study (mean age: 58 ± 6 , 20 male). After a 12-h fasting, we measured the fasting blood glucose and insulin in all patients. IR was measured with HOMA. All patients were evaluated by transesophageal echocardiography (TEE). Left atrial SEC was graded as 0, 1, 2, 3, 4. Patients who were

diagnosed with and without thrombus or SEC, were compared in terms of IR and other characteristics.

Twelve (27%) patients had SEC, 2 (5%) patients had thrombus on LAA. Ischemic stroke occurred in 2 (4.5%) patients and transient ischemic attack developed in 4 (9%) patients.

HOMA-IR was significantly higher in the patients who had SEC or thrombus (6.3 vs 2.4 , $p = 0.01$) and thromboembolic events (5.1 vs 1.5 , $p = 0.001$) compared with patients who had no. There was a significant correlation between the IR and SEC grade ($R = 0.464$, $p = 0.009$). In multivariable analysis, while independent variables for SEC and thrombus formation were LA diameter, IR, and the duration of AF and independent variables for cerebrovascular events were the existence of SEK and thrombus in LA, and IR.

Conclusions: IR may a contributing factor on development of SEC, thrombus, or thromboembolic events in patients with lone AF. Thromboembolic events despite the effective anticoagulation in patients with AF connote other possible mechanisms. One of them might be IR.

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Diastolic function of the left atrium and relation with recurrences of paroxysmal atrial fibrillation

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Background: The relationship between mechanical remodeling of the atria and chronic atrial fibrillation (AF) is well established. Few data exist valuating the effects of frequent recurrences of paroxysmal AF to the mechanical properties of the atria. The aim of our study was to assess possible correlations between the frequency of recurrences of paroxysmal AF and functional properties of the left atrium as obtained through transthoracic echocardiography.

Methods: 126 patients (58 male – 68 female, mean age: 63.6 ± 8.7 y) who presented with an episode of paroxysmal AF were studied. All patients were submitted to assessment of the systolic and diastolic function of the left ventricle (LV) and left atrium (LA) during the initial hospitalization for the episode of paroxysmal AF. The patients were thereafter followed prospectively for 1 year and new episodes of AF, if any, were documented. Based on the collected data the patients were divided into two groups: Group A (64 patients, mean age 61.5 ± 9.6) if no other episode of AF was documented and Group B (62 patients, mean age 64.8 ± 9.9) if they had one or more recurrences of paroxysmal AF.

Results: Impaired diastolic function of the LA concerning both relaxation and filling phases was observed in patients in Group B, as seen by the reduced S/D ratio of the pulmonary vein flow velocities (A: 1.38 ± 0.6 vs B: 1.14 ± 0.41 , $p = 0.04$) and the reduced deceleration time of D wave (A: 313.8 ± 99.6 ms vs B: 258.9 ± 87.1 ms, $p = 0.03$) compared with patients in Group A. Moreover, a negative correlation was found between the S wave velocity (pulmonary vein flow during LV systole and LA relaxation) and the frequency of recurrences of AF ($r = -0.43$, $p = 0.02$). No other significant differences were observed concerning clinical, epidemiological or the rest echocardiographic data between the two groups.

Conclusions: Frequent recurrences of paroxysmal AF alter the diastolic function of the LA resulting in remodeling of the latter, as estimated by the study of the pulmonary vein flow velocities with the transthoracic echocardiographic examination. These changes favour the recurrence of AF and possibly are partially responsible for creating a suitable environment for the formation of thrombi in the LA.

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Left atrial shape may influence volume underestimation using ellipse formula in patients with atrial fibrillation

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Background: complete geometrical and shape characterization of left atrium (LA) in patients with atrial fibrillation (AF) has not been per-

formed. Ellipse formula has been proved to underestimate the real LA volume. We hypothesized that atrial dilatation may evolve different than ellipsoidal shape. The aim of the study is to analyze the influence of LA shape in the assessment of the volume using two different formulas.

Methods: 116 patients (pts) aged 53 ± 27 years with paroxysmal and persistent AF, were included. The following parameters were assessed: LA dimensions (LAd = M-mode, parasternal long axis, LAt and LAI are the measurements of short- and long-axis in apical four chamber view), LA surface in apical four chamber view (LAS). Two new measurements were introduced, the basal and annular dimension of the LA (LAb/LAa) as the maximal transverse distance at the base/mitral annulus of LA, apical four chamber view. LA measurements were calculated at end-systole (maximal). Trapezoidal LA shape was defined if transverse dimension < basal dimension. LAv was calculated using both the ellipse formula $\pi/6(LAd \times LAt)$ and truncated cone (frustum) formula $\pi LAI/12(LAa^2 + LAb^2 + LAa \times LAb)$.

Results: LAS ranged 18.5–45.5 cm². Trapezoidal LA was found in 89 pts. LAS was 20 ± 2.5 cm² in patients with ellipsoidal shape and 28.5 ± 6.5 cm² in patients with trapezoidal shape ($p < 0.0001$). In the subgroup of ellipsoidal shape, LAv was 50.7 ± 7.5 cm³ (using ellipse formula) and 55.1 ± 8.9 cm³ (using truncated cone formula, $p = 0.07$). In the subgroup of trapezoidal shape, LAv was 65.7 ± 9.5 cm³ (using ellipse formula) and 95.1 ± 18.9 cm³ (using truncated cone formula, $p < 0.0001$). The simple regression analysis showed a significant moderate correlation between LAS and the difference in LAv using the 2 formulas ($r^2 = 0.46$), suggesting that the progressive LA dilatation evolve to trapezoidal shape. Trapezoid LA with atrialization of the pulmonary veins and predominant dilatation of basal atrium than annular side may explain underestimation of LA volume using ellipse formula.

Conclusion: complete characterization of LA remodeling in patients with AF should include shape definition and LAb, LAS (parameter independent of geometrical assumption); LAv calculation may be more accurate using truncated cone formula.

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Additional risk markers of thromboembolic stroke in patients with atrial fibrillation

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Atrial Fibrillation (AF) thromboembolic complications risk factors are well established nowadays, especially in elderly age groups. At the same time, the role of genetic mutations, coding coagulation factors, as increasing risk of thromboembolic complications in patients with AF is not clear. We found it useful to analyze conventional AF risk factors, clinical appearance along with distribution of 6 genetic determinants which determine a genetic predisposition to thrombophilia in patients with AF aged before 60 who had history of ischemic stroke or left atrium appendage thrombosis and those who had no thromboembolic complications.

Materials: Our study enrolled 67 patients with paroxysmal and constant AF (50 males, 17 females) mean age 52.5 ± 0.89 . The patients were divided into two groups: the first group consisted of 19 patient who had history of ischemic stroke or left atrium appendage thrombosis and the second consisted of 48 who had no history of thromboembolic complications, the second group was regarded as a controlled group. Allele types factor V (FV Leiden) genes, prothrombin G 20210 G/A, fibrinogen (FG G/A-455), methylenetetrahydrofolate reductase (C677T MTHFR), platelet receptor (P1A1/A2 GpIIIA), plasminogen activator inhibitor type-1(4G/5G PAI-1) were detected using polymerase chain reaction (PCR) with consequent restriction analysis.

Results: Thromboembolic complications happened more often in patients with persistent form of AF 63.2% cases ($p < 0.01$). A allele FGB happened more often in patients with thromboembolic complications compare to the controlled group 47.4% ($p < 0.05$). GA-genotype FGB showed an increased risk of left atrium appendage thrombosis and ischemic strokes (OR, 2.7; 95% CI, 1.30 to 5.40; $p = 0.01$). Significant risk factors

of stroke appear: duration of AF episodes (OR, 5.49; 95% CI, 1.76 to 17.2; $p = 0.001$), left ventricular hypertrophy (OR, 2.84; 95% CI, 1.23 to 6.56; $p = 0.01$), left atrium enlargement (OR, 4.44; 95% CI, 2.06 to 9.56; $p = 0.001$), more then two thromboembolic risk factors (OR, 3.42; 95% CI, 1.48 to 7.86; $p = 0.002$), mitral regurgitation (OR, 5.31; 95% CI, 1.70 to 16.64; $p = 0.002$).

Independent predictors of thromboembolic complications in patients with AF were -455A FGB (OR, 4.91; 95% CI, 1.03 to 23.51; $p = 0.05$), mitral regurgitation (OR, 5.44; 95% CI, 1.22 to 24.24; $p = 0.02$), duration of AF episodes (OR, 8.01; 95% CI, 1.66 to 38.69; $p = 0.01$)

Conclusions: In order to improve quality of risk group identification all risk markers of thromboembolic complication should be taken into consideration including genetic markers.

MONDAY, 25 JUNE 2007, 10:00–11:00

Poster Area

Clinical Pacing

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Prevention of pocket related complications with fibrin sealant in patients undergoing pacemaker implantation receiving anticoagulant treatment

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Aim: The aim of our study was to establish the efficiency of fibrin sealant in the prevention of pocket related complications in patients undergoing pacemaker implantation receiving anticoagulant treatment.

Methods: The study was performed upon 40 and 41 patients prospectively randomized into treatment and control groups who underwent pace maker implantation procedure. Patients in both groups were receiving anticoagulant treatment with heparin or warfarin. Surgical procedures between both groups differed only by the application of fibrin sealant prior to wound closure in the treatment group.

Results: In the treatment group, there were no pocket related complications while in the control group 6 patients (14.63%) had minor hematomas that didn't need any treatment. Four patients (9.76%) had significant hematomas (2 patients were treated conservatively and other 2 patient needed reintervention). INR in the treatment group was 2.76 ± 0.85 and in the control group 2.65 ± 0.79 . In the follow up period (2–27 months) no late complications were registered in both groups.

Conclusion: Fibrin sealant is an effective adhesive and hemostatic agent. The results obtained in our study show that the administration of fibrin sealant in patients receiving anticoagulant treatment eliminates postoperative hematomas after pacemaker implantation procedures.

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Temporary pacing using tunnelled active-fixation leads allows prolonged reliable pacing with a low rate of complications

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Conventional temporary transvenous pacing is frequently associated with complications such as infection, lead dislodgement, loss of capture and perforation. The aim of this study was to investigate the reliability and safety of temporary tunnelled pacing (TTP). All patients who were treated with TTP at our institution between 2001 and 2006 were included in the analysis ($n = 22$). TTP involved transvenous placement of a bipolar active-fixation permanent pacing lead into the right ventricle and in some cases the right atrium. The lead was then tunnelled subcutaneously 5–10 cm from the point of vascular access. Pacing was achieved using an external re-sterilised permanent pulse generator. Following implantation patients were allowed to ambulate freely. The mean patient age was

67±10.7 years with 73% being male. Indications for pacing included AV block (52.4%), sick sinus syndrome (55%), and ventricular tachycardia (14%). Indication for use of TTP were as follows: infected permanent pacing system (23%), systemic infection (32%), infection or failure of conventional temporary wire (14%), concurrent critical medical illness (14%) and as an alternative to conventional temporary pacing (18%). In the majority a single ventricular lead was placed (64%), although 8 patients (36%) also received an atrial lead to allow DDD pacing. There was one pneumothorax, no lead dislodgments, perforations, pacing failure, infections or deaths related to TTP. The median duration of TTP was 12 days (range 2–78 days) with 12 patients (55%) going on to have a permanent system implanted. Of the other 10 patients 2 (9%) had an ICD implanted, 4 (18%) died due to an intercurrent illness and 4 (18%) had resolution of their arrhythmias. Nine patients were transferred from the tertiary implanting centre to a secondary centre and one patient was sent home to await either resolution of bradyarrhythmias or permanent pacemaker implantation once their other medical problems had resolved. TTP is a reliable method of achieving prolonged temporary single of dual chamber pacing whilst allowing patients to ambulate freely and is associated with few complications.

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Long term effects of right ventricular pacing in patients with normal ejection fraction

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Introduction and Objectives: Right ventricular pacing alters the ventricular activation sequence and reduces left ventricular ejection fraction (LVEF) in patients with left ventricular dysfunction. The aim of this study was to evaluate right ventricular pacing effects on patients with normal left ventricular function.

Methods: Twenty one subjects, mean age 70±10 years, with transvenous dual-chamber Pacemakers (PM) because of carotid sinus hypersensitivity or sick sinus syndrome, intact atrioventricular (AV) conduction and normal left ventricular function were included. We analyzed several eicardiographic parameters (systolic and diastolic function, doppler tisular intra and inter ventricular dissynchrony), and the distance in the 6 min test walking (6MT). After a baseline evaluation, the PM were programmed in DDD at 70 beats/min and AV interval of 100 ms to assure stimulation percentage >90%. After one year these parameters were again measured and pacemakers reprogrammed to favour physiological activation.

Results: See the table. After one year stimulation, no differences in functional status and in the distance in 6MT were observed (468 vs 480 metres, p=0.5). We did not observe admissions for heart failure.

Conclusions: In our serie of patients with normal LVEF, right ventricular pacing was associated to: (1) A deleterious effect in inter and intra ventricular dissynchrony parameters, (2) A small reduction in LVEF; and (3) No clinical reperfusion in functional status.

Echocardiographic parameters

	LVEF (%)	Left preyeective interval (LPI)	Right preyeective interval (RPI)	LPI – RPI	TEI	Lateral Wall Contraction Duration	Septal to lateral wall motion delay (TDI)
Baseline	66±5	77±34	75±34	3±14	0.35	359±40	37±40
1 year	62±5	128±29	114±21	14.3±18	0.57	406±30	81±42
Significance	0.05	<0.01	<0.01	0.04	<0.01	0.001	0.01

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How to reduce unnecessary ventricular pacing: performance of “SafeR” mode in dual chamber paced patients

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Purpose: Aim of this prospective analysis is to evaluate, in patients (pts) implanted with dual chamber pacemaker (PM), the reduction of unnecessary ventricular pacing (%Vp) through a dedicated pacing mode (called “SafeR”), operating in AAI mode with a safety back-up Vp in DDD mode and to describe the incidence and distribution of atrio-ventricular blocks (AVBs).

Methods: Investigators were free to assign included pts to the programming of SafeR mode or to standard DDD (in case SafeR was contraindicated mainly due to permanent high-degree AVB). Pts underwent routine follow-up visits (FU) for 2 years. At each FU visit, data were retrieved from PM memories and analyzed to extract %Vp and incidence of AVBs.

Results: To date 158 pts from 9 Centers have been consecutively included (94 males, 69±14 y). Implant indications were (% of pts): Sinus Node Disease (SND) 84%, paroxysmal AVB 12%, SND + AVB 2%, permanent AVB 2%. SafeR mode was programmed at inclusion in 151/158 pts (95%). An interim analysis has been conducted on a subgroup of 82 pts with PM in SafeR mode. Results in terms of %Vp at 3, 6 and 12 months (M3, M6, M12) FU visits after inclusion are shown in Table 1. We also determined the distribution of AVBs (according to criteria used by the PM to classify AVBs and switch to DDD mode): results are shown in Table 2 (mean±std.dev, median, 3rd quartile).

Conclusions: SafeR resulted to be effective in reducing the amount of unnecessary Vp in our population of pts. The analysis reveals also a high incidence of paroxysmal AVBs often unknown at time of implant.

Table 1: % Ventricular Pacing

%Pts at M13 (n = 82)	110%	11–5%	61–10%	11–20%	21–30%	31–40%	41–50%	>50%
%Pts at M3 (n = 82)	49%	21%	3%	11%	3%	4%	2%	7%
%Pts at M6 (n = 58)	53%	21%	4%	4%	4%	4%	3%	7%
%Pts at M12 (n = 21)	62%	24%	0%	0%	0%	5%	0%	9%

Table 2: AVBs distribution

	I° AVBs			II° AVBs			III° AVBs		
	Mean ±SD	Median	3rd Quartile	Mean ±SD	Median	3rd Quartile	Mean ±SD	Median	3rd Quartile
M3	176±483	2	81	377±855	7	231	94±285	7	63
M6	140±504	1	31	548±1308	10	352	84±317	6	51
M12	111±367	2	26	272±792	3	19	278±687	5	23

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Cardiac remodeling secondary to right ventricular pacing

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Background: Chronic right ventricular (RV) pacing may lead to worsening symptoms in patients with heart failure. The purpose of this study was to measure the effects of chronic RV pacing on RV and LV end-diastolic (ED) and end-systolic (ES) volume (V, ml) and ejection fraction (EF).

Methods and Patients: Tomographic equilibrium radionuclide angiography was used to measure RV and LV end-diastolic (EDV), end-systolic (ESV) and ejection fraction (EF) in twenty-eight patients with LVEF < 0.50; fourteen (Group 1) with chronic (duration 4±2 years) persistent RV pacing (98±5% of RR intervals were RV paced beats) and in fourteen patients (Group 2) with no cardiac pacing.

Results: Comparisons between Group 1 and Group 2 are tabulated. Chronic persistent RV pacing compared to no pacing was associated with increases in RV and LV EDV and ESV and reductions in RV and LV EF; the increases in RV ESV and LV EDV and ESV were significant ($P < 0.03$, $P < 0.006$ and $P < 0.01$ respectively) and significantly fewer patients had $RVEF \geq 0.40$ in Group 1 compared to Group 2 (50% vs 93%, $p = 0.01$). **Conclusion:** In patients with $LVEF < 0.50$, chronic persistent RV pacing compared to no pacing was associated with enlargement of RV and LV EDV and ESV and decline in RVEF. Chronic persistent RV pacing may have led to adverse remodeling of the LV and RV.

Comparison of RV and LV

	RV			LV		
	EDV	ESV	EF	EDV	ESV	EF
Group 1	208±71	151±76	0.42±0.16	237±68	168±58	0.30±0.09
Group 2	179±51	89±31	0.51±0.11	176±36	119±33	0.33±0.08
P, 1 vs 2	0.23	0.03	0.12	0.006	0.01	0.36

Group 1 compared to Group 2

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Idiopathic ventricular rhythm: a cause of atrio-ventricular desynchronisation in AAI paced patients

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Pacing in AAI mode is usually performed in patients (pts) with sinus node disease (SND) in the absence of atrio-ventricular (AV) conduction disorder with the objective of permanent 1 to 1 AV conduction. Nevertheless AV desynchronisation may occur in case of paroxysmal AV block or of idiopathic junctional or ventricular rhythm (IVR). The incidence of this second mechanism is probably underestimated.

EVOCARD_{DS} is a trial assessing the influence of atrial overdrive pacing on AV conduction in SND pts paced in AAI mode + back-up ventricular pacing (AAIsafeR mode). While conducting this study, we documented episodes of AV desynchronisation related to IVR occurring during atrial pacing.

Population and Results: 100 SND pts were enrolled in the trial. A total of 60 pts (34F; 76±7 years; 36 with a history of AF) already completed the 3 months follow-up period. The pts were randomly assigned to AAI pacing at 50 bpm (Gr 1: n=31) or AAIR pacing at 60 bpm with a low reactive rate responsive function (Gr 2: n=29). No baseline differences were observed between the 2 groups. Occurrence of IVR was monitored using the specific device memories. In Gr 1, the mean atrial rate was 64±5 bpm and 14/31 pts demonstrated episodes of IVR. In Gr 2, the mean atrial rate was 68±4 bpm ($p = 0.02$) and only 7 out of 29 pts demonstrated episodes of IVR ($p < 0.05$). The mean rate of IVR episodes was 61±5 bpm in both groups. The number of IVR episodes per pt varies a lot from only one episode to more than 500 episodes over one month period. No different baseline characteristics were observed between pts with or without IVR, the only predictive factor being the pacing mode.

Conclusion: These data suggest the relatively high incidence of IVR leading to transient atrio-ventricular desynchronisation in SND pts paced in AAI mode. Optimization of atrial basic rate and rate responsive function programming are successful in lowering the number of pts presenting with IVR. IVR is mainly related to a hypochronotropic response of the atrial rate.

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The degree of mitral regurgitation in PM patients depends on LV dyssynchrony and is avoided by Hisian Pacing

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Background: Right ventricular (RV) apical pacing is detrimental for left ventricular function because it promotes ventricular dyssynchrony (VD) and Mitral Regurgitation (MR). In pts with preserved left ventricular synchrony and preserved Hisian-Purkinje conduction, a pacing system that could preserve both is desirable.

Aim of Study: To assess the relationship between MR and VD in different PM paced patient populations.

Methods: 117 Pts were implanted with a permanent PM according to the current guidelines. Pts have been divided into three groups in accordance to RV pacing site: (A) 63 pts (mean age 74±8 y and EF 50±16%) with a RV apical lead, (B) 24 pts (mean age 72±10 y and EF 53±17%) with a RV lead positioned in Para-his (PH) and (C) 30 pts (mean age 76±7 y and EF 61±13%) with a RV lead for Direct His Bundle (DHB) pacing. The three groups are homogeneous for diabetes, hypertension and ischemic cardiomyopathy. Through echocardiography we evaluated the VD as: (1) Electromechanical Latency (ELM, time for LV activation); (2) Yu index (SD of interventricular delays); (3) Degree of MR measured as Volume; (4) Tenting Area (TA, measured in 4 chamber view in systole between Mitral Ring and closed mitral leaflets).

Results: Different measurements have been done to evaluate the degree of VD and MR in the three groups A, B and C as shown in the table 1. A significant correlation between the TA and ELM – Lateral Wall has been observed ($r = 0.86$).

Conclusions: RV apical pacing leads to left VD and, due to the strong correlation between the ELM and MR, it leads to increased MR. DHB pacing, maintaining LV contraction synchrony, leads to a lower degree of MR compared to the other pacing sites.

	A	B	C	p A vs B	p A vs C	p B vs C
Yu	32±10	18±4	16±4	<0.05	<0.05	ns
ELM	133±23	106±19	92±15	<0.05	<0.001	<0.05
ELM – Lateral Wall	158±41	105±23	92±20	<0.05	<0.001	<0.05
MR (ml)	20±14	17±15	9.54±7	ns	<0.05	<0.05
Tenting Area cm ²	1.48±0.79	0.87±0.44	0.72±0.47	<0.05	<0.001	<0.05

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A randomized controlled trial for prevention of thrombosis after permanent transvenous leads implantation. Preliminary results

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Although the incidence of pulmonary embolism after permanent transvenous pacemaker and defibrillator implantation is not well established, the frequency of venous thrombosis is high, ranging from 30–50%. Previous temporary transvenous leads ipsilateral to the permanent implantation and lower left ventricular ejection fraction (LVEF) were associated with an increased risk of obstructions.

Aims: To study the efficacy of prophylactic six-months use of warfarin after transvenous leads implantation in patients with high risk of venous thrombosis.

Method: In this clinical, prospective, randomized and blinded study, a total of 200 patients submitted to first transvenous devices implantation with previous ipsilateral temporary pacing and/ or LVEF < 0.40 will be enrolled. The primary end-point is venous obstructions and secondary are morbidity, safety of anticoagulant therapy and overall mortality. Patients with history of previous venous extremity thrombosis and pulmonary embolism, coagulation disturbances, and malignancy are not included. Anti-bradycardia pacing was implanted in 45.5% of patients, cardioverter-defibrillators in 20.2% and devices for cardiac resynchronization in

34.3%. After device implantation, patients were randomly assigned to placebo or warfarin. Periodical clinical and laboratorial evaluations were performed to anticoagulant management. Following the six-month period, every patient was submitted to a digital subtraction venography. Chi-square or Student's t-test was used for statistical analysis between the two groups.

Results: From Feb/2004 to Oct/2006, 100 patients had undergone randomization. Base-line characteristics and the frequency of known risk factors were similar in both groups. Venographies analysis showed 61.5% of venous obstructions in patients assigned to placebo as compared with 33.3% in patients assigned to warfarin and absolute risk reduction of 28% (relative risk, 1.7 [95% confidence interval, 1.00 to 2.99]; $P < 0.0174$). The median international normalized ratio (INR) of patients in placebo group was 1.0 ± 0.3 , whereas the median INR in warfarin group was 2.5 ± 0.4 . This difference was maintained throughout the study period. In warfarin group, one patient had an episode of bleeding necessitating hospitalization.

Conclusions: Preliminary results of the prophylactic use of warfarin showed a significant absolute risk reduction of venous thrombosis after transvenous devices implantations.

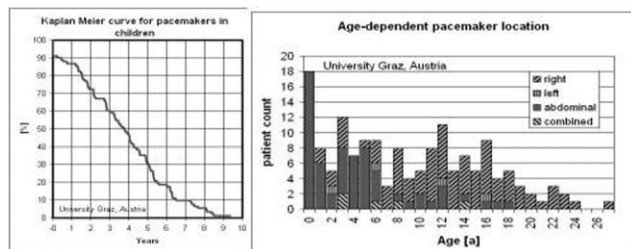
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20 years single centre experience in paediatric Pacing – conclusions

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Over a 20 years period, all pacemaker implantations, revisions and testings within the paediatric department were reviewed. 78 patients of all ages were seen on 500 occasions, 167 operations and 333 testings. In only 17% congenital bradycardia led to pacemaker implantation, perioperative events were much more frequent. During follow up patients received between 1 and 6 pacemaker exchanges (mean 2.0). Mean survival time of the explanted aggregates was 3.6 ± 2.3 years. In total 158 pacemakers, 54 atrial and 102 ventricular leads were implanted. 1 atrial and 18 ventricular leads were switched from epicardial to transvenous position. Modification from epicardial to transvenous systems begin in the second year of life and only patients with Fontan circulation will remain on epicardial pacing. For prospective planning in children, the longevity of a pacemaker is secondary to its physical dimension. Revisions are to be expected more frequent than in the adult population according to the patient's growth. After epicardial implantation in the newborn age, it is usually advisable to early switch to a transvenous system as growth adaptation is facilitated.



Pacemaker decay curve & lead strategies

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Aetiology of death among patients with electronic medical devices

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Objectives: Aim of the study was to determine aetiology of death among patient with implantable electronic medical devices (EMD) together with analysis of devices.

Methods and Patients: 66 patients with EMD (46 male, 20 female, age median 80.2 years – from 31.8 to 96 years), who died in Faculty Hospital Brno and who had autopsy at Department of Pathology during period from 01.01.2005 to 31.10.2006. Hearth weight, diameters of right and left ventricles, valvular pathology, signs of heart failure, signs of CAD, placement of electrode in vein system and presence of thrombi on the leads were obtained. We assessed the aetiology of death and other concomitant diseases. Data of battery status, stimulation mode, percentage of stimulation, AV delay settings were obtained by interrogation of EMD.

Results: Major aetiology of death was atherosclerosis in 74.2%, cancer in 12.1%, other in 13.6%. Immediate aetiology of death was: heart failure in 47%, bronchopneumonia in 25.8% acute myocardial infarction in 10.4, other causes 16.6%. Ischemic heart disease was present in 96.8% of patient (46.8% with signs of myocardial infarction (MI), 50% with coronary heart disease without MI). Fixation of electrodes in vein system: 42.2% of electrodes were free, 22.7% were fixated in vena cava superior, 18.2% in tricuspidal valve, 7.9% in pappillary muscles, 4.2% in right atrium. Insertion of electrodes: 42.4% in right ventricular (RV) apex, 27.3% in posterior wall of RV, 19.7% other places – septum, lateral wall or anterior wall of RV. Thrombi on electrode system were present in 4.5% cases. EMD: 61 pacemakers (62.3% VVI, 32.8% DDD, 4.9% VDD), 5 implantable-cardioverter defibrillators (2 with resynchronisation therapy, 3 with VVI pacing). There was no malfunction of EMD. Battery status: 6% of devices with ERI indicator. Median of RV pacing: 77.1%, RA pacing: 38.5%. There was no statistical correlation between type of pacemaker and aetiology of death, between percentage of RV stimulation and aetiology of death nor diameters of heart.

Conclusion: Major aetiology of death patients with EMD is atherosclerosis with heart failure. No death due to device malfunction was observed. There was no correlation between mode of stimulation and aetiology of death.

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Echocardiographic attempt to explain why RVOT is better than apex for patients after pacemaker implantation

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Echocardiography, including new methods as Tissue-Doppler Imaging, can indirectly help in resolving controversies on the optimal placement of the lead in the right ventricle by assessing cardiac function and evaluating dispersion of the electrical impulses in the myocardium.

Purpose: to evaluate influence of the localization of the RV lead on cardiac function assessed by echocardiography.

Methods: 91 patients with sinus node dysfunction and normal heart contraction, qualified for pacemaker implantation were included and next randomly divided into 3 groups: RVOT (Right Ventricular Outflow Tract), apex and IVS (Inter Ventricular Septum). Excluded were patients in which it wasn't possible to obtaine the previously random place of the implantation of the ventricular lead. In each patient a DDD pacemaker (Sigma 303 and Kappa, Medtronic Inc) with screw-in leads were implanted. In each patient a full echo including Tissue-Doppler Imaging (Vivid 7, GE) were performed twice: 2 days before and 5 days after implantation. All after-implantation examinations were performed on VDD pacing on short AV-delay (80 ms). Such parameters were evaluated: time velocity integral (TVI), mitral flow and contractility pattern using Inter-Ventricular Delay time (IVD) and IsoVolumetric Contraction time (IVC).

Results: All results are presented as difference between initial and post-implantation echo examination \pm SD. Middle mitral flow in % for RVOT = 3.84 ± 2.81 , IVS = 0.5 ± 3.74 , apex = -5.81 ± 6.41 . TVI in mm for RVOT = 3.47 ± 3.24 , IVS = 1.11 ± 3.45 , apex = -2.84 ± 2.76 . Middle IVD in ms was for RVOT = 25.3 ± 15.86 ; IVS = 25.36 ± 15.25 ; apex = 15.0 ± 12.5 . Middle difference between IVC was for RVOT = 20.2 ± 7.43 ; IVS = 48.2 ± 7.42 ; apex = 43.2 ± 6.79

Conclusions: Location of the lead in RVOT significantly increased mitral flow and VTI compared to initial parameters. Apex localization give opposite results. RVOT is the most optimal location of the pacemaker lead. Apex location seems to be a better alternative than IVS for RV

pacing using the contractility pattern, however, mitral flow and VTI seem to give opposite results.

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Right ventricular pacing reduction in non-selected dual-chamber ICD patients: overall performance of SafeR pacing mode

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Recent literature suggests the need to reduce the unnecessary amount of cumulative right ventricular pacing (Vp) to improve clinical outcome, in patients (pts) with ICD indications but no CRT indication. The SafeR pacing mode was designed to combine the advantages of AAI mode with the safety of back-up Vp in DDD mode. In this study the efficacy of SafeR mode was assessed in non-selected pts implanted with a dual-chamber ICD.

Methods: The SafeR mode behaves like a true AAI mode – no atrioventricular (AV) delay triggered after any atrial events – until AV conduction disorder occurs, triggering an immediate switch to DDD. While functioning in DDD, the device periodically attempts to switch back to AAI if spontaneous AV conduction resumes. The % of Vp cumulated from follow-up (f-up) to f-up was evaluated, selecting the longest available f-up period in 60 consecutive pts (88% males, 64±12 y old [min 22; max 84]) implanted with a dual-chamber ICDs programmed in SafeR mode. ICD indications were of primary / secondary prevention in 23%/77% of pts respectively. 25% of pts presented with bundle branch block and/or some degree of AV block, and 16% of pts had isolated sinus node dysfunction.

Results: On a mean f-up of 57±24 days [min 13 d; max 142 d], mean Vp was 5.7±18% ([min 0; max 89], median 0). 23% of pts had no switch at all to DDD. 71% pts had Vp < 1% and 18% of pts had 1% ≤ Vp < 10%. Interestingly, out of the 6 pts with Vp ≥ 10% that have appropriately frequently switched to DDD, only 1 pt had a reported history of AV conduction disorders. The trend of Vp over time was also evaluated on a subgroup of 29/60 pts with Vp statistics related to both f-up periods “implant to 1-month” and “1-month to 3-months” after implant. The table reports the resulting data.

Conclusions: The SafeR pacing mode is able to promote V spontaneous activity also in case of unexpected paroxysmal AV blocks, while maintaining Vp < 1% in 71% of non-selected pts implanted with a dual-chamber ICD. According to the available short time data, “time after implant” factor doesn't impact on the cumulative % of Vp in pts f-up.

Table 1: Comparing Vp data at 1M and 3M

Cumulative % of Vp (n=29 pts)	mean ±SD	median	min-max
Implant to 1M	6.1±18	0	0-70
1M to 3M	6.8±22	0	0-89

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Incidence and predictors of in-hospital events after first implantation of pacemakers

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Aims: Despite a rising number of patients receiving annually their first pacemaker (PM), current data on the incidence of early (in-hospital) events after (PM) implantation are inconsistent and have been obtained from studies that have only limited relevance for current practice. The purpose of this prospective study was to estimate the incidence of in hospital events after first PM implantation and to determine predictors.

Methods and Results: Patients with conventional pacing diagnosis are included in the Dutch multicenter Followpace PM registry that

prospectively documents patient prognosis and quality of life, and PM events after first implantation. Followpace is a prospective multicenter longitudinal cohort study, executed in 23 (of the 104) PM centres in the Netherlands. From these registry characteristics, implantation data and in hospital findings were analyzed as potential predictors for events in a sample of 797 patients. In 111 patients an in-hospital event occurred (incidence 13.9%, 95% CI: 11.5–16.3%). In the univariable analysis a lower Body Mass Index (BMI), presence of atrial arrhythmias, presence of heart failure, indication for implantation, use of antiarrhythmics, use of the vena subclavia for venous access, the implantation of a dual chamber system and pacing mode at discharge were associated (p < 0.20) with a higher incidence of in-hospital events. Five variables i.e. body mass index, history of atrial arrhythmias, vena subclavia for venous access, active atrial lead fixation, and pacing mode at discharge were found to be independent predictors of events after first PM implantation. The overall multivariable model yielded an ROC area of 0.70 (95% CI: 0.64–0.75).

Conclusion: This large prospective multicenter shows an incidence on in hospital events after first PM implantation of 13.9% (95% CI: 11.5–16.3%). We identified five independent predictors consisting of two patient characteristics and three implantation procedural and PM related ones. These predictors can support implanting cardiologists, surgeons and assisting technicians to identify patients at higher risk of events.

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Conventional dual-chamber right ventricular apical pacing in patients with preserved cardiac function: the predictors of clinical course

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Introduction. Permanent dual-chamber right ventricular apical pacing (RVAp) determines adverse changes in myocardial geometry and haemodynamics. However the long-term effects of RVAP in patients (Pts) with preserved left ventricular function still remains not clearly defined.

Aim: Prospectively investigate which parameters can predict the clinical evolution after long-term RVAP in Pts with preserved basal left ventricular ejection fraction (LVEF).

Population: 28 Pts (16M, 74±6 yrs) with advanced A-V block and indication to conventional DDD pacing. All Pts had a basal LVEF > 50%.

Methods: Pacemaker, clinical and echo-Doppler follow-ups were performed after implantation and at 12, 24 and 36 months. A-V interval was optimized by echo-Doppler. The following parameters were collected: QRS amplitude, left ventricular diastolic diameter (LVDD), LVEF, myocardial performance index (MPI), NYHA class, quality of life (QoL), the % of ventricular pacing and of A-V synchronism.

Results: The % of ventricular pacing was > 94% and of AV synchronism > 95%. Paced QRS duration >160 ms positively correlated with NYHA class (p < 0.005) and LVDD (p < 0.001).

Conclusions: In Pts with preserved left ventricular function RVAp determines worsening of MPI, but this index does not correlate with clinical course and has not practical impact in clinical setting. Post-implantation QRS amplitude can identify Pts with progressive impairment of clinical status who could benefit of integrated and/or alternative modality of pacing.

Data at follow-ups (mean value ± standard deviation)

	Basal	12 Months	24 Months	36 Months	P (36M vs. Basal)
LVEF	53.4±4.9	53.0±5.3	52.4±6.1	51.4±7.0	0.004
MPI	0.41±0.02	0.42±0.02	0.43±0.03	0.45±0.03	<0.0001
QoL	10.3±2.7	10.0±2.9	10.5±4.9	11.0±5.9	0.299
NYHA	1.43±0.5	1.54±0.64	1.71±0.76	1.82±0.94	0.039
LVDD	57.8±4.6	58.0±5.5	58.0±5.7	59.1±6.1	0.009
QRS	105.6±8.8	130.8±11.3	137.8±10.4	145.8±15.8	<0.0001

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Efficacy of structured pacemaker follow-up in paediatric patients

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Background: There are controversies about the optimal follow-up management to detect malfunctioning pacing systems in children. Aim of the study was to compare outpatient events in children with AutoCapture or conventionally programmed devices.

Patients and Methods: Data of children with AutoCapture (group AC, n=49, follow up 4.0 years (1.0–9.4)) and conventionally programmed devices (group Conv, n=41, follow up 10.5 years (3.8–11.9)) were retrospectively analyzed. Outpatient visits and Holter-recordings were screened for events necessitating device reprogramming or re-intervention: (1) Technical actions (change of A-/V-sensitivity, -output, pacing mode); (2) AutoCapture (AC) actions (change of Evoked response sensitivity, AC on/off) or (3) Acute actions (events leading to surgery). A total of 1106 outpatient visits and 147 Holter-recordings were analyzed (group AC: n=544 and 43, group Conv: n=562 and 104).

Results: Kaplan–Meier estimates at 2 and 5 years differed in freedom from acute (group AC: 96, 92%, group Conv: 88, 79%; p=0.049), and technical actions (group AC: 84, 71%, group Conv: 49, 20%; p<0.001). Number of technical actions/ year after correction for follow-up was lower for group AC than Conv (p<0.001). Length of follow-up correlated with a decreasing number of technical actions/ year in group Conv (rho=–0.55, p<0.001). In group AC, 0.19 (0.0–1.5) AC actions/ year were observed. Differences were seen for Holter-recordings leading to technical actions/ year (group AC: 0.0, group Conv: 0.33, p=0.01). One acute action after Holter-recording due to an indistinct problem during device interrogation was seen in both groups.

Conclusion: Estimated freedom from acute or technical actions was favourable for Group AC. The number of technical actions/ year was significantly lower for Group AC. As AutoCapture devices provide diagnostic features and automatic output adjustments, Holter-recordings are mandatory, if device interrogation remains unclear. In children, who are predominantly pacemaker-dependent, a 6-month follow up is adequate, independently of the device.

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A latent cardiac insufficiency of chronic right ventricular apex pacing patients without heart failure

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Background: Asynchrony induced by right ventricular (RV) apex pacing can cause various abnormalities in left ventricular (LV) function. However, patients paced from RV apex site for a long time without heart failure has not been fully elucidated.

Objective: To evaluate latent cardiac insufficiency of the chronic RV apex pacing patient without heart failure symptom.

Method: This study was intended of patients without heart failure symptom admitted for the exchange of exhausted pacemaker in our hospital from December, 2005 to November, 2006. As exclusion criteria, (1) Pacing site without RV apex, (2) renal insufficiency (Cre > 1.5 mg/dl) or hemodialysis patients, (3) no history of heart failure and (4) NYHA class ≥2. We defined more than 100 pg/ml of brain natriuretic peptide (BNP) levels as cardiac insufficiency (CI). We compared the following items in both group; RV pacing period, a ratio of RV pacing, presence of ischemic heart disease, use of angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB), left ventricular ejection fraction, left ventricular end-diastolic dimension, left atrial dimension, septal wall-thickness, grade of mitral regurgitation.

Result: During the period, consecutive 89 patients were admitted for exchange of exhausted generator as planned. Of 89 patients, 17 patients (19%) fulfilled the exclusion criteria and 3 patients (3.3%) underwent an upgraded to cardiac resynchronization therapy. A total of 69 patients

(29 men and 40 women, aged 76±8 years) constituted the study population. Patients with CI were 31 cases (45%). RV pacing rate was significantly higher in CI group than in the other group (91±21% vs 75±37%, P=0.035). With the exception of left atrium diameter (43±9 mm vs 38±9 mm, P=0.044), there were no significant differences in other parameters, when comparing the two groups.

Conclusion: Our data suggested that a half of RV pacing patients without obvious symptom were shown a latent cardiac insufficiency state and causes of them might be associated with RV pacing rate.

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Predictors of long-term clinical course in patients with permanent conventional dual-chamber pacing and different haemodynamic configurations

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Long-term conventional dual-chamber right ventricular apical pacing (RVAp) can deteriorate cardiac function but the prognostic implications in patients (Pts) with and without left ventricular dysfunction are undefined.

Aim: prospectively identify the predictors of clinical course in Pts with different haemodynamic configurations and permanent RVAP.

Population: 29 Pts (18M, 74±7 years) with advanced A-V block and indication to permanent DDD pacing. After implantation Pts were divided into 2 groups. Group I: left ventricular ejection fraction (LVEF) ≥ 50% and Group II: LVEF < 50%.

Methods: Echo-Doppler, pacemaker and clinical follow-ups were performed after implantation and at 12, 24, 36 months to evaluate: left ventricular diastolic diameter (LVDD), LVEF, right ventricular ejection fraction (RVEF), myocardial performance index (MPI), NYHA, Quality of Life (QoL), % of ventricular pacing and A-V synchrony. A-V delay was optimized by echo-Doppler.

Results: % of ventricular pacing was >94% and of A-V synchronism >95%. At Kaplan–Meier analysis Pts with RVEF < 40% had higher incidence of heart failure morbidity (0.005).

Conclusions: In group I RVAp worsened MPI, but this index was not correlated to clinical course. Group II presented deterioration of all parameters but uni-multivariate analysis didn't show a strong predictor of morbidity.

Data at follow-ups (mean±SD)

	Basal	12 Months	24 Months	36 Months	P
Group I					
LVEF	51.5±1.7	50.9±1.9	50.2±3.0	48.9±3.9	0.001
MPI	0.423±0.01	0.429±0.02	0.441±0.03	0.457±0.03	<0.0001
QoL	9.8±2.0	10.1±2.5	9.8±4.0	9.8±4.3	1
NYHA	1.40±0.6	1.53±0.5	1.60±0.6	1.60±0.6	0.334
RVEF	50.9±3.4	50.3±3.4	49.8±3.7	49.8±3.9	0.02
LVDD	57.5±4.2	57.9±5.0	58.3±5.7	59.4±6.1	0.029
Group II					
LVEF	46.4±2.0	45.5±2.5	44.2±3.2	43.4±3.3	<0.0001
MPI	0.419±0.02	0.435±0.02	0.445±0.03	0.462±0.03	<0.0001
QoL	15.4±3.4	17.4±4.2	19.3±3.6	20.1±3.9	<0.0001
NYHA	1.86±0.5	2.14±0.5	2.43±0.6	2.71±0.6	<0.0001
RVEF	42.8±2.1	40.0±2.2	38.6±2.8	36.3±3.5	<0.0001
LVDD	61.9±3.1	63.7±2.4	64.2±2.6	64.7±2.9	<0.0001

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Diagnostic messages and programming recommendations in a pacemaker advisory system-frequency & clinical correlation

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Purpose: To facilitate follow-up, some current pacemakers analyze diagnostic information and alert the physician to potentially important clinical events. In some cases, specific programming recommendations (ProgRec) are also suggested. However, the frequency and utility of this information remain uncertain.

Methods: We conducted a retrospective analysis of data from the VIBRANT Registry to assess relative frequency of Therapy Advisor messages (TAM) and programming advices in 158 patients (pts) with a T-series pacemaker, implanted between November 30, 2004 and April 29, 2005 (72M, 74±11 yrs).

Results: 141 (89%) pts received at least 1 TAM during 367 follow-up visits over 279±90 days of follow-up. TAM indicating the presence of high atrial rates (HAR) or atrial fibrillation (AF) occurred most frequently (78 pts). The 2 next most frequent TAM concerned the promotion of intrinsic AV conduction (76 pts) or sinus rhythm (72 pts). Acceptance of ProgRec to promote intrinsic AV conduction or sinus rhythm occurred in 23% and 33% of pts, respectively. TAM alerts for the presence of either an irregular and/or rapid ventricular rhythm occurred in 67 and 63 pts, respectively. Most of these pts had a history of rhythm abnormality & many also received an AF TAM.

Detection of retrograde conduction (28 pts; 15% ProgRec acceptance), P-wave sensing problems (25 pts; 62% acceptance rate), and infrequent AV synchrony (20 pts) were the only other TAM to occur in >10% of pts. Far-field R wave TAM were given for 7 pts and ProgRec to minimize the problem were followed in 31% of pts. Many TAM appeared repeatedly & most pts received >1 TAM.

Conclusion: Therapy Advisor Messages occur frequently, are internally consistent, and appear to reflect underlying clinical situations. The most frequent messages relate to the presence of rapid supraventricular rhythms. ProgRec are accepted a significant proportion of time, suggesting appropriateness and clinical relevance.

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Outpatient versus inpatient pacemaker implantation

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Background and Aims: In most current clinical practice, permanent pacemaker implantation is performed in an inpatient (IP) regimen with short hospital stay. We assessed the safety and feasibility of outpatient (OP) pacemaker implantation compared to IP implantation in a low-risk population with indication for permanent pacing.

Methods: We blindly distributed 124 consecutive patients with spontaneous rhythm and indication for pacemaker to IP implantation (1 night-long) or to OP implantation (observation during 8 hours before discharge).

Results: A group of 49 patients underwent IP implantation and 75 patients OP implantation. Baseline characteristics of the two groups of study are summarized in the table. Both groups were well balanced, and complications did not significantly differ between them. In the IP group, all complications were detected before discharge (1 pneumothorax and 3 lead dislocations), while in the OP group 4 of them (2 pneumothorax and 2 hematomas) were detected during hospital stay, what allowed initiation of treatment and required admission for at least 1 night, and 2 lead dislocations were detected at first follow-up at 15 days, which did not imply a vital risk for the patients as they had self spontaneous rhythm. Hospital stay taking into account the delay due to complications was

significantly shorter in the group of OP implantation, and this led to a significant decrease in hospital cost (see table).

Conclusion: Outpatient pacemaker implantation without need for a 1-night hospital stay is feasible, safe and significantly reduces hospital costs.

	Inpatient (IP) n = 49	Outpatient (OP) n = 75	p
Age (y)	75.1±11	74.9±10	NS
Male gender	67.3%	66.6%	NS
Indication for PM (%)	38.7/28.5/24.5	41.3/32/18.6	NS
(AV block/sinus dysfunction/slow AF)			
Type of device (%) (single-/dual-chamber)	53.1/46.9	46.7/53.3	NS
Active-fixation lead (n)	3	2	NS
Complications, n (%)	4 (8.1)	6 (8)	NS
Hospital stay (hours)	30.9±22	12.7±13	<0.001
Hospital stay (nights)	1.18±1	0.13±0.6	<0.001
Mean hospital-stay cost per patient (€)	349.2±299	132.7±156	<0.001

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Risk factors for survival of children with cardiac pacemaker due to post-operative atrioventricular block

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Objective: To evaluate the long-term outcomes of children submitted to permanent cardiac pacing due to postoperative atrioventricular (AV) block, searching risk factors for survival.

Methods: From 1980 to 2004, 113 children (5.7±5.0 years old) were submitted to permanent pacemaker (PM) implantation due to post-surgical A-V block. Time interval between heart surgery and PM implantation was 10.8±27.6 months (median = 21 days). The indication of PM implantation was persistent bradycardia (65.5%), heart failure (17.7%) and dizziness or syncope (16.8%). The surgery resulted in complete correction with no residual defect in 60.2%, with residual defect in 14.2%, with a valve prostheses in 15.0% and was palliative in 9.7%. Transvenous leads (79.6%) and ventricular pacing (80.5%) were preferred. Epicardial leads and other pacing modes were implanted only in specific indications. Age, gender, time from heart surgery until pace, pacing mode, lead type and surgical result were risk variable studied. Risk factors were studied using the Cox proportional model. The Kaplan–Meier method and the Log-Rank test were used to analyze survival.

Results: After a 5.6±6.0 years (maximum = 22.5 years) follow-up period, 11 patients were lost to follow-up, 23 died and 2 were submitted to heart transplantation. Reoperations to correct residual defects or to replace valve prostheses were performed in 18 patients and upgrade of pacing system in six. The 5-, 10-, and 15-year survival rates were 79.5±4.4%, 73.7±5.7% and 65.2±7.6%, respectively. The presence of residual defects was identified as the only independent risk predictor for mortality (p=0.038) increasing the risk of death 2.75 times.

Conclusion: Children with permanent pacemaker due to postoperative AV block presented with satisfactory evolution. The persistence of residual defects, valve prostheses or palliative corrections were predictors of poor results in these children.

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Technical aspects of apical and non-apical right ventricular pacing lead implantation

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Permanent cardiac pacing is widely used technique in the treatment of symptomatic bradycardia. A right ventricular apex stimulation was a golden standard for many years. Recent published papers demonstrate that it may deteriorate left ventricular function and may compromise the clinical course of pacemakers recipients. In order to avoid the latter alternative pacing sites should be considered.

In this communication we present intraoperative measurements of x-ray exposition, pacing threshold and R wave in 2 groups of consecutive patients whom pacemaker was implanted. We analyzed 168 patients. Group I consisted of 51 patient with apical pacing with the use of active and passive fixation electrodes. Group II consisted of 117 patients with non apical lead position, placed in right ventricular outflow tract or low or medium septum. In group II only active fixation electrodes were used. There were no electrode dislodgements or exit block observed in both groups.

Results: The measurements results are shown in the table.

Conclusions: (1) Non apical pacing of right ventricle is possible and does not demand much more x-ray time that apical to be established. (2) The intra cardiac signals are comparable. (3) Pacing threshold is higher in "new" position in comparison to conventional one, but acceptable. (4) The need for more studies to evaluate the potential benefit of specific pacing site is obvious. (5) The definition of criteria to get optimal electrode position should be established.

Group	Lead position	No. of pts	X-ray time (min)		Threshold (V)		R wave (mV)	
			Range	Mean	Range	Mean	Range	Mean
I (51 pts)	a	51	1.13–19.29	6.69	0.3–1.3	0.65	3.5–24	11.61
II (117 pts)	b	20	1.08–12.03	3.96	0.4–1.7	0.855	3.8–29	9.16
	c	56	1.14–28.48	5.87	0.4–1.5	0.785	3.7–38	11.17
	d	41	1.34–24.31	5.78	0.4–1.6	0.835	4–27.2	10.59

a: apex, b: low septum, c: middle septum, d: out-flow tract

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Dual-chamber pacing induced left ventricular remodelling for severe drug refractory symptomatic obstructive hypertrophic cardiomyopathy

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Purpose: Recently, several studies showed that dual-chamber pacing (DDD-pacing) in patients with symptomatic obstructive hypertrophic cardiomyopathy (HOCM) can relieve symptoms and decrease the left ventricular outflow tract (LVOT) gradients. However, it remains unknown whether LV remodeling occurs by chronic DDD-pacing.

Methods and Results: Fifteen patients (51.3±5.2 years) with HOCM and severe drug refractory symptoms were implanted a dual-chamber pacemaker. Echocardiographic studies were performed before and every 6 month after continuous DDD-pacing. They had LVOT gradient (mean 77.4±31 mmHg) by echocardiography at rest. There were no sudden cardiac death and worsening of heart failure. The LVOT gradients were significantly reduced (77.4±31 versus 22.8±7.2 mmHg, p<#65308;0.05) during 5.8±3.5 years (0.8–10.2 years). The interventricular septal thickness (21.6±3.1 to 16.9±2.4 mm, p<#65308;0.05) and posterior LV wall thickness (14.1±3.7 to 10.9±1.6 mm, p<#65308;0.05) were significantly reduced. LV diastolic dimension was significantly increased (40.8±5.6 to 47.8±3.1 mm, p<#65308;0.05) but LV systolic function did not changed (EF 71.6±7.5% to 69.0±5.5%, p=NS). Furthermore, NYHA classification (III to II in all patients) were improved as well.

Conclusions: Chronic DDD-pacing induced LV remodeling with reducing LVOT gradients and LV wall thickness and without deterioration of systolic function. Quality of life was remarkably improved.

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Direct His-bundle pacing preserves coronary perfusion compared to right ventricular apical pacing: a prospective, cross-over mid-term study

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Impulse propagation from right to left ventricle can cause an asynchronous contraction similar to that observed with left bundle branch

block. This altered contraction may lead to a change in strain and in myocardial perfusion. No data are available correlating the beneficial effects of His bundle pacing compared to right ventricular (RV) apical pacing. Aim of our study is the intra-patient comparison of myocardial perfusion corresponding to these two different pacing techniques.

Method: Pts with standard indication for PM implantation, with preserved atrio-ventricular (AV) conduction, were eligible for the study. Before enrolment, all pts in sinus rhythm were implanted with a triple-chamber PM: the atrial channel was connected to a atrial lead implanted in the right atrium and the ventricular channels were connected to: (1) the lead for His bundle in the RV port and (2) the RV apical lead in the LV port. Pts with chronic AF were implanted with a dual-chamber PM with the His pacing lead connected to the atrial port and the ventricular apical lead to the RV port. The PM was programmed in DVI mode. During His bundle pacing the channel connected to the RV apical lead was programmed as a back-up lead. After 3 months of His pacing all pts underwent the first follow-up and were submitted to a rest myocardial scintigraphy with Tc99m-SestaMIBI to evaluate myocardial perfusion. Then the PMs were reprogrammed to RV apical pacing and, after 3 months, all pts underwent the second scheduled follow-up, which included a new rest myocardial scintigraphy.

Results: Twelve consecutive pts (9M, 74±9 years) entered the study. Indications for PM were AF with slow ventricular rate (4 patients, 33%), second degree AV block (6 patients, 50%), third degree AV block (2 patients, 16%). The average values of perfusion were evaluated on a 20 segments basis. The perfusion score during His pacing was significantly better than during RV apical stimulation (0.44±0.5 vs 0.71±0.53 respectively, p=0.011). None of them showed a decreased perfusion with His pacing compared to RV apex.

Conclusion: Pacing the His bundle is superior to RV apical stimulation, preserving the physiologic myocardial coronary flow, while RV apical pacing induces perfusion defects.

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Impact of sequential and multisite biventricular pacing on left ventricular function and dyssynchrony in pigs with normal heart

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Introduction: Right ventricular pacing (RVP) is usually proposed in clinical practise for patients with complete atrio-ventricular block and normal left ventricular (LV) function. The respective impact on LV function and dyssynchrony of simultaneous, sequential and multisite biventricular pacing (BVP) in animals with normal LV function still needs to be investigated.

Methods: Experiments were conducted in 10 anesthetized open-chest pigs with normal ventricular conduction and normal LV function to compare the acute effects on LV function and on echocardiographic ventricular dyssynchrony of apical RVP, simultaneous BVP (RV apex + lateral LV wall), sequential BVP pacing (right to left ventricular delay from +60 ms to -60 ms in 20 ms increment) and multisite BVP (RV apex + lateral + anterior + posterior LV walls). The animals were paced in the VDD mode with short atrio-ventricular delay to ensure complete ventricular capture.

Results: The optimal settings were animal specific, however RVP was detrimental in all animals in terms of LV max +dP/dt and LV dyssynchrony as compared to simultaneous BVP.

– Comparison simultaneous vs sequential BVP: right to left ventricular delay optimization had no positive effects on LV max +dP/dt as compared to simultaneous BVP. Moreover, the level of LV dyssynchrony was minimal in 9 of the 10 animals with simultaneous BVP.

– Comparison simultaneous vs multisite BVP: Multisite BVP was not associated with a significant hemodynamic improvement as compared to simultaneous BVP. In contrast, we observed a significant decrease in terms of QRS width (65±08 vs 78±07 ms; p<0.05) and in terms of echocardiographic LV dyssynchrony (26±05 vs 37±06 ms; p<0.05) during multisite versus simultaneous BVP.

Conclusions: In pigs with normal heart, RVP was detrimental as compared to simultaneous BVP. Sequential BVP was not associated with a significant improvement in terms of LV function or dyssynchrony as compared to simultaneous BVP. In contrast, multisite BVP induced a significant decrease in electrical and mechanical dyssynchrony. This may have important implications in terms of long term LV regional remodelling.

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Do threshold trend fluctuations of epicardial leads predict pacing and sensing characteristics?

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Background: AutoCapture devices provide stored diagrams of long-term ventricular pacing threshold trends. Aim of this study was to evaluate whether amplitudes of fluctuation correlate with ventricular threshold and sensing changes over time.

Patients and Methods: A total of 56 children received AutoCapture devices (median age 6.7 years) connected to bipolar steroid eluting epicardial leads (Medtronic CapSure Epi 10366 or 4968). Maximum lead age at study closure was 12.2 years (median 4.0). Routine device interrogations were performed every 3 to 6 months and amplitudes of ventricular threshold fluctuation (Δ fluctuation) of stored diagrams were obtained. Regression slope coefficients to determine the incline as well as individual mean values of measured variables were calculated for each patient's course. Data are given as median.

Results: Δ Fluctuation correlated with higher thresholds ($\rho=0.68$, $p<0.001$), lower impedances ($\rho=-0.38$, $p=0.004$) and an incline of Δ fluctuation ($\rho=0.34$, $p=0.01$). Furthermore, an incline of Δ fluctuation correlated with an incline of thresholds ($\rho=-0.34$, $p=0.01$). Neither the mean nor incline of Δ fluctuation influenced ventricular sensing. No difference for Δ fluctuation was found for the pacing site ($p=0.75$). In children with congenital heart disease Δ fluctuation was higher compared to those without (0.73 versus 0.41, $p=0.02$). If lead age was >5 years, Δ fluctuation was higher compared to those <5 years (0.75 versus 0.55, $p=0.03$).

Conclusion: High amplitudes of ventricular threshold fluctuation are associated with higher and increasing pacing thresholds and lower impedances. Theoretically, this results from microinstability of the epicardial electrode on the heart surface with continued tissue irritation. Lower impedances suggest a fast conducting interface, such as local oedema. A higher Δ fluctuation was documented more than 5 years after lead implantation. A possible simultaneous decrease of the steroid-eluting potency of the electrode as course for this phenomenon can be hypothesized.

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Significant improvement of Quality of life in first year after pacemaker implantation

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Aims: In the last decade, health related quality of life (QoL) has become a useful and validated tool in the assessment of symptom-related outcomes, where the consensus exists that QoL should be assessed on the basis of several components, including physical condition, psychological well-being, social activities and everyday activity. The purposes of this prospective study were to estimate the QoL of pacemaker patients and compare the results with (age matched) average population and other patient groups, and to determine how QoL improves after pacemaker implantation and whether subgroup analysis could determine factors related to the change in QoL.

Methods and Results: Patients with conventional pacing diagnosis are included in the Dutch multicenter Followpace PM registry that prospectively

documents patient prognosis and quality of life, and PM events after first PM implantation. Followpace is a prospective multicenter longitudinal cohort study, executed in 23 (of the 104) PM centres in the Netherlands. For 341 patients all 9 subscales of the SF 36 detected a marked difference between PM patients before implantation and an age matched average Dutch population ($P<0.05$). After PM implantation all subscales of the SF-36 as well as all three subscales of the disease specific Aquarel and the EuroQoL QoL improved drastically. General health perception was significantly lower for patients with cardiac history and/or treated with anticoagulantia and antiarrhythmica. The indication for implantation was not related to QoL. For all SF36 subscales, except for "Change in Health" improvement of QoL was negatively related to female gender, older age, presence of cardiac history, anticoagulantia/antiarrhythmica use, indication for implantation and PM mode at discharge. The measurement of the improvement of QoL with the Aquarel questionnaire was less biased by these characteristics and therefore more susceptible to changes only depending on the PM implantation itself. The results showed a beneficial effect on improvement of QoL when the PM mode was set at DDD or DDDR at discharge as compared to VVV(R).

Conclusion: This large prospective multicenter study shows that QoL of patients before pacemaker implantation is dramatically low as compared to an age matched average population. The improvement of the QoL as measured by the SF36 is more susceptible to other factors as age and gender than the disease specific Aquarel questionnaire. When offered an option, discharging the patient on DDD or DDDR mode is the best choice to improve QoL after the initial implantation.

MONDAY, 25 JUNE 2007, 10:00–11:00

Poster Area

Catheter ablation of atrial fibrillation. Surgery for atrial fibrillation

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Drug induced atrial flutter during pulmonary vein isolation in patients with atrial fibrillation: Ablate or not?

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Introduction: Atrial fibrillation (AF) frequently coexists with atrial flutter (AFL) in the same patient. It has been demonstrated that AF can be transformed into AFL after administration of class IC antiarrhythmic drugs (ICA). It is not clear if pulmonary vein isolation (PVI) has influence on ICA induced AFL in AF patients.

Methods and Results: This study included 28 drug-refractory AF patients (5 women, mean age 59 ± 9 , 23 paroxysmal and 5 persistent). The patients were referred for PVI and did not have any pre-ablation history of AFL. All patients showed cavotricuspid isthmus (CTI)-dependent AFL during the ablation procedure under flecainide administration (intravenous 20 and long-term oral 8). The patients were randomized into two groups, A ($n=14$, 3 female) and B ($n=14$, 2 female). Both groups underwent PVI. Group A was during the same procedure subjected to additional CTI ablation with bi-directional CTI block as endpoint. The patients were followed for 11 ± 7 months. None of the patients in any of the two groups had documented AFL post-ablation. A total of 8 patients experienced recurrence of AF during follow-up, 4 of them were still using ICA. Two patients without recurrence were also still on long-term ICA. As shown in the table, there was no statistically significant difference in recurrence rate between group A and B. The patients also scored equal at one arrhythmia quality of life questionnaire (0 – no improvement compared to status before ablation, 10 – no arrhythmia related symptoms) at the time of follow-up.

Conclusion: We could not identify any differences in clinical outcome between patients with procedural AFL after PVI+CTI-ablation or PVI alone. CTI-ablation does not appear to be an important supplement to PVI in patients with drug induced AFL during AF ablation.

Patient group	Post ablation AFL	Recurrence of AF	Non-recurrence	Mean QoL Score (0–10)
All patients, n=28	0	8 (29%)	20 (71%)	7.6±3
Group A (PVI alone), n=14	0	5 (21%)	9 (64%)	7.4±3
Group B (PVI+CTI), n=14	0	3 (36%)	11 (79%)	7.9±4

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Effect of radiofrequency catheter ablation for atrial fibrillation on cardiac troponin I

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It is well known that minor myocardial necrosis due to radiofrequency (RF) lesions may be detected by the rise of cardiac specific biochemical markers, particularly cardiac troponin I (cTnI).

Aim: to assess the serum levels of cTnI in pts submitted to pulmonary veins (PV) electrical isolation (EI) for AF.

Methods: in 25 consecutive pts (20 males; 54±9 years old) with paroxysmal (14 pts) or persistent (11 pts) non-valvular drug-resistant AF submitted to ostial PV EI, we analyzed the levels of cTnI at baseline, at the end of ablation and 24 hours after the procedure (upper limit of normal range 0.06 ng/ml). Every RF pulse lasted 1 minute with maximum power of 30 Watts (irrigated-tip catheter). After ablation transtelephonic ECG monitoring was used.

Results: in our population EI was achieved in all the 82 targeted PVs (3.2±1 PVs/pt) by 65±22 RF pulses/pt. At the beginning of the procedure sinus rhythm (SR) was present in 14 pts and AF in 11 pts; in 8/11 pts cardioversion was necessary to obtain SR before PV EI. All the pts considered had normal values for cTnI at baseline. The levels of cTnI rose to 0.32±0.37 ng/ml and 0.72±0.51 ng/ml at the end of the ablation and 24 hours after the procedure, respectively, without significant differences in pts submitted to cardioversion. The number of RF pulses was significantly correlated with both cTnI release ($r=0.46$; $p=0.02$) and the number of PVs isolated ($r=0.73$; $p=0.0004$). In 9/25 pts (36%) with a temporary post-ablation period of early AF relapses (during the first 2 months after EI) both cTnI plasma levels (0.93±0.56 ng/mL in AF pts vs 0.51±0.33 ng/mL in AF-free pts; $p=0.05$) and the number of RF pulses (68±19 in AF pts vs 54±20 in AF-free pts; $p=0.02$) were significantly higher than in AF-free pts.

Conclusions: cTnI is a biochemical marker of even a minor myocardial damage, such as the one produced by RF during PV EI for AF. The good correlation between cTnI levels and the number of RF pulses suggests that monitoring of cTnI is a reliable way to quantify the size of myocardial necrosis induced by RF. Significantly higher levels of cTnI in pts with a temporary period of early AF relapses suggest that pts submitted to more aggressive procedures are more frequently, transitory, affected by arrhythmic episodes, as a possible consequence of irritative phenomena in a larger treated area.

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Arrhythmogenicity criteria of pulmonary veins in patients with paroxysmal atrial fibrillation

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Key Words: Arrhythmia, fibrillation, electrophysiology, pulmonary veins. The tenth anniversary of the pulmonary veins (PV) theory in origin of atrial fibrillation (AF) is coming up, but the electrophysiological properties of PVs still make interest.

Methods and Results: Research included 30 patients with paroxysmal AF, 22 male, (49.2±12.05 year). In 60% concomitant heart disease was presented. By using the programming stimulation of left atrium (LA) and PV, criteria of arrhythmogenicity of PVs were investigated.

We divided all arrhythmogenicity criteria into two groups. The first group represented pre-stimulation criteria (disorder of impulse conduction in

PV and LA, PV premature beats, bursts and spontaneous or mechanical origin of AF) and the second one was stimulation criteria (PV echo and arrhythmia during the programming stimulation). Moreover, effective and functional refractory periods (ERP, FRP) of PV and LA were compared. The results of electrophysiological investigation achieved that aforementioned arrhythmogenicity criteria exist in 67% of patients. 24 PVs were arrhythmogenic: 9 left superior PV, 7 right superior PV, 2 left inferior PV, 1 right inferior PV and all of 5 collectors of left PVs.

Pre-stimulation arrhythmogenicity criteria were found in 86% of arrhythmogenic PVs (Disorder of impulse conduction in PV and LA was presented in 20%, ectopic beats from PV – in 22%, bursts – in 27% and spontaneous or mechanical origin of AF episodes – in 17%).

Stimulation arrhythmogenicity criteria were found in 53.5% of arrhythmogenic PVs (PV echo during the programming stimulation – in 40% and arrhythmia during stimulation – in 13.5%).

The ERP and FRP of arrhythmogenic PV were significantly shorter than ERP and FRP of the LA. ($p<0.00001$, $p<0.0006$). ERP LA = 226.15±22.2 ms, ERP PV = 174.2±35.5 ms; FRP LA = 267.5±32.6 ms, FRP PV = 220±13.7 ms.

Conclusion: Using pre-stimulation and stimulation arrhythmogenicity criteria can help an electrophysiologist to select the most arrhythmogenic pulmonary vein that can decrease time and increase efficiency of ablation.

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Obesity is a major determinant of radiation dose in patients undergoing pulmonary vein isolation for atrial fibrillation

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Objectives: The purpose of this study was to evaluate the impact of obesity on patient radiation dose during atrial fibrillation (AF) ablation procedures under fluoroscopic guidance.

Background: Obesity is a risk factor for atrial fibrillation and its recurrence after ablation. It increases patient radiation dose during fluoroscopic imaging but this effect has not been quantified for AF ablation procedures.

Methods: Effective radiation dose and radiation-induced carcinogenic risk were calculated from dose-area product (DAP) measurements in 85 patients undergoing AF ablation guided by biplane low-frequency pulsed fluoroscopy (3 frames/sec). Two dose calculation methods were used (Monte Carlo simulation and dose conversion coefficients).

Results: Median DAP for all patients was 119.6 Gy cm² (range 13.9–446.3) for procedures with a median duration of 4 hours and 83±26 minutes of fluoroscopy. Body-mass index (BMI) was a more important determinant of DAP than total fluoroscopy time ($r=0.74$ vs. 0.37 , $p<0.001$), with mean DAP-values per hour of fluoroscopy of 58±40, 110±43 and 184±79 Gy.cm² in normal, overweight and obese patients respectively. The corresponding effective radiation doses for AF ablation procedures were 15.2±7.8, 26.7±11.6 and 39.0±15.2 mSv respectively (Monte Carlo simulation). Use of conversion coefficients resulted in overestimation of the effective dose, particularly in obese patients. Mean excess lifetime risk of all-cancer mortality was 0.060% (1/1666), 0.100% (1/1000) and 0.149% (1/671), depending on weight class.

Conclusions: Obese patients receive a more than 2 times higher effective radiation dose than normal weight patients during AF ablation procedures. Obesity needs to be considered in the risk/benefit ratio of AF ablation and should prompt for further measures to reduce radiation exposure.

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Recurrence of atrial fibrillation within 48 hours after ablation: impact on long-term outcome

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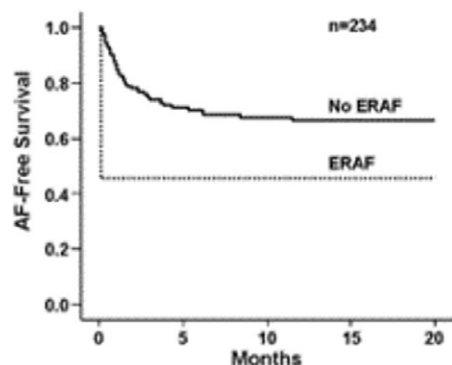
Purpose: Due to delayed structural and electrophysiological effects of radiofrequency ablation, early recurrence of atrial fibrillation (ERAF)

after ablation of atrial fibrillation (AF) does not necessarily indicate long-term ablation failure. The study was intended to assess the prognostic value of ERAF within 48h after ablation.

Methods: The study included 234 patients (23–80 yrs, 71.8% males) with symptomatic, drug-resistant paroxysmal (n=165) or persistent AF (n=69) who either underwent a Lasso-guided segmental pulmonary vein isolation (n=83) or a CARTO-guided left atrial circumferential ablation (n=151).

Results: After a median follow-up of 12.7 months 64% of patients with paroxysmal and 45% of patients with persistent AF were free of AF. ERAF occurred in 43% of patients and was a significant predictor of long-term ablation failure in univariate Cox regression analysis (HR=2.29, P<0.001). However, 46% of patients with ERAF were AF-free in the long-term follow-up compared to 68% of patients without ERAF. In multivariate analysis, ERAF (HR=2.23, P<0.001) and type of AF (HR=1.82, P=0.004) independently predicted ablation outcome. The prognostic value of ERAF did not significantly differ between the two ablation techniques and was found in both patients with paroxysmal (HR=2.05, P=0.005) and persistent AF (HR=2.35, P=0.013).

Conclusions: Regardless of the ablation technique and the type of AF, ERAF within 48 hours after ablation is a significant predictor of a poor long-term ablation outcome. However, as nearly half of the patients with ERAF remain free of AF on long-term, ERAF should not automatically result in an early repeat procedure.



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How to assess left atrium volume for evaluating reverse remodelling after atrial fibrillation ablation

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Background: Enlargement of the left atrium (LA) reflects structural remodelling and LA size has been considered to be a predictor of atrial fibrillation (AF).

Aim: To compare different methods to obtain a practical non-invasive assessment of LA volume as an accurate measure of LA remodelling.

Methods: Echocardiographic LA volume measurements with biplane ellipsoid formula (EEL) was compared with contrast enhanced spiral CT-scan (as a reference standard) applying the Simpson rule (CTSR) and the biplane ellipsoid formula (CTEL) using linear regression, a Pearson correlation coefficient (r) and Bland&Altman analysis.

Results: We measured LA volume in 46 consecutive patients (mean age 58±11 years, 80% men) with paroxysmal (67%) or persistent (33%) AF before and ±3 months after ablation (ABL). Mean LA volume before and after ABL was respectively 78 and 73 ml for CTSR, 71 and 64ml for CTEL and 68 and 61ml for EEL (all p<0.001). Irrespective LA volume, before and after ABL, CTEL was significant correlated with CTSR (respectively r1=0.77 and r2=0.74; p<0.001) and was even better correlated with EEL (respectively r1=0.77 and r2=0.76; p<0.001). LA volume could thus be derived from simple biplane ellipsoid echocardiographic measurements using the following formulas: before ablation CTEL = EEL × 0.44 + 40.4 ml and after ablation

CTEL = EEL × 0.5 + 33.3 ml. In a subset of patients (n=26) with LA volume >50 ml measured by EEL, CTEL and CTSR had the best correlation (r1=0.817; p<0.001). In addition, the mean of difference between these 2 CT-scan methods was 7±9 ml, indicating a good agreement.

Conclusions: Generally, contrast enhanced spiral CT-scan and echocardiography are equally applicable for LA assessment. LA volume measurements with echocardiographic biplane ellipsoid formula (EEL) provide the best correlation with contrast enhanced spiral CT-scan using the biplane ellipsoid formula (CTEL). Although this good correlation, lack of concordance between these methods implies a correction formula. In practice, echocardiographic biplane ellipsoid corrected measurements may serve as a valuable approximation of LA volume. Using all 3 different methods of LA volume measurements a significant reverse remodelling could be observed after atrial fibrillation ablation.

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Quality of life in patients with atrial fibrillation after circumferential pulmonary vein ablation – long term follow-up

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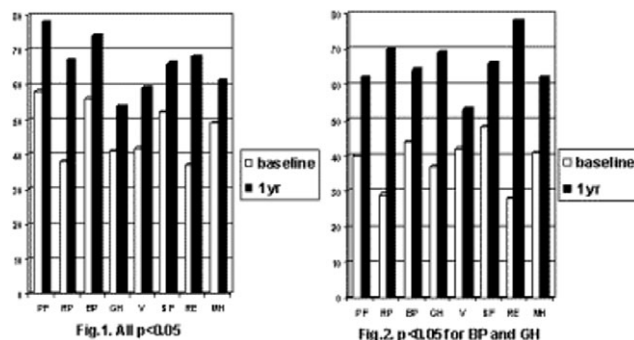
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Atrial fibrillation (AF) is the most common arrhythmia and is associated with deterioration of quality of life (QOL). Effectiveness of circumferential pulmonary vein ablation (CPVA) is still under assessment. The aim of the study: was to evaluate changes in QOL after CPVA.

Methods: Study population consisted of 33 patients (pts) (26 males, age: 54.2±9 yrs) with highly symptomatic drug refractory atrial fibrillation who underwent CPVA (Pappone technique). Clinical and echocardiographic examination (TTE, TEE), Holter ECG (1-, 7-days) were performed before and every 3 months after ablation. SF – 36 Medical Outcomes Survey Short-Form (QOL), scored on a 0–100 scale for each of eight domains: bodily pain (BP), general health (GH), mental health (MH), physical functioning (PF), role-emotional (RE), role-physical (RP), social functioning (SF) and vitality (V) and NYHA classification before and 1 year after CPVA were collected.

Results: After CPVA 27 of pts were free from AF and they reported significant improvement in all SF-36 categories (Fig. 1). Pts who had recurrence of AF after CPVA had a significant benefit in two (GH, BP) from eight subscales (Fig. 2). The NYHA classification improved from 2.7 at baseline to 1.5 (p<0.05) after CPVA.

Conclusion: Patients after successful CPVA experienced significant benefit in QOL and NYHA classification. Partially successful or unsuccessful in physician's opinion ablation also eliminated some symptoms of atrial fibrillation and partially improved QOL in those pts who were highly symptomatic before procedure.



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Treatment of different type atrial fibrillation by achieving electrical silence of the posterior inter-pulmonary-vein atrium (ESPIA) based on isolation of the pulmonary vein

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Introduction: Several studies have shown that the posterior left atrium (LA) can play an important role in triggering and perpetuating atrial fibrillation (AF). Electrical silence of the posterior inter-pulmonary-vein atrium can be achieved by surgery and catheter ablation. We sought to investigate results in different type AF treated by ESPIA technique and to analyze reasons for unsuccessful treatment.

Methods and Results: Three radiofrequency ablation steps are required to obtain ESPIA. (I) Segmental pulmonary vein (PV) isolation guided by a Lasso catheter; (II) Creating two lines of lesion between the two superior and inferior PVs. (III) Abolishing electrical signals between ipsilateral PVs if necessary. An electroanatomical mapping system (CARTO Merge®) was employed to achieve ESPIA. In 40 patients with AF (57±9 years, 3 women, 18 paroxysmal, 14 persistent and 8 permanent) ESPIA was completed. Voltage mapping was performed in all patients before and after ablation. The endpoint of ESPIA was voltage amplitudes in the region between the PVs and the two lines of lesion <0.1 mV. The mean perimeter and area of the electrically silent region created were 27±4 cm and 51±11 cm² (mean 31±4% of the total atrial surface). An average of 79±21 ablation applications were performed with an irrigated ablation catheter (40–60 s at each target site). Overall the recurrence rate was 22.5% (paroxysmal 11.1%, persistent 21.4% and permanent 50%) during a follow-up period of 11±4 months. Mapping results are shown in the table.

Conclusions: ESPIA based on PV isolation was effective particularly in the treatment of paroxysmal and persistent AF. Patients with low electrogram voltage prior to ablation in the LA, large LA volume and low percentage of silent area created by ablation may have high risk for clinical recurrence of AF.

	Pre-ablation voltage map in the LA (mV)				LA volume (mL)	Silent area created by ablation (%)
	Posterior wall	Appendage	PV ostia	Other parts		
Recurrence-free	1.42±0.66	2.41±0.75	0.53±0.30	1.47±0.57	107±28	31.6±3.8
Recurrence	0.81±0.49	1.72±0.90	0.26±0.09	0.92±0.48	149±53	26.7±2.6
P	<0.05	<0.05	<0.05	<0.01	<0.01	<0.01

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Paroxysmal atrial fibrillation originating from Limbus Fossa Ovalis: a report of three clinical cases

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Background: The efficacy of pulmonary vein isolation (PVI) for paroxysmal atrial fibrillation (PAF) is already recognized generally. However, it has been reported that about 20% of PAF have non-PV origin. A recent study reported that major non-PV foci originated from left atrial posterior wall, superior vena cava, ligament of Marshall, crista terminalis, coronary sinus ostium, and interatrial septum. Above all things, there is very little report concerning PAF originating from right interatrial septum. We describe 3 case reports with PAF originating from limbus fossa ovalis (LFO).

Cases: Case 1 is a 64-year-old woman who had been suffering from PAF. After PVI, atrial premature beats (APB) and PAF recurred soon. In second session of PVI, APB originated from right LFO, and this APB occasionally triggered AF. Complex fractionated atrial electrogram (CFAE) was also recorded at LFO during AF. Single radiofrequency (RF)

application at LFO terminated AF. Thereafter she is free from AF during 12 months follow-up period.

Case 2 is a 37-year-old man referred for RF ablation of incessant AT and PAF. Earliest atrial activation site during incessant AT was the right side of LFO. Very sharp spiky potential like His-bundle potential was recorded at LFO. And this potential preceded local atrial potential during AT, suggesting the presence of preferential conduction. AT occasionally degenerated to AF. Single RF application at LFO terminated incessant AT. Since then he was free from AT and PAF during 16 months follow-up period.

Case 3 is a 60-year-old man who underwent surgical Maze operation for lone AF 5 years ago. Recently PAF recurred and we mapped AF by CARTO system. Because interatrial septum was so hard that septal puncture needle was tough to punch through. Then we injected contrast medium into the atrial septum of foramen ovale. Just then, AF terminated spontaneously. Rapid pacing induced AF again, and we mapped both atrium by CARTO system. All left atrial potentials was organized. On the other hand, CFAE was recorded only at the right atrial septum and the sinus venosa region. Then, linear ablation from SVC to IVC via LFO terminated AF and rendered it noninducible.

Conclusions: We experienced 3 cases of PAF originating from LFO. We should bear in mind that LFO may be an important site of non-PV foci triggering AF.

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A randomized comparison of a pure circular mapping catheter based versus a combined circular catheter and non-fluoroscopic system (NavX) based ablation strategy in patients with atrial fibrillation

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Recent evidence suggests that a pure electroanatomical approach without a circular catheter based circumferential mapping of the pulmonary veins (PVs) may lead to electrically incomplete isolation during atrial fibrillation (AF) ablation.

Purpose: To compare the feasibility and the efficacy on long-term outcome of a pure circular catheter based circumferential PVs mapping approach (CCM) vs a combined CCM and electroanatomical mapping approach (CCEM) guided by the Ensite NavX® system in performing segmental PVs isolation.

Methods: Seventy-four consecutive patients (pts., age 53±15 years, 50 men) with symptomatic AF (paroxysmal 40; persistent 34) were randomized to a CCM (36) or a CCEM (38) ablation strategy. In the CCM approach a circular deflectable mapping catheter was used as the only tool to guide ablation. In the CCEM approach a 3D anatomical reconstruction of the left atrium and the PVs was obtained as a first step; consequently the positioning of the circular mapping catheter at the PVs ostium was optimized by the combined aid of the fluoroscopy and of the 3D visualization by NavX®. The endpoints of the ablation procedure were the electrical isolation of the PVs documented by the circular mapping catheter in the CCM group and the association of both an electrical isolation of the PVs documented by the circular mapping catheter and a complete electroanatomical circular lesion around each PV ostium in the CCEM group.

Results: An isolation of all PVs was reached in 38/38 (100%) pts of CCEM group and in 30/36 (83%) pts of CCM group (p=n.s.). In CCEM group, compared with CCM group, a significant reduction in the fluoroscopy time (31.8±11.4 vs 61.8±15.2 min, p=0.001) and in total procedural time (167.6±32.7 vs 208.3±45.2 min, p=0.03) was reported. A 48h ECG Holter was performed at 2 month intervals after ablation. During a mean follow-up of 12±4.0 months without antiarrhythmic medication, 31/38 (81%) of CCEM group patients were free of arrhythmia compared with 22/36 (61%) of CCM group patients (p=n.s.). Two non-fatal pericardial tamponade were reported, 1 in CCM and 1 in CCEM group.

Conclusions: An ablation strategy based on the combined use of a circular mapping catheter and the NavX® mapping system allowing catheter 3D visualization, is safe and significantly reduces fluoroscopy and total procedural time during AF ablation compared with the use of a pure circular mapping catheter based strategy. Furthermore the combined mapping strategy is associated to a higher complete successful PVs isolation rate and to a lower incidence of AF recurrence, although statistically not significant.

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Correlation between arrhythmia symptoms and confirmed atrial fibrillation paroxysm in patients after segmental isolation of the pulmonary veins

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Aim: Evaluation how ablation procedure influence on atrial fibrillation (AF) symptomatology

Material and Methods: 72 pts (50M, 22F; age 52±11 yrs) after segmental isolation of the pulmonary vein. After 19±12 months after successful ablation the history about arrhythmia symptoms were taken. All patients had more than 5 Holter monitorings and (if palpitation were present) ECG. Group 1 – 39 symptomatic patients, group 2 – 33 asymptomatic patients.

Results: Before procedure all patients registered AF as heart palpitation. 30 patient had also dyspnoe, 1 – presyncopal, another one – syncopal episodes.

After ablation heart palpitation was reported by 39 patients (55.1%). In 26 of them (33.3%) Holter monitoring or ECG registration during symptoms confirmed paroxysm of the AF. In 13 pts (16.6%) during heart palpitation AF was not presented (usually supraventricular or ventricular extrasystolies were observed).

In group 2 “silent” AF episodes were registered in 6 pts (7.7%). In 27 asymptomatic patients (92.3%) no AF was observed.

Patients in group 1 had significantly more often confirmed AF than asymptomatic ones ($p < 0.0001$).

Conclusions:

1. In our group recurrence of the AF after ablation was confirmed in 44% of patients.
2. Lack of symptoms is not a proof of successful procedure. 7.7% of patients have silent AF.
3. AF was confirmed only in 67% of symptomatic patients.

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Pulmonary vein related reentrant tachycardia after circumferential pulmonary vein isolation

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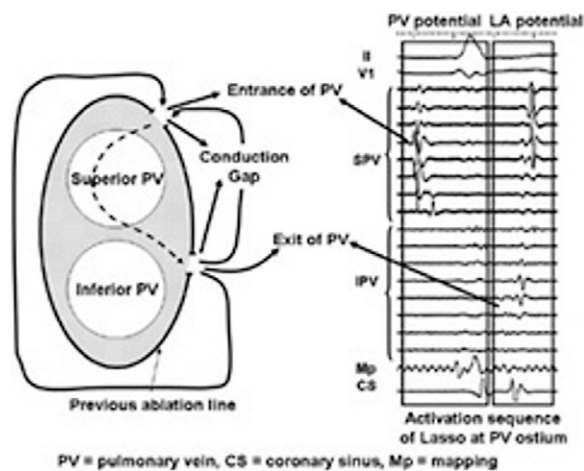
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Background: Recurrent organized left atrium (LA) tachycardias are sometimes observed after pulmonary vein (PV) isolation, and a focal tachycardia originated from the region around the reconnected PV ostia was reported as one of its mechanisms. The detailed electrophysiological aspects and mechanisms of this tachycardia were not fully investigated.

Methods and Result: Eight patients (6 male, aged 56±12 yr) underwent electrophysiological test and catheter ablation for an organized LA tachycardia originating from PV after PV isolation (PVI) for atrial fibrillation (AF). All patients had recurrent tachycardias 23±17 days after the ipsilateral PV isolation. The initial PV isolation and re-ablation were performed with 3D mapping and 2 Lasso catheters within the superior and inferior PVs. The mean cycle length of recurrent tachycardias was 297±38 ms. These tachycardias were originated from right PV in 6 patients, left PV in 2 patient. The electroanatomical mapping and the entrainment study demonstrated that all tachycardia had the reentrant circuit related with the 2 recurrent conduction gaps between PV and LA,

indicating that 1 gap acted as an entry of PV and another as an exit. All tachycardias were terminated by applications at the gap (5 cases in exit of PV and 3 in entrance). And according to the change of the sequence of PV signal during applications, at least 2 gaps between LA and the culprit PV for the tachycardia were confirmed to be closed after termination of the tachycardia in all patients.

Conclusions: After circumferential PVI, a reentrant tachycardia “PVRT” can be developed with the circuit conducting alternately between PV and LA via 2 gaps. And a slow conduction property at the gap or PV may play an important role in the mechanism of this tachycardia.



The schema of reentrant circuit

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Left atrial linear ablation and right atrial maze procedure to treat atrial fibrillation: first local experience

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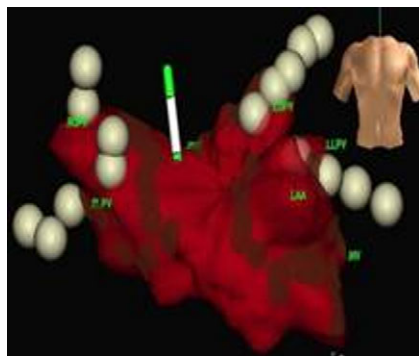
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Introduction: Recurrence of atrial fibrillation after pulmonary vein isolation is not uncommon and usually arises in the left atrial isthmus (area between the left lower PV and the mitral valve). This led to thinking of applying linear lesions in the left atrium.

Aim: The aim of this study is to evaluate the feasibility of performing left atrial linear ablation and the outcome of this type of ablation when combined with pulmonary vein isolation.

Materials and Methods: 28 patients (22 males and 6 females with mean age of 56 years) with history of AF refractory to pulmonary vein isolation were enrolled in the study. With the aid of the constellation Basket catheter and the Navix system a wide area of circumferential ablation (WACA) was applied to encircle the left and right PVs. This was followed by three lines of ablation; a roofline connecting the LUPV with the RUPV and two lines connecting the lower PVs to the mitral valve annulus. This was followed by right atrial maze procedure by creating two line of ablation in the right atrium; septal and anterior.

Results: A total number of 49 PVs were found to be electrically active (20 LUPV, 16 LLPV, 12 RUPV and 1 RLPV). Ablations attempted at all these veins and were successfully isolate. The average duration of WACA and left atrial linear ablation was 70.96 minutes and the average duration of right atrial maze was 33.11 minutes. The average duration of the whole procedure was 211.07 minutes. The average fluoroscopy dose was 1306.38 cGy cm². No immediate complications were recorded. During the first period of follow-up (1 month) majority of the patients hold sinus rhythm and reported no significant symptoms. Follow-up of these patients is still running. The success rate in maintenance of sinus rhythm will be feasible with the period of follow-up.



3-D image of LA showing the WACA.

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Basal plasmatic neuro-hormonal activation predicts the success of circumferential pulmonary veins ablation of atrial fibrillation

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Recent data suggest that renin-angiotensin system may act as a local profibrotic factor promoting and perpetuating atrial fibrillation (AF).

The aim of the study was to analyze, in patients undergoing circumferential pulmonary veins ablation (CPVA) for treatment of drug-refractory AF, if basal plasmatic neuro-hormonal activation is related to the success of the procedure.

Methods: Pre-procedural basal plasmatic neuro-hormones (renin activity, angiotensin-II (AT-II), aldosterone, AT-II converting enzyme and atrial natriuretic peptide) were determined in patients undergoing a first procedure of CPVA. Patients with structural heart disease were excluded from the study. Success of the ablation was defined as the absence of AF after a blanking period of 1 month.

Results: A series of 45 consecutive patients were included. Of them, 30 have completed a 4-month follow up and are presented. Mean age of the study population was 51±13 years, and 77% were males. Hypertension was present in 33% of patients, and 33% were endurance sport practitioners. In the remaining patients AF was considered idiopathic. AF was paroxysmal in 22 patients (73%), persistent in 4 (13%) and permanent in 4 (13%). Mean left atrial diameter was 40.6±6 mm. After a mean follow-up of 6.2±2 months, 20 patients (66.7%) remained in sinus rhythm. The univariable analysis showed that patients with AF recurrences had significantly higher basal plasmatic levels of AT-II (16.7±17 vs. 8.7±3 pg/mL, $p=0.03$) and aldosterone (13.2±4 vs. 5.2±2 ng/dL, $p<0.001$). Cox regression confirmed the basal plasmatic levels of aldosterone as the only independent predictor for AF recurrence in this series, with a hazard ratio of 1.24 (95% confidence interval 1.1–1.4; $p=0.001$). The area under the ROC curve for basal aldosterone was of 0.95, and levels of aldosterone higher than 11.35 ng/dL had a sensitivity of 80% and a specificity of 100% for identifying patients with AF recurrences after CPVA.

Conclusions: Basal levels of aldosterone predict AF recurrences after CPVA in patients without structural heart disease, and may help identifying patients with a worse outcome. These results suggest that having a profibrotic milieu may contribute to perpetuate AF and may worsen the success rate of CPVA.

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High thoracic epidural anaesthesia in atrial fibrillation ablation

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Purpose: During atrial fibrillation ablation, radiofrequency delivery in the left atrium induces pain usually not tolerated. Thus the need to utilize

a conscious or deep sedation plus analgesia with consequent problems of drug titration and overdose adverse effects or underdose insufficient analgesia. High thoracic epidural anaesthesia (HTEA) has been successfully utilized in cardiac and thoracic surgery showing improved perioperative analgesia.

Aim of the study is to verify feasibility, efficacy and safety of HTEA in atrial fibrillation ablation.

Methods: Eighteen consecutive patients undergoing atrial fibrillation ablation procedure were selected for HTEA. Informed consent was obtained from each patient. Exclusion criteria were: APTT > 45", INR > 1.4, platelet count < 80,000, contraindications to any of the drugs in the protocol. One hour before the procedure, 10 mg of Morphine IM were injected. An epidural catheter was inserted, via a 17-gauge Tuohy needle, at the T2-T3 or T3-T4 interspace, with a test dose of Naropine to confirm placement. Half an hour before RF ablation, 10–12 ml of Naropine 0.6% + 50–100 µg of Fentanyl were administered.

Results: 16 pts received HTEA. 2 pts were excluded because of INR > 1.4. Mean total procedure time was 221.5±38.3 min while mean RF ablation time was 41.5±6.3 min. No HTEA related complication were observed. In 15 pts (94%), complete analgesia was obtained all the ablation long. Only in 1 pt, analgesia was implemented with 5 mg of Morphine IV. In 2 pts, adjunctive sedation, with 2 mg of Midazolam IV, was required. No drug adverse effects were observed. Since heparin was administered during the procedure, the epidural catheter was removed after ACT normalization. Postoperative recovery was free of adverse events.

Conclusion: HTEA can be safely performed for atrial fibrillation ablation analgesia, with excellent pain control.

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Integrated approach for atrial fibrillation ablation under transesophageal echocardiography guidance

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Background: Different techniques are used for atrial fibrillation (AF) ablation. Procedures have evolved; from left atrial (LA) linear ablation, to ostial electrical isolation of the pulmonary veins (PV) or PV antrum isolation guided by intracardiac echocardiography.

Methods: Under general anaesthesia, 100 pts (mean age 47±12 yo, 81 paroxysmal, 19 persistent) underwent transesophageal echocardiography (TEE) guided hybrid AF ablation. Lone AF was present in 66 pts, hypertension in 18 pts and cardiomyopathy (CM) in 16 pts. Using only one catheter in the LA, an integrated AF ablation approach (anatomical and electrophysiological) was performed. We encircled the left- and right-sided PVs 1 to 2 cm from the ostia with circular PV lesions using 3D electroanatomical guidance. All PV ostia were marked on the 3D map based on PV angiography, TEE and/or prior CT imaging. Then, ostial PV potentials were targeted with the ablation catheter, and additional lesions were performed to achieve antrum and ostial electrical isolation. Additional roof and mitral isthmus lines were performed in CM and persistent AF. All procedures were guided by transesophageal echocardiography (TEE) to delineate the anatomy, guide the transseptal puncture and monitor for complications. The mean radiofrequency ablation and fluoroscopy times were 63±12 and 36±12 minutes respectively.

Results: After a single ablation procedure and a mean follow-up (FU) of 10±4 mo, 90% of the pts were improved including 72 pts who were free from recurrent AF. Left atrial tachycardia (AT) occurred in 14 pts including 6 pts with no recurrence after electrical cardioversion. A second LA ablation procedure was done in 15 pts. (AF ablation in 8, left AT in 7) After the second procedure, 12 more pts were cured increasing the success rate at 84%. The success rate was the same in the population with persistent AF and CM. The esophagus was located close to the left PV ostia in 38%, right sided in 28%, midline in 17%, with an oblique course in 17%. The right and left superior PV velocity were detected in 100%, the right inferior PV in 94% and the left inferior PV in 86%. Major complications (cardiac tamponade 1, PV laceration 1) occurred in 2 pts. These 2 serious complications were detected immediately by the

TEE with no long term adverse effect. No stroke occurred and no acute PV stenosis was detected by TEE.

Conclusions: A single AF ablation session using a hybrid approach is an effective treatment for AF. TEE is a valuable monitoring tool to confirm the PV antrum edge localisation and to diagnose acute complications.

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Circumferential pulmonary veins ablation for atrial fibrillation: results in creating 1 versus 2 ablation lines along left atrial posterior wall. A randomized study

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Circumferential pulmonary veins ablation (CPVA) is an effective treatment for atrial fibrillation (AF). Ablation scheme often includes lineal lesions not only to modify left atrial (LA) substrate but also to prevent subsequent LA reentries. Larger lesions may be associated with a higher risk of complications. The aim of this study is to compare the results of 2 CPVA ablation schemes.

Methods: CPVA consisted in continuous radiofrequency lesions encircling both ipsilateral PVs until voltage abatement is achieved plus anatomical ablation of mitral isthmus. Then, patients (pts) were randomized to CPVA-1 or CPVA-2 groups in which either 1 or 2 ablation lines were anatomically created along LA posterior wall.

Results: A total of 60 drug-refractory and symptomatic AF pts were included (74% men, 51±12 years, 62% paroxysmal AF, LA diameter 41±5 mm, 28% hypertensive and 18% with structural heart disease). There were no basal differences between both groups. Mean follow-up was 7.5±1.0 months. After the first ablation procedure: in CPVA-1 group, 7 pts (23%) experienced AF relapses and 2 pts (7%) had new-onset flutter; in CPVA-2 group, 7 pts (23%) experienced AF relapses and 3 pts (10%) had new-onset flutter respectively. Kaplan-Meier curves showed no differences in the mean predicted proportion for arrhythmia recurrence between both groups (Figure 1; solid line: CPVA-1 group, dots line: CPVA-2 group; Log-rank test p=0.85). In CPVA-1 group, there were 2 pts who suffered a transient cerebral ischemia and 1 pt who presented pericarditis. In CPVA-2 group, there was 1 pt with ST-segment elevation normalized by sublingual nitrates.

Conclusions: The addition of a second ablation line along the LA posterior wall did not show benefit regarding to AF or flutter recurrences after first CPVA procedure.

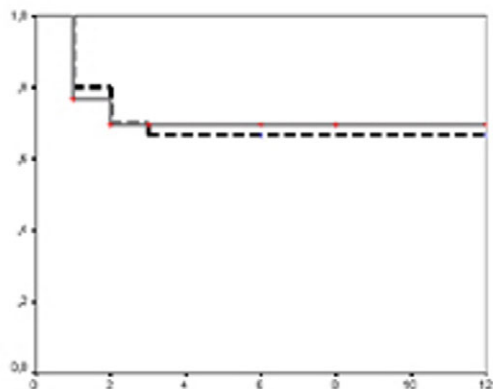


Figure 1

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Atrial scarring is an independent predictor for recurrence of atrial fibrillation but not for new onset atrial flutter after radiofrequency ablation of atrial fibrillation

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Purpose: Radiofrequency ablation of atrial fibrillation is associated with a high rate of recurrence of atrial fibrillation and occurrence of atrial flutter. The role of atrial scarring as risk factors of these rhythm disturbances is not well established.

Methods and Results: 204 patients with drug resistant atrial fibrillation (paroxysmal n=127; persistent n=77) who underwent CARTO-guided left atrial circumferential ablation were included in this study. Atrial scars defined as absence of electrical signals, were present in 80 cases at baseline. Patients were followed for at least 6 months (median follow-up 9.89 months). At 6 months 58% of patients with paroxysmal AF and 51% of patients with persistent AF remained free of AF (Table 1). Atrial flutter occurred in 28.4% of the patients. Presence of atrial scars at baseline was a significant predictor for AF recurrence in univariate (p<0.012; HR 1.67) and multivariate Cox regression analysis (p<0.003, HR 2.08), but not for the occurrence of atrial flutter.

Conclusion: Atrial scarring is an independent risk factor of recurrence of atrial fibrillation but does not predict atrial flutter after radiofrequency ablation of atrial fibrillation.

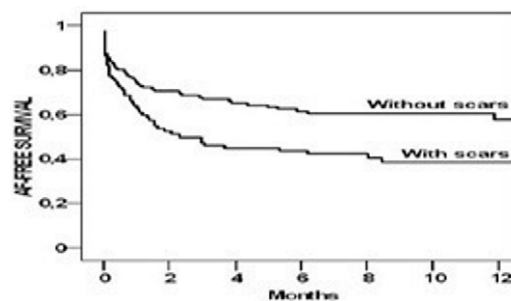


Figure 1

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Integration of 3-D left atrial magnetic resonance image into real-time electroanatomic mapping system: validation of a new registration method to guide catheter ablation of atrial fibrillation

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Background: The alignment of real 3D left atrial image acquired by magnetic resonance (MR) into the electrical and anatomical information obtained with the 3D mapping system is one of the most critical issues of the new technique of image integration for catheter ablation of atrial fibrillation (AF). Aim of the study was to assess the accuracy of a new simplified technique for the superimposition of 3D MR left atrial image on real time left atrial electroanatomic map obtained with 3D mapping system (registration).

Method and Results: Gadolinium-enhanced MR imaging of left atrium and pulmonary veins (PVs) was performed in 38 patients with drug-refractory AF. MR data were imported into the electroanatomic mapping system. Registration was obtained with a combination of "landmark registration" of 1 endocardial point and of "surface registration" of a limited number of points sampled only from the posterior wall and the septum of the left atrium. The accuracy of the registration was assessed through: (1) alignment between the PV virtual tubes and the 3D MR PVs anatomy; (2) a statistical algorithm integrated in the CartoMerge system; (3) the percentage of PVs in which electrical isolation was documented after the anatomical circumferential ablation without the need for supplemental ostial ablation.

Alignment between the PV virtual tubes and the 3D MR PVs anatomy was obtained in all but one patients. The average registration surface-to-

point distance and the average ablation surface-to-point distance resulted in a mean of 1.37 ± 0.97 mm and 1.49 ± 1.22 mm respectively. Upon completion of the circumferential anatomical ablation around the PVs, electrical PV isolation was confirmed by decapolar circular mapping catheter in 138/155 PVs (89%).

Conclusion: Our registration strategy mainly based on the surface registration of the posterior wall of the left atrium increases the accuracy of the image integration process and allows tailored catheter ablation according to individual anatomy in about 90% of PVs.

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Decrease in efficacy of repeat procedures of circumferential pulmonary vein ablation in patients with relapses of atrial fibrillation or left atrial flutter

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The success rate of circumferential pulmonary vein ablation (CPVA) to treat atrial fibrillation (AF) ranges from 60 to 90%. However, as many as 20 to 30% of patients underwent a second procedure. The aim of the study was to evaluate the efficacy of a second and third CPVA procedure in patients with relapses of atrial fibrillation or left atrial flutter.

Methods and Results: From a series of 210 patients who underwent a CPVA due to refractory AF, 150 patients have completed a minimum follow-up of 6 months. Of them, 29 (19%) underwent a second CPVA due to recurrences of AF or left atrial flutter (LAF) poorly controlled with antiarrhythmic medication. There were 25 men (86%) with a mean age of 50 ± 13 years. The repeat ablation procedure consisted of mapping and ablation of the flutter, whenever present, and a redo of CPVA, deploying circular lesions around right- and left-side pulmonary veins (PV) whenever electrical activity was detected inside the previous circumferential lesion. The procedure was guided by an electroanatomic mapping system (CARTO). Additionally, the linear ablation lesions on the posterior left atrial wall and mitral isthmus were revised.

After a mean follow-up of 13 ± 6 months, 13 patients (45%) were free of recurrences after a second procedure. Seven patients underwent a third ablation due to arrhythmia recurrence. The global efficacy of the latter was 28% (2 patients free from arrhythmia). Six patients were submitted to cardiac surgery: 3 of them after the second and 3 after the third CPVA procedure. A bilateral video-assisted thoracoscopic epicardial pulmonary vein isolation and left atrial appendage excision was performed, with a success rate of 83% after a mean follow-up of 9.2 ± 7.2 months.

Conclusions: The success rate of CPVA decreases when repeating the procedure, especially after the third ablation. Alternative options, such as minimally invasive surgery may be offered to such patients.

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Catheter ablation for atrial fibrillation using intracardiac echocardiography

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Background: Catheter ablation is effective in the treatment of atrial fibrillation (AF). During the procedure, visualization of left atrium and pulmonary veins (PV) is important. We assessed the role of intracardiac echocardiography (ICE) for the guidance of ablation.

Methods: The study included 220 patients (pts, 181 men, age 55 ± 9) with paroxysmal, persistent or permanent AF, in whom radiofrequency (RF) catheter ablation was performed using 8 mm tip catheter and electroanatomical mapping (CARTO). Moreover, guidance by ICE was used in 162 pts (group I), while the rest 58 pts underwent ablation without ICE (group II).

Results: Total procedure duration was shorter and time of RF delivery was longer in the group I than in the group II (258 ± 52 min vs. 282 ± 51 min and 2610 ± 743 sec vs. 2265 ± 624 sec, $p < 0.05$). During a mean follow-up of 9 months, 68% of cases in group I and 60% of cases in group II were arrhythmia-free ($p < 0.05$). Procedure was repeated in 13% and 9% of pts, respectively. Thrombus formation in the left atrium was

observed in 9 pts from group I. Higher degree of anticoagulation started before transeptal puncture diminished the risk of thrombus. Significant stenosis of one PV was detected in two pts, all in group II.

Conclusion: ICE is useful method for the guidance of ablation for AF. It allows to increase the efficacy of the procedure and reduce the risk of complications.

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Heart rate night drop after successful surgical ablation of paroxysmal atrial fibrillation may be possible marker of left atrial remodeling and autonomic reinnervation

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Background: Successful surgical pulmonary vein isolation (PVI) is highly effective treatment of paroxysmal atrial fibrillation (PAF) as it isolates triggering from PVs and as well as it isolates atrial area from autonomic ganglia. The aim of the study was to evaluate changes of heart rate night drop (HRND) in long-term follow-up as a possible marker of atrial remodeling and autonomic reinnervation of left atrium.

Material and Methods: 27 patients after successful surgical ablation of PAF with use of bipolar radiofrequency device were prospectively followed after 3, 6 and 12 months. In all patients 24-hours Holter ECG and echocardiography were performed. Proportional HRND was measured in patients free from PAF. Pharmacotherapy remained unmodified in all patients during observation period.

Results: Before ablation mean HRND was 27.04 (± 33.7)%. After 3 months mean HRND reduction was observed (13.4 ± 20.4 %) and lasted till 6 months after ablation (14.5 ± 22 %). After 12 months HRND significantly increased up to 40 (± 43.1)% ($p = 0.03$) showing no significant difference with preoperative value ($p > 0.05$). HRND significantly correlated with left atrial (LA) diameter and duration of PAF.

Conclusion: Dynamic changes of HRND and its return to preoperative level after 1 year after successful PVI with addition of significant correlation with LA diameter and PAF duration may suspect HRND as possible marker of LA reversal remodeling.

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Atrial arrhythmias after surgical treatment of atrial fibrillation using radiofrequency energy

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Creation of linear lesions in the left atrium has been suggested as a therapeutic option for patients (pts) indicated for cardiac surgery for valvular heart disease and/ or coronary artery disease (CAD) and concomitant atrial fibrillation (AF).

The aim of the study was to analyze the heart rhythm after surgical ablation, especially the clinical and electrophysiologic characteristics and management of recurrent tachyarrhythmias in symptomatic pts.

Methods: Since August 2000 till November 2006, 415 pts (163 female, mean age 67.5 years, range 25–84 years) with chronic or paroxysmal AF underwent left atrial (LA) linear endocardial radiofrequency (RF) ablation before valve surgery and/or coronary artery bypass grafting (CABG). Subjects with symptomatic recurrent atrial arrhythmias resistant to DC shocks and antiarrhythmic drugs underwent electrophysiologic study. Electroanatomical mapping by CARTO system (Biosense Webster) was used to guide catheter ablation.

Results: Restoration and maintenance of sinus rhythm after surgical RF ablation was achieved in 61 to 72% of cases in six months follow up depending on underlying disease. Majority of the remaining pts have AF. Regular atrial tachyarrhythmias occurred during follow up in 62 pts (15% of all patients) and were transient in majority of cases.

Twelve subjects (3%, 3 female), with symptomatic recurrent atrial arrhythmias underwent electrophysiologic study. Five pts had typical right

atrial (RA) flutter, four have documented LA macroreentry tachycardia. In two pts postincisional RA tachycardia was diagnosed. One pts had multiple arrhythmias (LA reentry, RA postincisional and typical RA flutter). All of 12 pts were treated successfully with RF ablation. At follow up 18 months (range 2–48 months) all of them were arrhythmia-free without antiarrhythmic drugs.

Conclusions: Incisional atrial flutter seems to be a common finding in this group of patients, occurring in nearly one-half of those with recurrent symptomatic arrhythmias. Catheter-based mapping and ablation of these arrhythmias is feasible and effective.

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Transcatheter pulmonary vein isolation after Mitral Valve replacement

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Objectives: Report our data about pulmonary vein isolation (PVI) in patients after mitral valve replacement.

Background: PVI is widely used to treat patients with atrial fibrillation. The combination of AF and structural heart disease is thought to be associated with a different substrate and possibly with a higher risk of procedural complications.

Methods: 19 patients after mitral valve replacement (MVR) underwent PVI for Atrial Fibrillation (AF). A matched group of 38 ablated patients without MVR acted as control subjects. After a blanking period of three months, a follow-up of 12 months was considered for MVR patients and controls. Holter recordings were performed in all subjects at 3, 6, and 12 months.

Results: The mean duration of and mean procedural time (175±30 vs 180±23) minutes and fluoroscopy time (51±7 vs 35±6) minutes was higher in the MVR group. Radiofrequency delivery (11±1 vs 10±3 minutes) was similar in both groups.

At the end of follow-up, 7 patients (42.10%) of MVR group were in sinus rhythm vs 29 patients (76.31%) of control group. 5 patients in the MVR group developed a left atrial flutter vs 1 patient in the control group. No complications occurred in both groups.

Conclusions: PVI is feasible after mitral valve replacement with a poor outcomes compared to patients without structural heart disease. Complications were similar in both groups.

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Left atrial remodelling and function after radiofrequency catheter ablation for atrial fibrillation: a real-time 3D echocardiography study

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Background: Radiofrequency catheter ablation (RCA) has demonstrated its effectiveness in the treatment of atrial fibrillation (AF). However, its impact on atrial remodelling and function has not been studied extensively.

Objectives: Our aim was to evaluate the effect of RCA on LA volumes and function with the use of real-time 3D echocardiography (RT3DE).

Methods and Results: 34 pts with paroxysmal (n=16) or persistent (n=18) AF were treated with RCA with 3-dimensional electroanatomic mapping/ablation system (CARTO). Left atrial (LA) volumes (maximum, pre-A and minimum) and function (reservoir, conductance and active contraction) were assessed with RT3DE before and 4.8±2.7 months after RCA. All patients underwent 24 hours ECG Holter registry at follow-up and were consequently divided into responders (sinus rhythm (SR)) or failed RCA (RAF). LA volumes and LA function are shown in the Table.

Conclusions: RCA induces a reduction in LA size, without a significant impact on LA active contraction. Patients with recurrent AF after RCA had larger LA volumes. RT3DE could be a useful imaging method to assess LA geometry and function after RCA.

		Vmax	Vmin	Vp	ActEF	VTI A	LACF
All	PRE	55.5±15.7	28.4±13.2	35.1±17.4	24.8±20.2	6.3±2.9	27.7±18.4
(N=34)	POST	48.1±15.9*	25.9±11.3	33.4±19.6	27.9±18.8	6.2±2.9	37.3±15.4*
SR	PRE	50.3±11.4	26.2±13.7	30.8±13.2	25.5±21.1	6.2±2.7	32.1±19
(N=21)	POST	45.4±10.2	23.7±7.6	29.4±8.7	26±21	6.1±2.2	37.1±16.4
RAF	PRE	64±18.5	32.1±8.1	48±23.4	22.6±19.3	6.6±3.8	20.5±15.5
(N=13)	POST	52.6±22.1*	29.6±14.8	39.9±28	17.9±11.5	5.6±2.6	37.6±14.2*

Vmax = Maximum LA volume; Vmin = Minimum LA volume; Vp = LA volume at P wave; ActEF = LA active emptying fraction; VTI A = velocity time integral A wave; LACF = left atrial conduit function. *p < 0.05.

MONDAY, 25 JUNE 2007, 10:00–11:00

Poster Area

Pacing

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AF suppression pacing does not increase the atrial effective refractory period

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Background: Atrial effective refractory period (AERP) may serve as an accurate measure of electrical remodeling of the atria and can be evaluated noninvasively using extrastimulus techniques available in modern pacemakers. The atrial fibrillation (AF) Suppression algorithm (AFS) has been demonstrated to be effective in reducing symptomatic AF burden, but the mechanism of action has not been ascertained. It was hypothesized that AFS may halt or reverse electrical remodeling by lengthening AERP in patients with paroxysmal atrial fibrillation and a symptomatic bradycardia for which pacing was indicated.

Methods: This prospective, randomized, multicenter study included a total of 29 pts (43% male, age 75±8 years, Ejection Fraction 60±10%). Patients with a history of documented paroxysmal or persistent AF were implanted with a St. Jude Medical (SIM) Identity ADx DR pacemaker. The right atrial lead was implanted at the atrial appendage for 94% of the patients. At device implantation, each patient was randomized to either AFS ON or OFF for the entire follow-up period of 6 months. During the implantation and follow-up visits, AERP was measured by using the Non-Invasive Programmed Stimulation (NIPS) feature in the pacemaker. AERP measurements were taken at S1 cycle lengths of 600 ms (AERP6) and 500 ms (AERP5).

Results: Fourteen pts were randomized to AFS ON and 15 pts to AFS OFF. In AFS ON pts, there was a 2.3% increase in AERP6 and in AFS OFF pts, there was a 4.7% increase in AERP6 (Table). AERP5 measurements decreased by 1.3% in AFS ON pts and increased by 2.8% in AFS OFF pts.

Conclusion: After 6 months of pacemaker implantation, AFS pacing does not increase the AERP. Any efficacy of the AFS algorithm may be due to factors other than lengthening of AERP, at least based on this small sample size. The apparent difference between AERP in the AFS ON and OFF groups at implant and 6 months follow-up of approximately 20 ms was not statistically significant and probably reflects the small number of patients who were studied.

Table 1

	AERP5			AERP6		
	AFS ON	AFS OFF	p-value	AFS ON	AFS OFF	p-value
Implant	275.7±46.4	252.1±35.4	0.3	270±52	254.6±37.4	0.3
6 Month	272.1±34.9	259.3±23	0.2	276.4±37.4	266.7±27.9	0.4
p-value	0.7	0.35		0.6	0.25	

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Atrial pacing dipole for termination of atrial flutter during transesophageal echocardiography

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Transesophageal atrial pacing (TAP) is an established therapy for termination of atrial flutter (AFL) after exclusion of atrial thrombus by transesophageal echocardiography (TEE).

Purpose of the study was to evaluate transesophageal atrial pacing dipole (TAPD) with a novel TEE tube electrode for termination of AFL by simultaneous TEE and directed TAP.

Method: Eleven AFL patients (age 61 ± 17 years; 8 males) with mean AFL cycle length of 207 ± 13 ms ($n=6$) and mean ventricular cycle length of 423 ± 17 ms ($n=5$) were atrial paced using a TEE tube electrode (Dr. Osypka GmbH, Rheinfelden, Germany) with fore hemispherical electrodes with 6 mm diameter on the heart side of the TEE probe. Bipolar TAP between two hemispherical electrodes was analysed with 90 mm TAPD ($n=5$) and 60 mm TAPD ($n=6$) after exclusion of atrial thrombus by TEE.

Results: AFL could be terminated by directed bipolar TAP with induction of atrial fibrillation (AF) ($n=6$), with induction of AF and spontaneous conversion to sinus rhythm (SR) ($n=4$) and with conversion to SR ($n=1$). TAP capture threshold with 60 mm TAPD was lower than TAP capture threshold with 90 mm TAPD and 10 ms stimulus duration (15 mA versus 18 ± 2.7 mA, $P=0.02$). The minimum of the TAP rate was 300/min and the maximum of the TAP rate was 1200/min. AFL cycle length was not different between 60 mm and 90 mm TAPD (213 ± 15 ms versus 200 ± 9 ms, $P=0.3$).

Conclusion: AFL can be terminated by directed rapid TAP with 60 mm TAPD of the novel TEE tube electrode with low TAP capture threshold. TAP with directed TEE tube electrode is a simple and useful method for termination of AFL. TAP during TEE allows the treatment of AFL during a necessary TEE examination without an additional study.



AFL Termination to SR by TAP during TEE

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Comparison of the haemodynamic effects of different dual-site right atrial pacing configurations in patients with recurrent atrial fibrillation

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Biatrial pacing (BiA) diminishes intra- and interatrial conduction disturbances, which may contribute to preventing atrial fibrillation (AF), however the best BiA pacing configuration with regard to the hemodynamic consequences has not been determined yet. Recently a “double resynchronization” of the atria consisting of pacing of the two most vulnerable atrial places namely the Bachmann bundle (BB) and the coronary sinus (CS) has been proposed.

The aim of the study was to compare the effects of the “classical resynchronization”: right atrial appendage and coronary sinus (RAA+CS) and the “double resynchronization”: Bachmann bundle and CS (BB+CS) pacing modality on cardiac hemodynamics. In 24 patients with paroxysmal AF and a biatrial pacemaker (12 patients with leads in RAA and CS and 12 patients with leads in BB and CS) cardiac output (CO), right (RV) and left ventricular (LV) filling, right-left atrial contraction sequence [PA(m-t)] and the difference in A wave duration [Adiff(m-p)] at the level of the mitral valve (Am) and pulmonary veins (Ap) were examined by echo-Doppler measurements. The results are reported in the table.

Conclusions: (1) Biatrial pacing configuration has no influence on CO, (2) BB+CS in comparison to RAA+CS pacing accelerates left atrial contraction, reverses of the usual right-to-left atrial contraction sequence and prolongs Ap due to an altered activation pattern, decreased pulmonary venous return, or increased LA pressure. (3) when considering the hemodynamic aspects of BiA pacing RAA+CS is superior to BB+CS.

	RAA+CS	BB+CS	p
PAm [ms]	175±12	150±13	<0.01
PA(m-t) [ms]	167±10	170±11	ns
Am [ms]	9±11	-21±9	<0.01
Ap [ms]	177±19	172±12	ns
Adiff(m-p) [ms]	136±12	149±14	ns
VTI Am [cm]	41±10	24±13	<0.1
VTI At [ms]	8.7±0.9	8.4±1.0	ns
VTI Ao [ms]	6.3±0.6	6.6±0.7	ns
	30±3	30±2	ns

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Evaluating the effect of atrial overdrive pacing after cardioversion in pacemaker patients with persistent atrial fibrillation

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Background: Electrical or chemical cardioversion is used successfully to terminate persistent atrial fibrillation (AF) and to restore patient (pts) to normal sinus rhythm. Recent clinical studies have reported that atrial overdrive pacing (AOP) algorithms may be effective in suppressing atrial ectopy and thus effective in preventing paroxysmal AF. However, the effect of combining cardioversion to restore and AOP to then maintain normal sinus rhythm in pacemaker (PM) pts with persistent AF has not been evaluated. The purpose of this study was to evaluate the effect of this combination.

Methods: This prospective, multicenter, randomized study included a total of 130 pts (59% males, 75 ± 8 yrs, EF of $50 \pm 13\%$). Pts were implanted with St. Jude Medical PMs equipped with the AF Suppression (AFS), a dynamic AOP algorithm. Of the 130 pts enrolled, 68 pts underwent cardioversion (electrical or chemical) for persistent AF and were randomized to either AFS ON ($n=28$) or AFS OFF ($n=40$). The randomized pts were followed until their first identified AF event or 6 months, whichever came first. The presence of AF was confirmed by documentation from device diagnostics and stored electrograms. The pacing base rate was set to 60 ppm or less with an atrial tachycardia detection rate of 200 ppm.

Results: In the AFS ON group, 57.1% ($n=16$) of pts had experienced an AF episode compared to 55% ($n=22$) of pts in the AFS OFF group ($p=NS$). The mean time to first identified AF episodes in the AFS ON and OFF groups was 21 and 28 days respectively ($p=NS$).

Conclusion: In this small sample, AFS did not reduce the incidence of AF within the first 6 months for pts with persistent AF receiving cardioversion. Further investigation to identify potential clinical predictors of AFS efficacy in pts with persistent AF may be warranted.

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Reduction of AF with AF Suppression pacing and antiarrhythmic drug therapy in patients with Persistent or Paroxysmal AF: Results from the RAPTOR trial

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Clinical trial data have shown that the use of overdrive pacing algorithms can suppress atrial ectopy and may be effective in reducing recurrent Atrial Fibrillation (AF). St. Jude Medical has developed an overdrive suppression algorithm, AF Suppression (AFS), which has been shown to reduce symptomatic AF burden. However, there has not been extensive investigation on the possible increased efficacy of the algorithm with concomitant antiarrhythmic (AA) drug therapy. The RAPTOR trial evaluates the benefit of AFS pacing in combination with AA drug therapy in pacemaker patients with a history of paroxysmal or persistent AF.

Methods: This prospective, double-blinded, randomized study enrolled patients with a market released dual chamber pacemaker with the AF Suppression feature. A majority of this patient cohort (79%) received ACE Inhibitors, Antiarrhythmic drugs (Class III), or Beta Blocker drug therapies (p=ns between the baseline therapies of patients). At implant, each patient was randomized to AF Suppression "ON" or "OFF" for the entire 12 month follow-up period, with data collected at 3, 6, 9, and 12 months. AF Burden from auto mode switch (AMS) diagnostic reports and the change in AA drug therapy were analyzed for each pt.

Results: A total of 71 patients (53% male, 73.7±9.6 years) were enrolled and followed through the 1-year follow-up period. 51% of the pts were randomized to AFS "OFF" (n=36). AFS "OFF" patients had an average AF Burden of 15±6%, whereas "ON" patients had an average AF Burden of 21±10% (p=ns). 50% of the AFS "OFF" patients and 49% of the AFS "ON" patients changed their drug regimen over the 12 month follow-up period (p=ns). Patients with AF Suppression "OFF" and Beta Blocker drug therapy had an average AF Burden of 18±7%, and those patients on Beta Blocker drug therapy with AF Suppression "ON" had an average AF Burden of 3±1% (p<0.001)

Conclusions: AFS does not reduce AF burden in the overall pt population with concomitant AA drug therapy. AFS does not have an effect on changing AA drug regimen. However, AFS reduces the AF Burden in pts specifically on BB drug therapy.

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Asymptomatic atrial fibrillation. The incidence in a non-selected population

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Aim: To evaluate, the incidence of asymptomatic episodes of atrial fibrillation (AF) and correlate the reported symptoms with the telemetric data supplied by the atrial arrhythmias registry.

Methods: Since March 2005, 99 patients (73±7 years, 59M, 40F) implanted with a dual chamber PM have been enrolled. The device (VITATRON, Selection 9000 or T70), is designed to store data about the atrial rhythm and equipped with algorithms for AF prevention. Patients (Pts) were followed up every three months to evaluate the AF burden, the number of episodes and the heart rate during the episodes; a symptoms diary was delivered to every patients.

The indications for pacemaker implantation were: SSS in 83 pts; AV block (BAV) in 8 pts, SSS+BAV in 3 pts, bradycardia in 2 pts, and

neuromediated syncope in 1 pt. 45 Pts had hypertensive cardiomyopathy, 8 ischaemic cardiopathy, 5 dilated cardiomyopathy, 12 valvular cardiopathy, 6 ischaemic and hypertensive cardiomyopathy, 1 ischaemic and valvular disease, 20 had no history of underlying heart disease. The antiarrhythmic drugs therapy was: amiodarone in 22 Pts; flecainide in 7 Pts; beta blockers (BB) in 16 Pts; propafenone in 8 Pts; amiodarone+BB in 2 Pts; flecainide+BB in 1 Pt, Sotalolol in 13 Pts; Sotalolol+Flecainide in 2 Pts; no antiarrhythmic drugs in 26 Pts. 50 Pts took Warfarin, 72 Pts had history of AF (68) and FIA (4).

Results: Till now 237 controls have been carried out. 60.3% of patients had at least 1 episode of AF recorded by the PM. 81.3% of the patients had asymptomatic episodes of AF. 88% of these had episodes that lasted less than 1 hour, while only 6% had episodes lasted more than 1 day. 20% perceived symptoms confirmed by the recorded episodes. 71% reported symptoms even if not having episodes of AF.

Conclusions: The analysis of the data in our possession evidences that there is low correlation between the arrhythmic episodes recorded by the pacemaker and the symptoms reported by the patients. A consisting percentage of them has asymptomatic episodes AF and others report symptoms without having recorded episodes.

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Usefulness of mode switching algorithms in detection of symptomatic and asymptomatic atrial tachyarrhythmias

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Automatic mode switching (AMS) is defined as the ability of a pacemaker to reprogram itself from tracking to non-tracking mode in response to atrial tachyarrhythmias, and to regain tracking mode as soon as the tachyarrhythmia terminates. In patients with permanent pacemakers, AMS events often are interpreted as surrogate markers for atrial tachyarrhythmias. The purpose of this study was to correlate patient-reported symptoms of atrial tachyarrhythmias and clinical features with AMS occurrence

Methods and Results: The charts of 93 (46 male) patients with SSS after dual chamber pacemakers (Affinity and Verity DR – St Jude Medical) with AMS algorithms were reviewed retrospectively. Three months period was analyzed and correlated with symptoms of paroxysmal atrial fibrillation (PAF). The mean age of study population was 72±10 years. There were sixty five pts with history of PAF, 51 symptomatic, 55% with hypertension (HT), 60% with chronic coronary heart disease (CHD), valvular heart disease 23% (VHD) and 20% with diabetes mellitus (DM). PAF and atrial tachycardia were noted by AMS if the rate was sensed above the 250 beats/min and 150/min respectively.

27 patients had PAF documented in ECG. In the same time AMS occurred in 82 pts (328.9±1185.7 times) with the total burden of AMS 4.49±11%. Symptoms related to PAF were observed in 31% of atrial tachyarrhythmia episodes identified by the pacemaker. There was significant correlation between total time of AMS occurrence and: age of pts (r=0.189, p=0.025); HT (0.247, p=0.014); VHD (0.248 p=0.014). In pts with DM there was a correlation between AMS lasting more then 24 hrs and burden of atrial pacing (r=0.228; p=0.002). Most of AMS episodes were less then 1 minute long (83%). The presence of symptoms related to PAF was correlated with the duration of AMS events (r=0.375, p=0.001) and atrial rate (r=0.332, p=0.0001). PAF detected by the pacemaker was correlated with the percentage of ventricular stimulation (p=0.009) and with the time from the pacemaker implantation (p=0.001). Long lasting PAF (>24 hours) was significantly related to the percentage of atrial (p=0.0001) and ventricular (p=0.0001) stimulation.

Conclusion: Automatic Mode switching assessment may serve as a valuable tool for research into the natural history and burden of atrial tachyarrhythmias. Among patients with sick sinus syndrome and a history of atrial fibrillation most of atrial tachyarrhythmias were clinically

silent. The occurrence of paroxysmal atrial fibrillation was significantly dependent on burden of atrial and ventricular stimulation.

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Atrial electrical remodelling in patients with drug refractory atrial fibrillation after implementation of dual-site interatrial septum pacing

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P wave prolongation on the standard ECG is considered to indicate abnormal atrial conduction, that is the presence of inter- and intra-atrial local activation delays. Decrease in P wave duration obtained with atrial pacing represents manifestation of electrical resynchronization of the atria and improvement in atrial activation time.

The aim of the study was to assess the influence of a new method of multisite atrial pacing on global atrial electrical activation in patients with drug refractory AF, sinus bradycardia indication for pacing, prolonged atrial conduction (sinus P wave ≥ 120 ms), and normal AV conduction.

Methods: All measurements were performed in lead II at a paper speed of 100 mm/s on the pacemaker electrogram obtained from the programmer. The sinus (SR) P wave duration was measured before pacemaker implantation and at the last control after atrial pacing insertion, that incorporated one lead implanted at the Bachmann's bundle (BB) region and the other lead near coronary sinus ostium (CS).

Results: A novel pacing method was successfully applied in 105 patients (34 male, 69 \pm 9 years), however 8 patients were lost during follow-up and were censored from the long-term analysis. After a mean 1.4 \pm 0.4 year follow-up 92% of patients remained in sinus rhythm and in 22% no AF recurrences were documented. Multisite atrial pacing resulted in significant reduction in P wave duration, when compared to spontaneous sinus rhythm. This was predominantly due to pre-excitation at the BB area, as pacing at this site alone produced significantly shorter P wave, in comparison to the CS ostium pacing.

Conclusions: Dual-site interatrial septum pacing results in improvement in global intra- and interatrial conduction, as was manifested by decrease in P wave duration with pacing. Shortening of the sinus P wave after > 1 year of pacing may indicate beneficial electrical reverse remodelling, corresponding to antiarrhythmic efficacy of this novel pacing modality.

Changes of the P wave duration

Variable	Baseline (N = 87)		Study end (N = 87)		Last control (N = 77)		
	Sinus rhythm (SR1)	Sinus rhythm (SR2)	Sinus rhythm (SR2)	BB pacing (BB)	CS pacing (CS)	Multisite pacing (BB+CS)	
P-wave duration [ms] \pm SD	143 \pm 15*	141 \pm 15*	141 \pm 13 \ddagger	139 \pm 18 \ddagger	144 \pm 17 \ddagger	117 \pm 13 \ddagger	

*Baseline vs study end $p < 0.01$; Last control ANOVA $p < 0.001$; post hoc: $\ddagger p < 0.0001$ BB+CS vs BB, vs CS, vs SR2; $\ddagger p < 0.01$ BB vs CS.

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Continuous ventricular pacing versus ventricular backup pacing for patients with chronic atrial fibrillation and normal left ventricular systolic function

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Aim: Both heart rate irregularity during atrial fibrillation (AF) and ventricular desynchronization imposed by ventricular pacing (VP) may compromise ventricular function. We aimed to investigate whether rhythm regularization achieved through continuous VP at the price of inducing ventricular dyssynchrony may be advantageous compared to irregular AF with intrinsic ventricular activation.

Methods: We studied 27 patients (mean age 72 \pm 7 years) with chronic AF, normal left ventricular (LV) systolic function and narrow QRS complexes, who were implanted with a common VVIR pacemaker. Cardiac function

was assessed by using serial echocardiographic conventional Doppler, tissue Doppler imaging (TDI) and color M-Mode (CMM) examinations, and B-type natriuretic peptide (BNP) measurements. Baseline echocardiographic and BNP data were obtained during AF (mean heart rate 58 \pm 5 beats/minute) with the pacemakers programmed to ventricular mere back-up pacing at a lower rate of 45 beats/min. These data were compared with corresponding measurements following a 2-week VP period after the devices had been programmed in VVIR mode with lower rate 70 beats/min, ensuring most of the time continuous VP.

Results: VP compared to AF, significantly reduced the LV cardiac index ($p < 0.05$), increased the isovolumetric relaxation time ($p < 0.01$), and decreased the TDI-derived systolic mean mitral velocity ($p < 0.05$), the diastolic right ventricular velocity ($p < 0.01$) and the CMM-derived transmitral early diastolic flow propagation velocity ($p < 0.05$). Both E/Ea and E/VP ratios indicating LV filling pressures showed a clear albeit non-significant trend toward increase ($p = NS$). The BNP levels following the 2-week VP period increased by 25.5% ($p < 0.01$).

Conclusion: It is concluded that continuous VP in patients with AF worsens the left and right ventricular function and may lead to elevations of the LV filling pressures.

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Dynamic ventricular overdrive for rate regularization during atrial fibrillation

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Purpose: Atrial fibrillation (AF) is a common comorbidity in patients (pts) with cardiac resynchronization therapy (CRT) devices and frequently leads to loss of stimulation and ventricular rate irregularity. Irregularity of ventricular contractions is often highly symptomatic and a reduced amount of pacing decreases the benefit of CRT pacing. We evaluated if a new pacing algorithm could reduce the rate irregularity at a minimal overdrive with a high amount of ventricular pacing which would be especially attractive during AF episodes in CRT pts.

Methods: We tested a dynamic ventricular overdrive (DVO) algorithm based upon the AF Suppression algorithm in pts with intact AV nodal conduction and AF undergoing an EP study. Upon the second of two intrinsic beats among the prior sixteen beats, DVO increases its pacing rate for fifteen cycles up to a programmable upper rate limit (120 bpm in this study). Then, DVO gradually decreases the rate toward the base rate. Three DVO settings (Low, Medium, and High) modulating the rate increase as a function of the intrinsic heart rate (HR) were evaluated in all pts and compared to no pacing. Pacing regimens were randomized and consecutively applied for five minutes each with a 1-minute rest period between each setting. ECG and event markers were recorded for off-line analyses.

Results: We report here on the first five pts (4 male, 66 \pm 10 y, all in chronic AF) completing the study. Sensing and pacing were performed at the RV apex via a transveous catheter. We analyzed the mean HR, the coefficient of variation of intervals (COV), the beat-by-beat difference of intervals durations, and the percentage of ventricular pacing (%Vp) for the last four minutes of each setting. Results (mean \pm SD) are reported in Table 1.

Conclusions: The DVO algorithm provided for a high %Vp and greater HR regularity compared to intrinsic conduction, while modestly increasing the HR. Further investigation is needed to determine long term effects of this novel pacing algorithm.

Table 1: DVO performance

	No pacing	Low	Medium	High
HR (bpm)	73 \pm 17	84 \pm 15*	90 \pm 14**	91 \pm 13**
COV	0.24 \pm 0.06	0.12 \pm 0.02*	0.13 \pm 0.04*	0.14 \pm 0.03*
Interval difference (ms)	236 \pm 98	72 \pm 23*	52 \pm 17**	51 \pm 10**
%Vp	0	83 \pm 3	91 \pm 3***	92 \pm 3***

* $p < 0.05$ vs. Off; ** $p < 0.05$ vs. Low and Off; *** $p < 0.05$ vs. Low.

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Long-term effects of dual-site interatrial septum pacing in patients with drug refractory atrial fibrillation

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Selection of optimal site(s) for atrial pacing in patients with recurrent AF is an unresolved issue. Interatrial septum due to its electrophysiological properties seems to be a promising area for pacing to prevent AF. The aim of the study was to assess the antiarrhythmic efficacy and safety of a new method of multisite atrial pacing in patients with drug refractory AF, sinus bradycardia, prolonged atrial conduction (sinus P wave ≥ 120 ms), and normal AV conduction.

Methods: Two atrial leads: at the Bachmann's bundle region and near coronary sinus ostium were implanted in 105 pts (34 male, 69 \pm 9 years) and DDD pacing with inter-atrial delays of 15 ms or 0 ms was established. Patients survival and stroke events were evaluated. Main outcomes were: maintenance of rhythm control, that was defined as the absence of permanent AF, and the absence of documented or symptomatic AF. A change in frequency of symptomatic AF episodes with pacing, when compared with pre-implant period, was also assessed. AF episodes were defined occasional if they occurred <1 per month, recurrent AF if it was reported from 1 episode per week to 1 episode per month and very frequent in case of AF episodes >1 per week.

Results: Eight patients were lost during follow-up and were censored from the analysis. For the remaining 97 pts follow-up ranged from 1 to 2.7 years (1.4 \pm 0.4). One patient died and 4 experienced a stroke. Eight patients developed permanent AF, after a mean of 1 \pm 0.6 years after implantation. Rhythm control efficacy was 92%, and 21 patients had no evidence of AF. The need for reoperation was 5% and at the last control 97% of patients maintained multisite atrial pacing. Antiarrhythmic drugs were administered to 96% of patients.

Conclusions: Dual-site interatrial septum pacing is safe, and in combination with antiarrhythmic drugs provides effective rhythm control and alleviation of symptoms during >1 year of follow-up in patients with abnormal atrial conduction referred for permanent pacing.

Frequency of AF episodes	Before implantation (N = 89)	Last control (N = 89)	p
Occasional AF (<1/month)	40	25	0.03
Recurrent AF (from 1 episode/week to 1/month)	36	12	0.0001
Very frequent AF episodes (>1/week)	13	5	0.08
No symptomatic arrhythmia	0	47	<0.0001

MONDAY, 25 JUNE 2007, 10:00–11:00

Poster Area

Mechanisms of atrial fibrillation

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Atrial fibrillation and inflammation markers

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Background: Atrial fibrillation (AF) is associated with atrial structural changes that may have an inflammatory basis. The failure in preventing the recurrence of AF has led to new searches in its pathogenesis. Perhaps inflammation is one of most popular mechanisms of AF. A classical marker of inflammation, C-reactive protein (CRP) and proinflammation agent Interleukin-6 were found elevated in patients with AF.

In this study we aimed to investigate the role of inflammation markers in different categories of AF.

Methods: 98 patients with AF (mean age 53.6 \pm 9.3) were enrolled in this study. AF was subdivided on paroxysmal and chronic types. Control group was consisted of 30 healthy persons. After the enrollment the echocardiography examination and 24-hour ambulatory Holter monitoring ECG were registered in each patient. Blood samples were tested on the serum level of high-sensitive C-reactive protein (hs-CRP) and plasma level of Interleukin-6 (IL-6).

Results: The obtained results have shown that the level of hs-CRP in both chronic (0.78 \pm 0.51 mg/dL) and paroxysmal (0.51 \pm 0.42 mg/dL) types of AF were significantly higher in comparison with control group (0.28 \pm 0.11 mg/dL, $p < 0.001$). The level of IL-6 in chronic type (32 \pm 21 vs 12.1 pg/ml, $p < 0.05$) and in paroxysmal type (27 \pm 25 vs 12.1 \pm 8.9 pg/ml, $p < 0.05$) was significantly higher than those in control group. Moreover there was no difference in inflammation markers between paroxysmal and chronic types of AF.

Conclusion: hs-CRP and IL-6 inflammation markers play important role in pathogenesis of AF.

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Quantification of the arrhythmic area for atrial fibrillation using high density CARTO mapping during sinus rhythm: Differences between paroxysmal and persistent atrial fibrillation

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Background: For symptomatic patients suffering from drug refractory atrial fibrillation (AF) catheter ablation represents the therapy of choice. In clinical studies it was shown that patients with persistent AF in opposition to paroxysmal AF benefit from placing additional linear lesions or ablation of regions with complex fragmented electrograms. Most likely differences in the degree of the arrhythmogenic substrate seem to be responsible for this observation. The aim of this study was to analyse and compare altered atrial myocardium in patients with persistent and paroxysmal AF. Using electroanatomical mapping (CARTOTM, Biosense/Webster) areas of reduced bipolar voltage were measured and taken as surrogate parameters for affected left atrial (LA) myocardium. Moreover the correlation between the extent of these areas and p-wave-duration as well as age was analysed.

Methods: We evaluated 25 consecutive patients undergoing catheter ablation (age 56.1 \pm 9.7 years, 19 (76%) males) with paroxysmal (n = 13) or persistent (n = 12) AF. A detailed electroanatomical reconstruction of the left atrium (LA) was created in sinus rhythm using CARTOTM. An average of >100 scanning points was allocated as equally as possible over the map. For each point catheter wall contact was confirmed by fluoroscopy and catheter stability. In a bipolar voltage map areas with a voltage ≤ 1.5 mV, ≤ 1.0 mV and ≤ 0.5 mV were measured offline using the "area measurement tool" and expressed as percentage of the total area of the electroanatomic LA reconstruction. Regression analysis was used to investigate the correlation between these values and p-wave duration as well as age.

Results: For reconstruction of the LA a mean of 104 \pm 40 points per patient was taken. The mean area of reconstruction amounted 131.5 \pm 15.8 cm². Patients with persistent AF had significant larger areas with a bipolar voltage ≤ 1.5 mV ($p = 0.015$) and ≤ 1.0 mV ($p = 0.045$). P-wave duration was longer ($p = 0.013$) and LA-diameter was bigger ($p = 0.026$) compared with patients with paroxysmal AF. The extent of the area with low bipolar voltage correlated significantly with the patients age (≤ 1.5 mV, $p = 0.009$; ≤ 1.0 mV, $p = 0.042$) and p-wave duration (≤ 1.5 mV, $p = 0.040$; ≤ 1.0 mV, $p = 0.026$).

Conclusion: Patients with paroxysmal AF show a less degree of areas with reduced voltage compared with persistent AF. The size of these areas correlates with p-wave duration and age. Our findings indicate substantial differences in the extent of the arrhythmogenic substrate of AF depending on its clinical manifestation.

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Continuous wavelet transform and fast Fourier transform analysis of arrhythmia termination pulmonary veins recordings in atrial fibrillation

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Emerging experimental evidence suggests that certain cases of AF are maintained by small reentrant sources (rotors) that result in a hierarchical distribution of frequencies throughout the atria. RF ablation of the rotor area may result in arrhythmia termination. We evaluate the sites of AF termination by performing fast Fourier transforms (FFT) and continuous wavelet transform (CWT) of pulmonary veins (PVs) electrograms recorded before RF ablation.

Methods: Electrograms of 82 PVs from 30 consecutive patients (pts) aged 54 ± 9.6 with ongoing AF (paroxysmal $n=24$ or short-lasting persistent $n=6$) were analyzed. Electrogram recordings (10 sec) at PV junctions were obtained before PV isolation. Cumulative RF time and % of ablated PV segments were assessed. PVs were divided into 2 groups depending on effect of PV isolation on arrhythmia termination: I-AF terminated, II-AF persisted. Each PV signal was assessed with FFT and CWT. 2048-point and 4096-point sliding window FFT were performed. FFT profiles were analyzed to determine the dominant frequency (DF). To detect local activity we used CWT with Morlet base wavelet. Inter wavelet interval (IVI) was calculated from maximum values of the magnitude in wavelet spectrum by peak detection algorithm. Standard deviations of 2048 FFT DFs and CWT inter wavelet intervals (IVI SD) were calculated to assess the level of frequency stability. Predictors of AF termination were determined with multivariate logistic regression.

Results: AF terminated after ablation of 13 PVs (gr. I) and persisted after ablation of 69 PVs (gr. II). There was no significant difference in FFT DF (2048-points and sliding window 4096-points), average IVI, RF time and % of ablated segments between the groups. Stability of the signal frequency was higher in gr. I (IVI SD = 29 ± 11 ms) vs. gr. II (IVI SD = 41 ± 16 ms) independent of age and left atrial size $p=0.009$.

Conclusions:

- High stability of PVs signal frequency predicts AF termination.
- CWT but not FFT analyze reveals discrete frequency changes of AF electrograms.
- CWT may be more effective than FFT in AF signal analyze considering high time and frequency resolution of this method.

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Characterization of high frequency complex fractionated electrogram maps in both atria during atrial fibrillation as a potential guide for ablation

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Introduction: Complex fractionated electrogram (CFE) mapping in the atria has been introduced as a potential guide for ablation of atrial fibrillation (AF). Systematic evaluation of CFE distributions in patients has not been previously reported. We performed global high-frequency CFE mapping in both atria during AF to characterize the distribution of high frequency.

Methods and Results: 11 AF patients (7 men, 4 women, mean age 55 ± 10 , 8 paroxysmal, 2 persistent and 1 permanent) referred for ablation therapy were included. The EnSite NavX CFE mapping tool (St. Jude Medical) was applied during stable AF (3 persistent and 8 induced). Electrograms were sampled for 8 seconds at each site with the CFE value calculated as the mean cycle length (CL) of all detected time intervals during the 8 seconds. Detection was based on $-dV/dt$ with a deflection-duration and refractory threshold of 10 and 30 ms, respectively. We defined a CFE value of < 80 ms as "high frequency". Sites were collected from the coronary sinus (CS) and the entire right (RA) and left atria (LA), including the proximal pulmonary veins (PV). The mean number

of collected sites was 8, 52 and 81, respectively. Average CFE values were 82 ± 17 , 123 ± 27 and 113 ± 32 ms, respectively. High frequency sites were observed more often in the LA appendage (LAA, 11), the mid-CS (10), the left (8) and right superior PV antrum (8), the RA appendage (RAA, 8), the left (7) and right side of the atrial septum (6) and the cavotricuspid isthmus (CTI, 6). Mean shortest CFE values are summarized in the table by site. The highest frequency was usually located in the LA or CS. High amplitude CFEs were observed in LAA, RAA and CTI.

Conclusions: Sites with high frequency CFEs are consistent with previous reports of sites measured by the dominant frequency of the Fast Fourier Transform. High frequencies observed in the superior PV antrum, CS and CTI may help explain why PV isolation can be effective and additional linear lesions at these locations may improve clinical results of AF ablation. Global CFE mapping in both atria may provide a guide for patient specific extension of the AF ablation strategy.

	LAA	Mid-CS	Left septum	Left superior PV antrum	Right superior PV antrum	Right septum	RAA	CTI
CL (ms)	69 ± 12	71 ± 14	73 ± 19	74 ± 17	75 ± 23	77 ± 20	79 ± 24	80 ± 14

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Comparison of atrial fibrillation signal properties at thoracic veins – fast Fourier transform and continuous wavelet transform analysis

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Recent studies have demonstrated spatiotemporal organization in atrial fibrillation (AF), with a highest dominant frequencies (DF) at pulmonary veins ostia (PVo). However, the other thoracic veins have also been implicated in the AF process. We evaluate the relative contributions of the thoracic veins by performing fast Fourier transforms (FFT) and continuous wavelet transform (CWT) analysis of electrograms from each vein.

Methods: 30 consecutive patients (pts) aged 54 ± 9.6 with ongoing AF (paroxysmal $n=24$ or short-lasting persistent $n=6$), scheduled for RF ablation were included. Simultaneous recordings (10 sec) at veno-atrial junction and coronary sinus (CS) were obtained before isolation. Veins with prominent electrical activity during AF were included. Each sequence (2 sec.) of digitalized signal was assessed with FFT and CWT. FFT profiles were analyzed to determine the dominant frequency (DF). To detect local activity we used CWT with Morlet base wavelet. Local activation time was calculated from maximum values of the magnitude in wavelet spectrum by peak detection algorithm. Standard deviation of CWT inter wavelet intervals (IVI SD) was calculated to assess stability of the signal frequency.

Results: Data of 95 veins (24 right superior pulmonary veins (RSPV), 15 right inferior pulmonary veins (RIPV), 26 left superior pulmonary veins (LSPV), 17 left inferior pulmonary veins (LIPV) and 13 superior caval veins (SVC)) were analyzed (DF: RSPV = 6.9 ± 2.8 Hz, LIPV = 6.5 ± 1.5 Hz, LSPV = 6.2 ± 1.2 Hz, RIPV = 5.5 ± 1.1 Hz, SVC = 4.5 ± 0.9 Hz). There was no medial DF and IVI SD difference between pulmonary veins (ANOVA $p=NS$). If SVC was included there was a statically significant difference in DF ($p=0.0001$). Lower DF was associated with SVC ($p=0.002$) independent of age, LA size, or prior history of AF. Moreover, stability of the signal frequency was significantly lower at SVC (IVI SD = 47 ± 19 ms) comparing to PVs (IVI SD = 33 ± 13 ms) $p=0.02$.

Conclusions:

- FFT and CWT analysis revealed lower dominant frequency and lower frequency stability at superior vena cava comparing to pulmonary veins.
- Superior vena cava seems to contribute less to AF maintenance, in most patients with paroxysmal or short-lasting persistent AF.

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The role of the post cardioversion time course of hs-CRP levels in clarifying the relationship between inflammation and persistence of atrial fibrillation

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Purpose: Although recent studies suggest that inflammation is involved in the pathogenesis of atrial fibrillation (AF), it remains controversial whether it is a consequence or a cause of the arrhythmia.

Methods and Results: In 52 patients with persistent, long lasting AF, high-sensitivity C-reactive protein (hs-CRP) was measured before and after electrical cardioversion (CV). All patients were successfully cardioverted to sinus rhythm (SR), although in twelve of them AF recurred. Baseline hs-CRP was higher in patients with AF recurrence compared to those who remained in SR (0.5 ± 0.18 mg/dl vs. 0.29 ± 0.13 mg/dl, respectively, $p < 0.001$). Similarly, arrhythmia recurrence was associated with greater left atrial diameters (45.4 ± 3.3 mm vs. 40.7 ± 3.1 mm, respectively, $p < 0.001$). However, logistic regression analysis showed that hs-CRP was the only independent predictor for AF recurrence ($p < 0.001$). Additionally, patients who were in SR on final evaluation had significantly lower hs-CRP levels than at baseline (0.10 ± 0.06 mg/dl vs. 0.29 ± 0.13 mg/dl, respectively, $p < 0.001$), while those who experienced AF recurrence had similar values on final and on initial evaluation (0.56 ± 0.24 mg/dl vs. 0.50 ± 0.18 mg/dl, respectively, $p = 0.42$).

Conclusion: High levels of hs-CRP are associated with an increased risk of AF recurrence after CV. The restoration and maintenance of SR results in a gradual decrease of hs-CRP levels while AF recurrence has an opposite effect, suggesting that inflammation is a consequence, rather than a cause, of AF.

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The effect of beta-adrenergic stimulation and blockade on the spatio-temporal dispersion of atrial repolarization and atrial fibrillation

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Background: Recent studies demonstrated that there are growing evidences showing a linkage between the alternans of atrial repolarization and susceptibility to initiation or maintenance of atrial fibrillation (AF). Moreover, many studies shows vagal tone play an important role of AF. Although beta-blocking agents are common drug for the treatment of AF, it remains unclear whether the sympathetic tone to the atrium is associated with heterogeneity of atrial repolarization and vulnerability of AF. The aim of this study was to investigate the relationship between the spatio-temporal variability of the atrial repolarization and vulnerability of AF under beta-adrenergic stimulation and blocking condition.

Methods and Results: Nineteen patients with atrial tachycardia and without structural heart disease were included in this study. Monophasic action potentials (MAPs) were recorded simultaneously from two separate sites in the right atrial appendage during progressively shorter pacing cycle length (PCL) until AF was induced or loss of 1:1 captures. We repeated this study during isoproterenol infusion (ISP) and then propranolol administrated (Prop), respectively. Four patients were excluded as the results of the frequent ectopic beats during ISP. AF was induced after discordant alternans (DA) was developed. All patients developed discordant alternans under control condition and after Prop. Only 2 patients did not developed DA during ISP, and they did not induced AF. The longest PCL of occurrence of DA was 293 ± 23 ms in control, decrease to 245 ± 92 ms during ISP ($p < 0.01$ vs control), and then increase to 315 ± 31 ms after Prop ($p < 0.05$ vs control, $p < 0.001$ vs ISP). AF was induced 11 patients in control, 8 patients during ISP, and 14 patients after PP by rapid atrial pacing. The incidence of pacing induced AF was significantly ($p = 0.04$) higher after propranolol administration than during ISP infusion. The pacing cycle length of the AF induction was 194 ± 19 ms in control, and then decreased to 169 ± 12 ms during ISP, increased to 201 ± 30 ms after

Prop ($p < 0.01$, vs. control). AF was sustained in 2 patients after Prop. The duration of AF was significant longer after Prop (median 20 sec) than control (median 3.4 sec) and during ISP (median 1.9 sec).

Conclusion: Spatio-temporal alternans developed at closed site in the right atrial and AF was induced only after DA. Although beta-adrenergic stimulation increased the incidence of ectopic atrial beats, it decreased the threshold of occurrence of DA and attenuated the vulnerability of AF. While, beta-adrenergic blocking had reverse effects of it.

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Pulmonary vein potential conduction delay during segmental isolation procedures for atrial fibrillation relates to vein anatomy, age and focal activity

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Arrhythmogenic activities in the pulmonary veins (PV) play an important role in triggering and perpetuating atrial fibrillation (AF). PV isolation (PVI) is widely used for treatment of AF. Conduction delay (CD) and amplitude of PV potentials can vary before disappearance during ablation.

Methods and Results: We studied 385 consecutive AF patients (74 female, mean age 54 ± 11) who underwent segmental PVI. A 10-pole Lasso catheter was employed to record electrograms at the PV ostia. The PV potentials were recorded during distal coronary sinus pacing for the left PVs and during sinus rhythm for the right PVs. The time delay from local atrial signal to PV potential was monitored in each PV. CD was defined as the maximum time delay greater than 20 ms during the PVI procedure. The results of CD are shown in the table. Compared to PVs without CD, more ablation applications (12.4 ± 8.2 vs. 9.9 ± 6.3 , $P < 0.01$) and higher ablated segmental fraction of PVs ($72.3 \pm 22.9\%$ vs. $63.7 \pm 25.4\%$, $P < 0.01$) were performed in PVs with CD during the first PVI. In addition, we observed CD in 75.2% (109/145) of the PVs where focal activity was identified. Older patients tended to have a higher incidence of PVs with CD than younger patients. There were no significant differences between genders.

Conclusions: The left common and the superior PVs which are usually larger in diameter have a higher incidence of CD during the first PVI. In addition, CD was more frequently observed in older patients and in the PVs with focal activities. The PVs with CD demand more applications and larger area of ablation around the ostia. These features were not found during repeat procedures.

PVs	First procedure			Repeat procedure		
	Subtotal	Number (%) with CD	Mean CD (ms)	Subtotal	Number (%) with CD	Mean CD (ms)
Left common	38	32 (84.2)	51.3 ± 37.5	6	5 (83.3)	43.7 ± 33.3
Left superior	225	149 (66.2)*	38.8 ± 31.1	36	17 (47.2)	24.9 ± 27.2
Left inferior	219	119 (54.3)*§	30.0 ± 29.6	29	12 (41.4)	25.3 ± 33.3
Right superior	280	190 (67.9)	38.4 ± 34.7	37	17 (45.9)	30.6 ± 30.5
Right inferior	272	109 (40.0)‡	22.6 ± 25.7	46	19 (41.3)	24.7 ± 26.3
Right middle	26	8 (30.8)‡	21.5 ± 30.8	3	0 (0.0)	13.0 ± 4.6
Total	1060	607 (57.3)	33.1 ± 32.1	157	70 (44.6)	26.7 ± 28.9

* $P < 0.01$ compared to left common PV. § $P < 0.05$ compared to left superior. ‡ $P < 0.01$ compared to right superior PV.

MONDAY, 25 JUNE 2007, 10:00–11:00

Poster Area

Antiarrhythmic drugs

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The very early effects of propafenone and amiodarone on atrial vulnerability for atrial fibrillationP. Kyriakou¹, G. Sakantamis¹, A. Hatziyianni¹, J. Kanonidis¹, P. Kotridis¹, C. Papadopoulos¹¹Aristotelion University, Cardiology, Thessaloniki, Greece

Background: Atrial fibrillation (AF) is the most frequent SVT, and the treatment of it, is addressed to both targets cardioversion and maintenance of sinus rhythm (SR). The onset of AF has been related to the existence of atrial premature beats. Propafenone and Amiodarone have been successfully used for both targets of AF therapy, with amiodarone been superior for the maintenance of SR and propafenone superior for rapid cardioversion. The purpose of this study was to define the effects on the electrophysiological background related to atrial vulnerability for AF, of these two clinically effective pharmaceutical agents.

Methods: In 25 patients with a history of lone AF while they were in sinus rhythm, an electrophysiological study (EPS) was performed before and after the intravenous administration of propafenone [(group A: n=15 patients: effusion: 2 mg/kg in 3–5 min) or amiodarone (group B: n=10 patients: effusion: 5 mg/kg in 20 min)]. The Interatrial conduction time (ICT_{AFRP}) of the last conducted in the atrial premature beat and the atrial functional refractory period (AFRP) were estimated, during basic rate and pacing rates of 100, 120, 140 b/min.

Results: In group A the AFRP was prolonged at all heart rates but significantly and more profound at the rate of 120 b/min ($p < 0.05$), whereas the ICT_{AFRP} was depressed strongly at all pacing rates especially the higher ones. In group B amiodarone resulted to prolonged AFRP during intrinsic rhythm and pacing rates of 100, 120 b/min, not for the rate of 140 b/min whereas it did not affect the ICT_{AFRP} at all. In both groups AF was not inducible after both antiarrhythmic administrations even in patient with inducible AF before the administration.

Conclusion: The alterations of ICT and atrial FRP in combination, suggest that both anti-arrhythmic agents partially suppress the vulnerability for AF via different electrophysiological ways taking into account that both suppressed the inducibility of AF.

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Are atrial fibrillation recurrences after sinus rhythm restoration in patients on antiarrhythmics plus angiotensin II ATI receptor antagonists predictable by brain natriuretic peptide (BNP) levelsE. Simeonidou¹, G. Tsigas¹, H. Sichelimiris¹, A. Arseniou¹, D. Damelou¹, D. Papandreou¹, D. Alexopoulos¹¹Patras University Hospital, Cardiology Dept, Patras, Greece

Purpose: It has been known recently that brain natriuretic peptide levels (BNP) increase in atrial fibrillation (AF) regardless of heart failure coexistence and decrease after sinus rhythm restoration. It appears AF triggers activation of the renin-angiotensin system, which plays important role in atrial remodeling. Blockade of the above system seems reducing AF recurrences.

Aim of the study was the assessment of BNP levels as prognostic index of AF recurrences after restoration of chronic and paroxysmal AF in patients (pts), who apart from antiarrhythmic medication receive angiotensin II ATI receptor antagonist (AIIRA).

Methods: Ninety pts with preserved LV systolic function were enrolled. Forty (29 ♂ and 11 ♀), mean age 68±11 years, who were admitted for persistent AF selective cardioversion, (1st group) and 50 with paroxysmal AF, duration <48 hours, (34 ♂ and 16 ♀), mean age 50±8 years (2nd group). Plasma brain natriuretic peptide (BNP) was evaluated before and 24 hours after sinus rhythm restoration, after 3 months and in any case of AF recurrence and compared with the development or not of AF. Plasma concentration of BNP was measured by Triage BNP test (5–1300 pg/ml). All the pts apart from antiarrhythmic therapy received irbesartan in dosage

determined by their blood pressure. All the patients underwent basic cardiac echo assessment before and after the cardioversion.

Results: Measurements were expressed as mean±SD. In the 1st group LV ejection fraction before sinus rhythm (SR) restoration and left atrium (LA) dimensions were 50±8% and 43±3.5 mm while in the 2nd group 55±7% and 40±3.5 mm respectively. In 1st group BNP levels before were 188±120 pg/ml and BNP 24 hours post SR restoration were 122±85 pg/ml ($p = 0.002$) while in the 2nd group BNP levels before 170±138 pg/ml and BNP levels 24 hours post restoration 116±100 pg/ml ($p = 0.002$). There were 10 recurrences in the 1st group and 6 recurrences in the 2nd group. We found positive association between highest BNP levels (>100 pg/ml) which maintained 24 hours post SR restoration and AF recurrences during 3 months of follow-up ($r = 1.003$, 95% CI 1.001–1.006, $p = 0.02$). There was positive association between LA dimensions and BNP levels before SR restoration in the 1st group ($r = 0.2$, $p = 0.04$).

Conclusions: Failure of BNP levels to get normalized 24 hours after sinus rhythm restoration in pts with chronic or paroxysmal AF, who apart from antiarrhythmic drugs are treated with irbesartan, is an independent prognostic marker of AF recurrences until 3 months post cardioversion.

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Prevention of arrhythmia recurrences by nonconventional antiarrhythmics after the first episode of paroxysmal atrial fibrillationG.-A. Dan¹, A. Dan¹, A. Buzea¹, I. Dahan¹, C. Adam¹¹Colentina University Hospital, Cardiology, Bucharest, Romania

Targeting the substrate and the electrophysiological vulnerable parameters seems to be equally important for the atrial fibrillation (AF) recurrences prevention. Nonconventional antiarrhythmic drugs are especially suitable for patients (pts) with AF because of the physiological mechanism of action and the lack of proarrhythmic properties.

The aim of our study was to assess the rhythm control efficacy of 3 nonconventional antiarrhythmic regimens in pts with paroxysmal AF.

139 pts (mean age 54±13 yrs) with normal left ventricular systolic function, no ischemic heart disease and first symptomatic episode of paroxysmal AF were randomly assigned to one of three regimens in an open prospective fashion: 46 pts on omega-3 polyunsaturated fatty acids esters (PUFAe – 1 g/day), 49 pts on irbesartan (150 mg/day) and 44 pts on atorvastatin (80 mg/day). 31 matched pts with paroxysmal AF were recruited as a control group. The basal characteristics (age, sex, atrial size) of the four groups were comparable and the mean follow-up period was 27±13 mo. During the follow-up period the ECG, 24 h Holter monitoring, laboratory evaluation and quality of life questionnaire were scheduled for all pts in a pre-specified algorithm. No antiarrhythmic drug was permitted during the study period, but the heart rate was controlled in the case of an AF paroxysm with beta-blockers, digoxin or diltiazem. The primary end-point was the freedom of symptomatic AF recurrences. After the follow-up period the event-free Kaplan–Meier curve showed no significant differences for patients treated with PUFA or statin compared to control group (log rank 2.74, $p = 0.10$). Treatment with irbesartan was associated with a 13 percent risk reduction ($p < 0.05$). For all the cohort, a multivariate model controlling for different variables demonstrated that age and hypertension are positive predictors for recurrences (OR: 1.2 and 1.3 respectively, $p < 0.05$) and the use of irbesartan is inversely correlated to AF recurrences (OR: 0.85, $p < 0.05$).

Conclusions: In patients with paroxysmal AF treatment with irbesartan but not with PUFAe or atorvastatin is protective against AF relapse. This antiarrhythmic protective capacity of the angiotensin receptor – blockers could point at the mechanism of AF relapse in paroxysmal AF.

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Atrial excitation patterns of refractory to propafenone paroxysmal atrial fibrillationG. Dakos¹, V. Vasilikos¹, I. Chouvarda¹, H. Karvounis¹, N. Maglaveras¹, S. Mochlas¹, G. Parharidis¹¹Aristotle University of Thessaloniki, 1st Cardiology Dept, Thessaloniki, Greece

The aim of this study was to associate the effects of propafenone on the atrial excitation patterns of a multiple recurrent paroxysmal atrial fibrillation (PAF), with P wave wavelet analysis.

Methods: Thirty-three PAF patients (20 males, mean age 60±11 years) were divided into 2 Groups, after received propafenone and followed for 2.3±0.4 years. Nine patients (5 males, mean age 61±7years) with multiple AF recurrences (>5/year) consisted Group A, while twenty-four patients (15 males, mean age 60±12 years) with less than 2 recurrences/year consisted Group B. Two consecutive recordings were obtained, before and 37±6 days after propafenone administration, during sinus rhythm with a 3-channel digital recorder (Galix Biomedical Instrumentation, Inc., USA) for 10 minutes and digitized with a 16-bit accuracy at a sampling rate of 1000 Hz. The P wave was analyzed using the Morlet wavelet and wavelet parameters expressing the mean and max energy of P wave were calculated in the three orthogonal leads (X, Y, Z) and in the vector magnitude (VM), in three frequency bands (1st: 200–160 Hz, 2nd: 150–100 Hz and 3rd: 90–50 Hz). The P wave duration was also measured in these axes and in the VM. Paired-samples T-test was used for comparing continuous variables.

Results: Group A patients had, after propafenone administration, higher mean and max energy values in the 2nd and 3rd frequency bands at Z axis. In contrast, Group B patients had smaller P wave duration at X axis along with higher max energy values in the 1st and 3rd frequency bands at X axis and mean and max energy values in all frequency bands at Y axis, after propafenone administration.

Conclusion: The multiple recurrent PAF refractory to propafenone associated with specific effects on atrial excitation patterns, along the Z axis, that can be revealed with P wave wavelet analysis.

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A comparison of the occurrence of Atrial Tachyarrhythmias in Dual Chamber Pacemaker Patients with and without Statin medication:**Analysis of ATOS-Trial data**B. Huegl¹, T. Karow¹, F. Kandari¹, Z. Findeisen¹, J.C. Geller¹, F. Biedermann¹, S. Sack¹, A. Cuijpers¹¹Weimar, Germany; ²Luedenscheid, Germany; ³Kuwait, Kuwait;⁴Bad Berka, Germany; ⁵Duesseldorf, Germany; ⁶Essen, Germany;⁷Maastricht, Netherlands

Background: In a dual chamber (DC) pacemaker (PM) population little is known about the incidence of new atrial tachyarrhythmias (AT). The ATOS study evaluated the incidence of new-onset AT in patients (pts) implanted with a DC-PM with extended AT diagnostics. In this retrospective sub-analysis the occurrence of AT episodes was compared for pts with or without statin medication.

Methods: 395 pts without a history of AT and a Class I (AHA/ACC) indication for DC-PM were enrolled in this prospective trial. All stored AT-episodes with intra-cardiac electrograms were analyzed and classified by the investigators. Long-term detailed AT information was stored in the daily log ("Cardiac Compass").

Results: Data from 387 patients (age: 70±10 years, males: 59%, NYHA I: 55%, NYHA II: 40%, EF: 58±12%, CAD: 33%) were collected over a follow-up period of 666±187 days. A total of 167 pts showed AT episodes lasting >1minute during this follow-up period. Sixteen percent (n=26) of these pts were treated with statins. Median duration of episodes (12.9 vs 4.5 minutes), median number of episodes per patient (7 vs. 12 episodes) median time between episodes (4.8 vs 3.0 hours), were calculated for the statin pts and non-statin pts respectively. The incidences of AT episodes for both pt groups were represented by Kaplan Meier graphs. The risk of developing AT/AF for statin users is significantly lower than for non-statin users (Odds Ratio: 0.53; 95% CI: 0.30–0.91).

Conclusion: DC-PM pts who are taking statin medication without any prior history of AT, have a lower risk of AT/AF, tend to have fewer AT episodes but of a longer duration. Further analysis on potential confounding variables will be necessary.

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Effects of intravenous administration of propafenone on the atrial vulnerability to atrial fibrillation (AF)P. Kyriakou¹, G. Sakantamis¹, A. Hatziyianni¹, J. Kanonidis¹, C. Papadopoulos¹¹Hippokraton General Hospital, Thessaloniki, Greece

Introduction: Atrial fibrillation (AF) is the most frequent SVT, and the treatment of it is addressed to both targets cardioversion and maintenance of sinus rhythm. Propafenone has been used for both, successfully mainly for rapid cardioversion. The purpose of the study was to define the effects of propafenone on the atrial electrophysiological properties that characterize the vulnerability of the atrial to AF.

Methods: Electrophysiological study was performed in 15 patients before and after intravenous administration of propafenone at 2 mg/kg. The Interatrial conduction time (ICT_{AFRP}) of the last conducted in the atrial premature beat and the atrial functional refractory period (AFRP) were estimated.

Results: AFRP was prolonged at all heart rates but this was significant and more profound at the rate of 120b/min, whereas the ICT_{LAP} was depressed but strongly at higher pacing rates. At basic rate the mean alterations of ICT_{AFRP} was 36.25±65.92 (p=0.083), mean alteration of AFRP was 44.17±77.04 (p=0.073). For the pacing rate with a cycle length of 600 ms mean alteration of ICT_{AFRP} was 35±58.35 (p=0.051) and of AFRP was 39.23±78.26 (p=0.096). For the pacing rate with a cycle length of 500 ms mean alteration of ICT_{AFRP} was 19.62±29.12 (p=0.032) and of AFRP was 20.77±30.4 (p=0.03). For the pacing rate with a cycle length of 430 ms mean alteration of ICT_{AFRP} was 41.82±37.57 (p=0.004) and of AFRP was 16.82±35.66 (p=0.149). Sustained or not sustained AF was induced before but not post propafenone administration to all patients.

Conclusion: The alterations of ICT and atrial AFRP in combination suggest that propafenone partially suppress the vulnerability for Atrial Fibrillation.

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Safety of oral propafenone for conversion of acute – onset atrial fibrillation – Dubai experienceG. Radaideh¹¹Rashid Hospital, Cardiology, Dubai, United Arab Emirates

Aims: To evaluate the effectiveness and safety of an oral loading dose of propafenone in the conversion of acute onset atrial fibrillation in Arab and Asian patients with or without underlying heart disease.

Setting: Coronary care unit at Rashid Hospital, Dubai, UAE. Patients: 162 patients with acute onset atrial fibrillation.

Intervention: Single oral dose of propafenone (600 mg).

Measurements: Conversion rate at 1, 3 and 8 hours.

Results: Oral propafenone was associated with 26% conversion rate within 3 hours and 66% within 8 hours. The best response was seen in patients with "lone" AF, however the response in those with hypertension and underlying heart disease was also satisfactory. There were no serious side effects.

Conclusion: A single oral dose of propafenone allows quick conversion to sinus rhythm in the majority of patients with acute onset AF. Its efficacy is unaffected by the cardiac status. The safety profile is excellent in the absence of heart failure.

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Influence of n-3 fatty acids intake on secondary prevention after cardioversion of persistent atrial fibrillation to sinus rhythm

P. Margos¹, D. Leftheriotis¹, G. Katsouras¹, E.G. Livanis¹,
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Background: Early and late recurrences of atrial fibrillation (AF) after conversion to sinus rhythm (SR) remain a clinical problem. The aim of our study was to evaluate the effect of n-3 fatty acids on recurrence of AF after successful biphasic waveform cardioversion of persistent AF to SR, in patients that rhythm control is the goal for the management of this common type of arrhythmia.

Methods: Forty patients (pts) underwent cardioversion for persistent AF (PAF) to SR. Pts were randomized to receive n-2 fatty acids (group A = 20 pts, 17 males, aged 54±45 years) and the rest served as controls (group B = 20 pts, 11 males, 57±16 years). All pts were euthyroid and under optimal anticoagulation therapy. Evaluation prior to cardioversion included, among other examinations, transesophageal echocardiography and CRP measurement. Pts with left ventricular ejection fraction (LVEF) ≤40%, left atrial diameter (LA) >55 mm or at least moderate valvular heart disease in echocardiographic examination, were excluded. Follow-up at months 1, 3 and 6 included electrocardiogram and recording of any documented new episode of AF since cardioversion. Twenty-four hour rhythm recording (Holter monitoring) was performed at month one.

Results: Basic characteristics were similar between group A and B: Duration of PAF: 3.8±2.1 months vs 3.8±1.7 months, history of cardioversion for PAF in the past: 5/20 pts (25%) vs 4/20 pts (20%), LVEF: 55.9±5.8% vs 58.6±4.8%, LA: 45.4±5.3 mm vs 44.3±4.6 mm, use of group I or III antiarrhythmic drugs (mainly amiodarone): 11/20 pts (55%) vs 12/20 pts (60%), heart rate before/after cardioversion: 69±9 bpm/60±9 bpm vs 74±13 bpm /66±9 bpm, CRP: 1.9±2.2 mg/dl vs 2.1±2.1 mg/dl. Seven recurred (35%) of persistent AF in group A vs 8 (40%) in group B (p=NS). Onset of new AF episodes after cardioversion was detected in 4.6±7 weeks (median 1 week) in group A vs 12.8±9.4 weeks (median 8 week) in group B (p=0.08). Runs of paroxysmal AF and premature atrial beats (PACs) in Holter monitoring were more common in group B [group A: runs of AF in 2/20 pts (10%) and 170±212 (median 62) PACs/24 hour, group B: runs of AF in 7/20 pts (35%) and 380±202 (median 267) PACs/24 hour, p=0.04 and p<0.01, respectively].

Conclusions: N-3 fatty acids intake did not reduce the incidence of AF recurrence after cardioversion of persistent AF to sinus rhythm when added to the conventional drug therapy, compared to control group. Pts under n-3 fatty acids showed a trend towards earlier recurrence of AF and less atrial arrhythmias (PACs and runs of AF) in one month Holter monitoring.

Monday, 25 June 2007

Oral Sessions

MONDAY, 25 JUNE 2007, 11:00–12:30

Guimaraes

Extension of indications for cardiac resynchronisation therapy

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Totally epicardial cardiac resynchronization therapy system implantation in patients with heart failure undergoing coronary artery bypass graftingJ. Bis¹, K. Goscinska-Bis¹, M. Krejca¹, P. Szmagala¹, R. Ulczok¹, A. Bochenek¹, W. Kargul¹¹Ist Department of Cardiac Surgery, Katowice, Poland

Background: Systolic asynchrony as an indication for cardiac resynchronization therapy (CRT) is present in a considerable subset of patients with congestive heart failure undergoing surgical coronary revascularization. Coronary artery bypass grafting (CABG) procedure offers an optimal setting for totally epicardial CRT system implantation. We sought to determine whether the implantation of epicardial CRT system concomitant with surgical coronary revascularization is associated with additional benefit in this group of patients.

Methods: Patients with New York Heart Association (NYHA) class III heart failure resulting from ischemic cardiomyopathy (left ventricular ejection fraction, LVEF \leq 35%) and systolic asynchrony (inter- and/or intraventricular), receiving optimal pharmacological treatment underwent a combined procedure of coronary artery bypass grafting (CABG) concomitant with totally epicardial CRT system implantation. The single-blind, randomized, controlled crossover study assessed the efficacy of treatment during two periods: the three-month period of inactive pacing and a three month period of active (atrioventricular) pacing. At the end of these periods several clinical (6-minutes walk test, quality of life) and echographic parameters (LVEF, LVEDD, mitral regurgitation, asynchrony) were analyzed.

Results: A total of 19 patients were enrolled in the study. Postoperative period was uncomplicated in 18 cases. All these 18 patients completed both phases of follow-up with excellent pacing and sensing parameters. In the group of active biventricular pacing the mean distance walked in 6 minutes was 12% greater, the quality of life according to the MLwHF questionnaire increased by 15% and LVEF by 10% when compared to inactive pacing group. None of the patients was worsened, 15 pts (83%) clinically improved during active pacing and 3 pts (17%) did not report any difference between inactive and active pacing phase. 16 pts (89%) preferred to be programmed to biventricular pacing after the randomized crossover period.

Conclusion: Cardiac resynchronization therapy can be regarded as an important supplement to surgical revascularization in the growing population of patients with severe heart failure and systolic dyssynchrony, for optimization of treatment results.

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Evaluation of mechanical dyssynchrony in patients with end stage heart failure and right bundle branch blockA. Bagherzadeh¹, M. Haghjoo¹, M. Moshkani Farahani¹

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Objectives: Cardiac resynchronization therapy (CRT) has emerged as an established therapy for congestive heart failure due to severe left

ventricular systolic dysfunction. Clinical trials of CRT have not included many patients with right bundle branch block (RBBB). Focusing these issues is important in identification of patients most likely to respond to CRT. This study aimed at defining the prevalence of interventricular and intraventricular dyssynchrony in heart failure patients with RBBB.

Methods: A total of 174 consecutive patients (90 patients with left bundle branch block (LBBB) and 84 ones with RBBB) with severe heart failure were prospectively included. Different parameters of inter and intraventricular dyssynchrony was measured by tissue Doppler echocardiography and was compared between two groups.

Results: Baseline demographic characteristics were not different between two groups (mean age 55.1 \pm 13.2 vs 58.3 \pm 11.9 years; male gender 86% vs 89%; Ischemic heart disease 72% vs 75%; QRS width 138.7 vs 131.4 ms; ejection fraction 32% vs 30%; All P=NS). All the parameters of intraventricular dyssynchrony were significantly higher in patients with LBBB compared with those with RBBB (Total asynchrony index 67% vs 48%; P=0.004, Septal posterior wall motion delay (SPWMD) 57% vs 41%; P=0.051, Septal lateral wall motion (SLWMD) delay 70% vs 49%; P=0.032). Interventricular mechanical dyssynchrony did not seem to have any significant difference between two groups (55% vs 50%; P=0.18). The patients with bifascicular block had significantly higher SPWMD and SLWMD compared with those with isolated RBBB (P=0.023 and 0.02 respectively).

Conclusion: The majority of heart failure patients with RBBB do not have any significant mechanical dyssynchrony in tissue Doppler echocardiography and have significantly lower incidence of dyssynchrony in comparison with heart failure patients with LBBB and bifascicular block. This study does not support the use of CRT in RBBB patients unless tissue Doppler study demonstrates significant mechanical dyssynchrony.

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Upgrading existing ICDs to biventricular technology versus de-novo CRT implantation: Prospective comparison of procedural outcomes and response ratesG.Z. Duray¹, C.W. Israel¹, F.T. Wegener¹, D. Pajitnev¹, J.R. Ehrlich¹, S.H. Hohnloser¹¹J.W. Goethe University, Div. of Clinical Electrophysiology, Frankfurt, Germany

Purpose: Cardiac resynchronization therapy (CRT) with implantable defibrillators is widely applied to patients with congestive heart failure. It has been argued that upgrading existing single- or dual-chamber ICDs or pacemakers (PM) to CRT-ICD technology may be more difficult and associated with more procedural complications than de-novo CRT implantation. The aim of this prospective observational study was to assess implant success, complications and short-term outcome of CRT therapy in pts with pre-existing ICDs or de-novo CRT therapy.

Methods: Consecutive pts undergoing de novo CRT implantation or upgrading of a pre-existing ICD/PM between 1/2005 and 10/2006 were enrolled in the study. We analysed the implantation success rate, procedural outcomes and response rates.

Results: There were 76 pts (64 \pm 11 ys, 61 male, 37 ischemic cardiomyopathy, 39 non-ischemic cardiomyopathy) undergoing CRT implantation (59 de novo CRT and 17 upgrade to CRT). In two cases of CRT-upgrade the procedure was challenged by occlusion of the vena subclavia with the need of recanalisation. Two (33%) of the 6 pts where the CRT implantation was unsuccessful died in the following 6 months compared to 4/70 pts (6%) with successful CRT implantations (p=0.068).

Conclusions: Upgrading a pre-existing non-CRT ICD or PM to a CRT ICD is similarly successful as de novo CRT implantation, with slightly higher procedural efforts. The clinical response rate after a CRT upgrade is similar to that of de novo CRT implantation. Accordingly, upgrading

pre-existing ICD/PM systems to CRT should be attempted in all pts meeting current CRT indications.

Procedural outcomes and response to CRT

	De-novo CRT	Upgrade CRT	p-value
Implant success	55/59 (93%)	15/17 (88%)	0.61
Procedure time (min)	153±44	172±60	0.16
Total X-ray time (min)	25±18	35±22	0.10
Total X-ray dose (Gy cm ²)	43±35	53±51	0.46
Response to CRT	64%	73%	0.59

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CRT for narrow QRS patients: final results of the DESIRE study

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The aim of the Desire study was to identify potential responders to chronic biventricular stimulation in a "narrow" QRS population presently not specifically studied, and to evaluate the respective merits of ECG and Echo. This prospective controlled longitudinal trial gathered heart failure patients (CHF pts) at the only condition that their QRS width was <150 ms. All patients were implanted and classified in a dyssynchronized (D) or non D group on the basis of an immediate pre-implant echocardiography focusing on simple basic D parameters. Response to therapy was assessed at 6 months using a clinical composite criterion (CCC) including successively mortality, hospitalization and functional assessment. ECG value.

64 CHF pts, in NYHA Class III or IV, 54 Males, mean age 64.2±12.5 years, EF = 27±8% and end-diastolic diameter 69±9 mm, 27 of ischemic origin, mean QRS = 121±19 ms and axis = 2±59° under optimized medical treatment were included and 60 could be implanted with a Talent MSP CRT device. Basic echocardiographic D parameters were: Left Ventricular Filling Time (LVFT%) reported to cardiac cycle <40%, Interventricular Delay (IVD) >40 ms, or temporal intraventricular D assessed by prolongation of Left Preejection Period (LPEP) >140 ms and/or Diastolic left lateral wall Contraction after closure of aortic valve (DC) persisting 50 ms after onset of next cardiac cycle filling phase (Overlap).

Results: 27 pts were classified as D and 33 as non D (echo data presented in Table 1). 33 pts improved according CCC. Pre and post-operative ECG had no value for predicting positive response. D patients improved more than non D (p < 0.04).

Conclusions: (1) 55% of implanted narrow QRS patients took advantage from CRT implantation and ECG was useless for selecting responders, (2) Presence of at least one basic D parameter at baseline echo was predictive of more favourable outcome. (3) Standard Echo D parameters should be considered before implantation in narrow QRS pts candidates for CRT

Table 1

Baseline echo	LVFT%	LPEP	IVD	DC	Overlap	Responders
D (27)	44±11	151±23	33±24	108±93	-50±58	70%
Non D (33)	50±7*	123±14 [‡]	13±13 [†]	27±45*	-80±112	40%*

*p < 0.05; [†]p < 0.01; [‡]p < 0.001

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Presence of ventricular dyssynchrony and haemodynamic impact of right ventricular pacing in adults with tetralogy of fallot and right bundle branch block

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Introduction: Late after surgical repair, adults with Tetralogy of Fallot (TOF) are used to present with right ventricular (RV) dysfunction and right bundle branch block (RBBB). The aims of the present study were (1) to investigate whether this prolonged right ventricular conduction induced detrimental electromechanical right and left ventricular dyssynchrony; (2) to determine the acute hemodynamic effects of atrio-synchronized RV pacing at different pacing sites.

Methods: (1) We performed an echocardiography, coupled with tissue Doppler (TDI) and Strain rate (SRI) imaging, in 20 adults (mean age 24±6 years) with TOF, sinus rhythm and RBBB. The interventricular dyssynchrony (IVD), the intra-RV dyssynchrony (IRVD), the intra-left ventricular dyssynchrony (ILVD) and the extent of RV myocardium displaying delayed longitudinal contraction (DLC) were assessed and compared with measurements of 30 healthy matched patients. (2) We performed an acute hemodynamic study in 6 patients (mean age 26±3 years) with TOF, RV dysfunction, class NYHA 3 or 4 and RBBB. Cardiac output was measured during spontaneous ventricular rhythm and during atrio-synchronized ventricular pacing at 4 RV sites (infundibulum, apex, septal and lateral walls).

Results: (1) We observed higher IVD (45±21 vs 18±10 ms; p < 0.01), IRVD (41±19 vs 13±06 ms; p < 0.01), intra-RV DLC (31±14 vs 05±01%; p < 0.01) and a trend to a higher ILVD (29±07 vs 18±10 ms; p = 0.06) in TOF patients than in controls. (2) Atrio-synchronized ventricular pacing improved significantly (p < 0.05) the cardiac output as compared with the spontaneous rhythm. The lateral wall was the optimal pacing site in 83%.

Conclusion: TOF adults with RBBB and RV dysfunction exhibit major electromechanical dyssynchrony. In symptomatic patients, atrio-synchronized ventricular pacing improves hemodynamic performance. The lateral wall may be the optimal pacing site. RV resynchronization is a promising novel therapy for patients with RV failure.

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Cardiac mortality in New York Heart Association functional class IV patients treated with Cardiac Resynchronization Therapy

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Background: Although the beneficial role of cardiac resynchronization therapy (CRT) in selected patients with heart failure is well proven, its effect on cardiovascular mortality in New York Heart Associations (NYHA) functional class IV patients is unclear. The present study evaluated cardiovascular mortality in NYHA functional class IV patients treated with CRT as compared to patients on pharmacological treatment.

Methods and Results: A series of 40 consecutive patients in NYHA functional class IV treated with CRT (CRT-group) were included. They were matched 1:1 with 40 patients in NYHA functional class IV by age, gender, and etiology of cardiomyopathy treated with optimal medical therapy (OPT-group). There were 80% of men, mean age 65±10 years, 62.5% ischemic, 32.5% idiopathic and 5% valvular heart disease. There were no differences among CRT-group and OPT-group in left ventricular (LV) diastolic diameter (71±6 vs 73±9 mm), LV systolic diameter (58±7 vs 61±11 mm), LV ejection fraction (22±5 vs 22±6%). There were 12 (30%) cardiovascular deaths in CRT-group during a mean follow-up of 13.8±10.5 months and 23 (57%) cardiovascular deaths in OPT-group during a mean follow-up of 33.7±47.9 months. Kaplan-Meier analysis showed no differences in the cumulated survival to cardiovascular death between both groups (Log rank test p = 0.65; Figure-1, solid line is CRT-group and dots line is OPT-group).

Conclusions: CRT did not show significant benefit on cardiovascular mortality in comparison with pharmacological therapy in NYHA functional class IV patients.

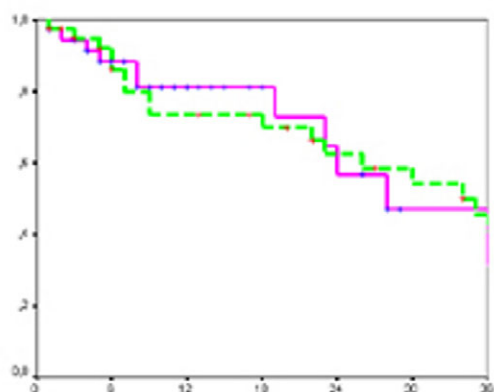


Figure 1

MONDAY, 25 JUNE 2007, 11:00–12:30

Evora

Mechanisms of atrial fibrillation

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Prediction of conversion from paroxysmal to permanent atrial fibrillation

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Background: Paroxysmal atrial fibrillation (PAF) transits to permanent atrial fibrillation (PEAF).

Objectives The current study was to determine whether a P wave triggered P wave signal averaged ECG (P-SAECG) and chemoreflexsensitivity (CHRS) are useful to predict a conversion to PEAF in patients with PAF. **Methods:** The filtered P wave duration (FPD) and the root mean square voltage of the last 20 ms of the P wave (RMS 20) were measured by P-SAECG. The ratio between the difference of RR intervals in the ECG and venous pO₂ before and after 5-minutes oxygen inhalation is measured (ms/mm Hg) for the determination of CHRS.

Predictive values of measurements

	Specificity	Sensitivity	PPV	NPV	Accuracy
FPD ≥ 145 ms and RMS 20 ≤ 3.0 μV	77	74	47	92	
CHRS ≤ 2.0 ms/mmHg	52	68	28	86	
Left atrial size ≥ 41 mm	57	74	31	89	
FPD ≥ 145 ms and RMS 20 ≤ 3.0 μV, left atrial size ≥ 41 mm and CHRS ≤ 2.0 ms/mmHg	34	96	68	84	

PPV, positive predictive value; NPV, negative predictive value; CHRS, chemoreflexsensitivity.

Results: A total of 180 patients with PAF were enrolled and followed for a mean of 22.5 months. PEAF occurred in 38 patients (21%) and these patients had a significantly larger left atrial size (43.2±4.9 vs. 41.0±5.4 mm, P=0.021), a significantly longer FPD (158.8±18.2 vs. 136.7±16.6 ms, P<0.0001) and a significantly lower CHRS (1.96±0.99 vs. 2.44±1.19 ms/mm Hg, P=0.024) than patients with PAF. Patients with PEAF tended to have a lower RMS 20 (2.38±0.65 vs. 2.75±1.18 μV, P=0.067) than patients with PAF. The chi-square test showed that the combination of FPD ≥145 ms, RMS 20 ≤3.0 μV, left atrial size ≥41 mm and CHRS ≤2.0 ms/mmHg had the best predictive power for PEAF.

Patients who fulfilled these criteria had a 12-fold increased risk for a conversion from PAF to PEAF.

Conclusions: Our results show that a P-SAECG, an analysis of CHRS and left atrial enlargement are clinical predictors of a progression from PAF to PEAF.

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Pre-procedural Predictors of Atrial Fibrillation Recurrence after Circumferential Pulmonary Vein Ablation

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Success rate of circumferential pulmonary vein ablation (CPVA) to treat atrial fibrillation (AF) ranges from 60 to 90%. The objective of the study was to identify predictors of AF recurrence after a CPVA procedure.

Methods and Results: A series of 148 consecutive patients undergoing CPVA for symptomatic paroxysmal (60.8%), persistent (23.6%) or permanent (15.5%) AF were included. CPVA with creation of supplementary block lines along the posterior wall and mitral isthmus was performed and a minimum of six months follow-up completed. Structural heart disease was present in 19.6% and hypertension in 33.8% of patients. After 13.1±8.4 months follow-up, 73.6% of patients were free of AF recurrences after a mean of 1.18±0.45 procedures/patient. Univariable analysis showed that patients with AF recurrence were older (50.6±11.0 mm vs 55.1±10.4, p=0.031), had more often permanent AF (11.9% vs 25.6%, p=0.042) and previous hypertension (53.8% vs. 26.6%, p=0.002), larger anteroposterior left atrial diameter (LAD) (43.9±5.8 mm vs. 40.4±5.3 mm, p=0.001) and larger left ventricular end systolic diameter (LVESD)(34.4±4.5 mm vs. 32.0±5.2 mm, p=0.029). Multivariable analysis showed that hypertension (OR=2.8; 95% CI: 1.5–5.4; p=0.002) and LAD (OR=1.1; 95% CI: 1.05–1.19; p<0.001) were independent predictors of AF recurrence. The mean predicted proportion of patients with AF recurrence after CPVA of the multivariable model showed a linear relationship with the increase of LAD previous to the procedure. The presence of hypertension further increased the mean predicted proportion of patients with AF recurrence at each LAD.

Conclusions: Hypertension and LAD are independent pre-procedural predictors of AF recurrence after CPVA to treat AF. These data may help in patient selection for AF ablation.

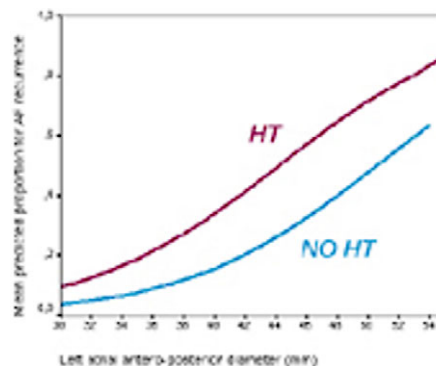


Figure AF

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The predictive value of inflammatory and oxidative markers for sinus rhythm maintenance in persistent lone atrial fibrillation

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Although there is evidence that inflammation and oxidative stress contribute to the pathogenesis of atrial fibrillation (AF), the predictive value

of inflammatory and oxidative stress markers in patients with AF has not been systematically assessed. Aim of this study is to evaluate these markers, along with echocardiographic parameters, as predictors of sinus rhythm (SR) maintenance, in patients with persistent lone AF.

Methods: Out of 268 patients with symptomatic AF, we studied 46 patients suffering their first episode of recently established persistent lone AF. We measured the circulating levels of high sensitivity CRP, TNF- α , IL-6, IL-10, sICAM-1, sVCAM-1, malondialdehyde (MDA) and nitrotyrosine (NT) before, one hour, twenty four hours, one, two, four and six weeks after cardioversion. Transthoracic echocardiography was performed 48 hours after cardioversion. During a 12-month follow-up period, AF recurrence was evaluated by Holter ECG recordings every month and when symptoms were reported.

Results: SR maintenance was associated with baseline MDA values $<4.25 \mu\text{M}$, a decrease in IL-6 $> 36.1\%$ from baseline, one week after cardioversion, and a decrease $>5.2\%$ and $>22.2\%$ in sICAM-1 and NT, respectively, two weeks following SR restoration (ROC analysis, Table). Echocardiographic parameters were not found to be predictive of SR maintenance.

Conclusions: In patients with lone AF, IL-6, sICAM-1, MDA and NT, assessed prior to and within two weeks after the first cardioverted episode of persistent arrhythmia, are reliable, early predictors of SR maintenance during the following year.

Table

Rank	Time	AUC	SE	Sig.	Cut off points	Sens.	Spec.	95% CI
IL-6	1 wk	0.845	0.078	0.001	-36.1%	89%	79%	0.693-0.997
	2 wks	0.831	0.077	0.002	-22.5%	83%	79%	0.680-0.983
sICAM-1	1 wk	0.809	0.086	0.002	-3.2%	96%	71%	0.641-0.977
	2 wks	0.831	0.079	0.001	-5.2%	87%	79%	0.676-0.986
NT	1 wk	0.890	0.061	0.0005	-12.2%	82%	87%	0.641-0.977
	2 wks	0.910	0.056	0.0005	-22.2%	88%	84%	0.676-0.986

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Prevalence of lower loop reentry or of typical atrial flutter with circuit posterior to the superior vena cava. Use of entrainment at the atrial roof

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Background: Superior part of the reentry circuit in typical atrial flutter (AF) has been shown to locate in front or behind the superior vena cava (SVC). Lower loop reentry (LLR) is a variant form of typical atrial flutter (AF) dependant on cavo-tricuspid isthmus (CTI) but involving only the lower part of the right atrium. Prevalence of AF circuits located behind the SVC as well as prevalence of LLR are unknown.

Methods: 43 consecutive pts (40 men, 68 ± 8 yo) successfully ablated of counter-clockwise typical AF were investigated. No multipolar catheter was used in order to check the high lateral right atrial activation. Low lateral right atrial activation checked on a single quadripolar catheter was descending in all pts. Prior to RF deliverance, AF was entrained by pacing 10 ms shorter than the AF cycle length (AFCL). Post-pacing interval (PPI) at the CTI and at the atrial roof (AR) between SVC and the high tricuspid annulus was measured and compared to the AFCL. AR was considered to be part of the AF circuit when local PPI was no longer than 30 ms compared to the AFCL or, in case of long PPI at the CTI isthmus despite successful RF ablation, if difference between local PPI and CT-PPI was no more than 10 ms.

Results: Mean AFCL was 252 ± 32 ms. AF pattern on 12-lead ECG was typical in all pts (e.g. negative sawtooth pattern in inferior leads and positive in V1). Heart disease was present in 31 pts (ischemic in 13 and valvular in 6). Previous AFib had been documented in 19 pts. Antiarrhythmic drug was prescribed in 30 pts at the time of the procedure (chronic amiodarone in 15, acute amiodarone in 14, sotalol in 1). CTI-PPI were closed to AFCL in 39 pts (mean difference 8 ± 6 ms). In those, AR-PPI was >30 ms longer than AFCL in 11 pts (mean difference 55 ± 16 ms). In the remaining 4 pts, CTI-PPI $>$ AFCL by more than 30 ms (mean

difference 38 ± 4 ms): in this group, AR-PPI was closed to AFCL in 2 and closed to the CTI-PPI in 2.

Conclusion: PPI measured at the atrial roof was longer than AFCL in 28% of patients with exact CTI-PPI and was never longer than CTI-PPI in the rare cases where typical AF was associated with long CTI-PPI. Taken together, 25% of pts presenting with typical AF do have reentry circuit passing behind the SVC or present with LLR.

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Age-related changes in the left atrium shape and electrophysiologic properties in patients without structural heart disease and no history of atrial fibrillation

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Background: atrial fibrillation (AF) is a common arrhythmia associated with atrial dilatation, premature beats and decreased atrial conduction velocities, but little is known about age related changes in left atrial shape and the relation to electrophysiological properties. In the other hand prevalence of AF is increased in elderly. The aim is to evaluate and analyze the relation between age, atrial shape/size and a new index of dynamic interatrial conduction time in a homogene population of patients (pts) with structurally normal heart without AF.

Methods: 56 patients (pts) without structural heart disease aged 42 ± 15 years referred for electrophysiologic study or ablation were analyzed. Echocardiographic LA surface (LAS) was assessed at end-systole (maximal). Trapezoidal LA shape was considered if transverse dimension $<$ basal dimension (four chamber view). To examine the atrial electrophysiologic characteristics we studied interatrial conduction time and fragmented atrial activity during premature stimulation of high right atrium using two extrastimulus method; decremental index (DI) was calculated as previously described as maximal percentage prolongation of interatrial conduction time during atrial extrastimulation. Pts with vulnerable atrium (inducible AF) were excluded. DI $>50\%$, repetitive atrial activity and fragmented electrograms was defined as susceptibility to vulnerability.

Results: age ranged 15-72 years; LAS ranged $10.5-32 \text{ cm}^2$; DI ranged 16-58%. Simple regression graph show a direct moderate correlation between LAS and DI ($r=0.65$, $r^2=0.42$, $p < 0.0001$). Trapezoidal LA shape was found in 15 pts (27%). Mean age in this group was 51 ± 15 years, while in pts with ellipsoidal shape mean age was 39 ± 15 years ($p=0.005$). Comparative data for LAS: trapezoidal/ellipsoidal shape group 22 ± 3.56 vs $16 \pm 2.9 \text{ cm}^2$ ($p < 0.0001$). Susceptibility to vulnerability was demonstrated in 19 pts, aged 45 ± 15 years, LAS $>20 \text{ cm}^2$ in 15 pts. Simple regression analysis demonstrated a statistically highly significant linear correlation between age and percent proportion of pts with trapezoidal LA shape ($r=0.97$, $r^2=0.95$, $p < 0.0001$).

Conclusions: this study shows that left atrial shape and electroanatomic remodeling changes with age in a population with structurally normal heart without AF, suggesting that higher incidence in AF in elderly might be also a consequence of higher incidence of atrial conduction disturbances and atrial dilatation.

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Enhanced dispersion of atrial refractoriness as an electrophysiological substrate for atrial fibrillation vulnerability in patients with paroxysmal atrial fibrillation

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Electrical remodeling plays a part in atrial fibrillation (AF) recurrences. It has been related to an increase of atrial heterogeneity of refractoriness that facilitates the occurrence of multiple wavelets of reentry and vulnerability to AF.

Aim: To examine the relationship between atrial refractoriness dispersion (Disp_A) and vulnerability (A_Vuln) for the induction of AF in pts with clinical paroxysmal AF (PAF).

Methods: 31 pts (18M, 13F; 55±13 yrs) with ≥1 yr history of PAF – 15 pts with systemic hypertension and 16 without underlying structural heart disease. They underwent electrophysiologic study while off drugs. Atrial effective refractory period (AERP) was assessed at five different sites – high (HRA) and low lateral right atrium (LRA), high interatrial septum (IAS), proximal (pCS) and distal coronary sinus (dCS) – during a cycle length of 600 ms. AERP was taken as the longest S1-S2 interval that failed to initiate a propagation response. Disp_A was calculated as the difference between the longest and shortest AERP. A_Vuln was defined as the ability to induce AF with 1–2 extrastimuli or with incremental atrial pacing (600–300 ms) from the HRA or dCS. Age, left atrial size, left ventricular function, duration of PAF, documentation of atrial flutter/tachycardia, and Disp_A were analysed to determine any association with A_Vuln for AF induction. We considered three groups: group A – AF not inducible (n=12); group B – AF inducible, self-limited (n=8); group C – AF inducible, sustained (n=11).

Results: There were no significant differences with regard to clinical characteristics and echocardiographic data between the groups. AF was inducible in 61% of the pts and noninducible in 39%. Pts with A_Vuln showed self-limited AF in 42% and sustained AF in 58%. The AERP increased from the HRA, LRA, and IAS to the pCS and dCS (HRA vs dCS, $p < 0.01$), without differences between the values measured in the three groups at any of the five sites. Group A had a lower Disp_A compared to the group B (49 ± 18 ms vs 133 ± 97 ms; $p < 0.01$), but not when compared to the group C (49 ± 18 ms vs 76 ± 39 ms; $p = 0.06$). There was no significant difference in Disp_A between group B and group C. Using logistic regression, the only predictor of A_Vuln was Disp_A ($p < 0.05$).

Conclusion: In pts with PAF, Disp_A is a major determinant of A_Vuln. Increased Disp_A enhances AF inducibility, whereas the degree of the nonuniformity of AERP appears to be less important in promoting AF maintenance. These findings suggest that Disp_A contributes not only for A_Vuln to AF but also to the type of induced AF.

MONDAY, 25 JUNE 2007, 11:00–12:30

Guarda

Evaluation of patients with syncope

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Complications of tests for the diagnostic assessment of patients with syncope

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Purpose: To evaluate the risk of complications of the main tests for the diagnostic assessment of syncope, as performed during 2005 in a wide sample of first-level, District Italian Hospitals.

Methods: The data presented are relative to the 2nd “Censimento Italiano dei Centri per lo studio della sincope”, recently undertaken with the endorsement of the Associazione Italiana di Aritmologia e Cardioritmologia. During the early 2006 dedicated questionnaires were posted to about 600 Italian Hospitals. About each test informations were requested relative to: test protocol, laboratory equipment, number of patients evaluated during 2005, complications occurred.

Results: One hundred twenty six Hospitals answered the questionnaire. A syncope-dedicated office (at least once a week) was available during 2005 in 86/126 Hospitals, and in 81 was dependent by the Cardiology Division. Carotid sinus massage was systematically performed in 94 Centres, of which 74 followed the “symptoms method” to define the positivity of the test. Out of 9318 tests performed during 2005, the following

complications were reported: prolonged asystole: 3; stroke: 1; transient ischaemic attack: 5. Tilt testing was performed in 109 Hospitals; in 91 Centres the methodology of the test was consistent with the European Society of Cardiology Guidelines’ recommendations. Out of 8461 tests performed, the following complications were reported: prolonged asystole: 8; prolonged hypotension: 1; persistent atrial fibrillation: 2; finger’s accidental crushing: 1. Adenosine test was performed in 40 Hospitals, with a 18 mg median dose (range 6–20); only 1 prolonged asystole was reported out of 504 tests performed. Implantable loop recorder was available in 88 Centres. Only 1 surgical pocket late erosion was reported out of 462 implant procedures performed during 2005.

Conclusions: As expected, the diagnostic assessment of syncope carried a reasonably low risk of complications also when undertaken as a routine activity in not strictly specialised Centres. Such data are in favour of a further increase, among the District Italian Hospitals, of structured models of care and management of syncope.

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Brugada syndrome and autonomic nervous dysfunction

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Purpose: The purpose of this study was to evaluate autonomic function in patients (pts) with Brugada syndrome with a head-up tilt-test (HUT) and sympathetic innervation of the heart assessed by I-123 metaiodobenzylguanidine (MIBG) single photon emission tomography (SPECT).

Methods: The study included 15 pts with the Brugada syndrome, mean age 40 ± 7.7 years. Thirteen pts had syncopal and/or presyncopal episodes (5 pts had 1.4 ± 2.4 syncopal episodes and 8 reported presyncope) and 2 pts were totally asymptomatic. Eleven pts had inducible ventricular tachycardia/fibrillation and had a defibrillator implanted. All pts underwent a HUT with clomipramine challenge whereas the I-123 MIBG test was performed in 13. The myocardium uptake was studied in 6 segments (anterior, posterior, inferior, septum, lateral from the short axis and apex from long vertical axes) using a 5-point scale (0 = normal, 1 = moderately diminished, 2 = intermediately diminished, 3 = severely diminished and 4 = no uptake).

Results: Ten pts (66.67%) had a positive HUT during the 8.6 ± 4.3 min of the test. Eight of the 13 pts with syncope/presyncope and the two asymptomatic pts had a positive HUT. The response of the test was mixed in 7, cardioinhibitory in 1 and vasodepressive in 2. All pts with a positive HUT had an abnormal uptake of I-123 MIBG with a mean score of 6.3 ± 2.5 . Reduced uptake was noted mainly in the inferior, posterior wall and apex. Five pts (33.3%) had a negative HUT and their MIBG score was 1.8 ± 2.9 (ANOVA $p = 0.015$ when compared with the positive HUT group).

Conclusions: Autonomic abnormalities expressed as abnormal responses to head-up tilt testing and areas of sympathetic denervation in the left ventricle are present in a subgroup of pts with the Brugada syndrome. It is therefore possible, that many syncopal episodes in pts with Brugada syndrome could be pathophysiologically related to abnormalities of autonomic nervous function.

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Evaluation of palpitation among patients with unexplained syncope

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Objectives: The aim of this study is to assess the clinical significance of palpitation among patients with unexplained syncope.

Background: Syncope of unknown etiology represents a great challenge to electrophysiologists. Palpitation is one of the premonitory symptoms that occur with both vasovagal syncope and syncope with cardiac origin. There is controversy about clinical significance of palpitation in patients with syncope of unknown origin.

Material and Methods: Two hundred and twenty seven consecutive patients with unexplained syncope were prospectively enrolled in this study since October 2004 to December 2006. Each patient was interviewed using a standard questionnaire. Electrophysiologic study (EPS) was performed in patients with suspected cardiac causes for syncope and head up tilt test was performed in patients with suspected vasovagal syncope or negative EPS.

Results: Thirty-five percent of patients in EPS group had abnormal EPS and 53% of patients in HUTT group had positive HUTT. Thirty-four percent of patients with positive head up tilt test and 33% of patients with abnormal EPS had palpitation. There was not significant difference in the presence of palpitation between patients with vasovagal syncope and syncope of cardiac origin ($P=0.48$).

Conclusion: Palpitation is a frequent symptom among patients with unexplained syncope. Palpitation before syncope is an insignificant symptom without any relation to cause of syncope.

Key words: head up tilt test (HUTT), Electrophysiologic study (EPS), unexplained syncope, palpitation

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Reproducibility of electrocardiographic findings in patients with reflex neurally-mediated syncope

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Aim: To analyse the reproducibility of electrocardiographic findings in patients with an implantable loop recorder (ILR) and recurrent suspected neurally-mediated syncope.

Methods and Results: From 417 patients with an implanted ILR because of suspected recurrent neurally mediated syncope, 106 had at least one documented syncope (index syncope): an additional syncope was documented by ILR in 20 patients; a presyncope was documented in 14 patients and ILR ECG recordings not associated with syncope or presyncope were documented in 22 patients. ECG findings were reproducible in 19/20 patients with 2 documented syncopal episodes (95% reproducibility rate): 3 with asystole, 1 with ventricular tachycardia and 15 with sinus rhythm. There was 1 patients with asystole at index syncope and sinus rhythm at recurrent syncope. ECG findings were reproducible with those recorded during index syncope in 10/14 patients with presyncope (71% reproducibility rate): 1 with asystole, 2 with supraventricular tachycardia and 7 with sinus rhythm. Four patients had asystole at index syncope and sinus rhythm at presyncope. The stored ECG findings not associated with syncope or presyncope were reproducible with those recorded during index syncopoe in 17/22 patients (77% reproducibility rate): 4 with asystole, 2 with supraventricular tachycardia and 11 with sinus rhythm. There were 3 patients with asystole and 1 patient with supraventricular tachycardia at index syncope, that had sinus rhythm during non syncopal or presyncopal episode, and 1 patient, that was in sinus rhythm during index syncope, had an asystole recorded during a stored episode not associated to syncope or presyncope.

Conclusions: The electrocardiographic findings during recurrent syncope are highly reproducible. The presence of an asystole or a tachyarrhythmia during non-syncopal episodes is highly predictive of the mechanism of syncope, whereas the absence of an arrhythmia during non syncopal episodes, does not rule out the possibility of such arrhythmias during syncope.

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Head-up tilt testing responses with different nitroglycerin dosages: experience in elderly patients with unexplained syncope

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The importance of head-up tilt testing (TT) has been demonstrated in the evaluation of elderly patients (pts) with unexplained syncope. Protocols using sublingual nitrates are increasingly used to improve diagnosis accuracy. Nevertheless, exaggerated responses to nitrates have been frequently described, particularly in elderly pts.

Objective: To evaluate in a population of elderly pts with unexplained syncope, if the impact of nitroglycerin (NTG) as a provocative agent is dose-dependent.

Methods: We studied 100 pts (≥ 65 years) submitted to TT using NTG after an asymptomatic drug-free phase. Pts were divided into 3 groups according to the NTG dosage used: 500 μg (73 ± 6 years; $n=37$), 375 μg (75 ± 6 years; $n=16$) and 250 μg (72 ± 8 years; $n=37$). The protocol included a stabilization phase, a passive phase of 20 min at a tilt angle of 70° and a provocation phase of further 20 min after NTG. Continuous monitorization of the ECG and blood pressure was obtained. The test was considered positive when there was reproduction of symptoms with bradycardia and/or arterial hypotension (cardioinhibitory, vasodepressive or mixed). A gradual and parallel decrease in blood pressure after NTG administration was considered an exaggerated response to nitrates.

Results: There were no differences in age and gender distribution between the groups or any significant difference in terms of response. There was only a trend to a higher incidence of a cardio-inhibitory pattern in the 250 μg vs. 375 μg group.

Conclusions: In a population of elderly pts with syncope of unknown origin, TT potentiated by NTG: 1. is safe and provides a significant contribution for the etiological diagnosis of syncope 2. the response to nitrates is not dose-dependent, with no differences in terms of exaggerated responses to nitrates.

	500 μg (n=37)	375 μg (n=16)	250 μg (n=47)
Female gender (%)	57	38	26
Negative test (%)	32	50	34
Positive test (%)	51	31	51
Vasodepressive (%)	63	40	46
Mixed (%)	26	20	50
Cardio-inhibitor (%)*	11	40	4
Exaggerated response (%)	16	19	15

* $p=0.07$ for 250 μg vs. 375 μg . $p=NS$ for other comparisons.

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Cardiovascular responses of Carotid Sinus Massage in adults with no history of syncope or falls

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Background: There is a causal association between carotid sinus hypersensitivity (CSH) and syncope especially in elderly patients. The prevalence of CSH is unknown in the general population but it is reported to be associated with various conditions. The aim of our study was to determine possible correlations between CSH and general epidemiologic features, specific diseases, way of living (abuse of alcohol and smoke) and use of drugs that affect the cardiovascular and autonomic nervous system, in a randomly selected adult population with no history of syncope or unexplained falls.

Methods: Toward this end, 193 randomly selected adults (mean age 58 ± 16 years, 92 male) were submitted to carotid sinus massage (CSM). Massage was performed first on the right and then on the left side, both in the supine and in the upright position, while heart rate and systolic blood

pressure were monitored. Patients were divided to those with a positive response (Group A) and to those with a negative response (Group B).

Results: CSH was documented in 11 individuals (5.7%). The response was cardioinhibitory in 6 (54.5%), vasodepressor in 4 (36.3%) and mixed in 1 subject (9.1%); 4 (36.3%) of these patients had a positive response to massage in the upright position following negative supine massage. Group A patients were older (A: 69 ± 13 v B: 57 ± 16 , $p=0.021$), were more likely to be male (A: 90.9% v B: 45.1%, $p=0.004$) and were more likely to have a medical history of hypertension (A: 81.8% v B: 42.3%, $p=0.013$), hyperlipidemia (A: 45.5% v B: 13.7%, $p=0.015$), coronary artery disease (A: 45.5% v B: 11.0%, $p=0.007$) and cerebrovascular disease (A: 18.2% v B: 1.6%, $p=0.027$). No significant differences concerning the use of certain drugs and habits (smoke, alcohol) were observed between the two groups. In multivariate analysis, age ($p=0.049$), male sex ($p=0.013$), hypertension ($p=0.047$) and hyperlipidemia ($p=0.033$) were found to be the predominant predictors of CSH.

Conclusions: CSH was observed in 5.7% of our population, more commonly in male, older patients with a medical history of diseases related to arteriosclerosis, in the absence of syncopal attacks or unexplained falls. Therefore clinicians should be cautious in attributing symptoms to carotid sinus syndrome, when a positive response after CSM is elicited during the investigation of patients with the above characteristics who present with syncope or unexplained falls.

MONDAY, 25 JUNE 2007, 14:00–15:30

Guimaraes

New aspect of cardiac resynchronisation therapy treatment

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Effects of cardiac resynchronization therapy on coronary blood flow: evaluation by transthoracic doppler echocardiography

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Background: Cardiac Resynchronization Therapy (CRT) provides hemodynamic and functional benefits in heart failure patients with left ventricular dyssynchrony. However, the effects of CRT on coronary blood flow (CBF) are not completely known.

Methods: In twelve patients (62±12 yr), successfully treated by CRT for 10±11 months, left anterior descending coronary artery (LAD) flow was assessed by transthoracic Doppler echocardiography during 4 programming modes: intrinsic conduction (IC), right ventricular (RV) pacing, simultaneous biventricular pacing (BIV 0 ms), and biventricular pacing with left ventricle (LV) activated 40 ms before RV (BIV LV 40 ms). Mean coronary flow velocity (CFV) and gradient, peak CFV and gradient, LAD flow velocity/time integral (VTI) and slope, and time of CBF were measured during each pacing modality.

Results: Mean CFV increased mostly during BIV LV 40 ms (0.23 ± 0.04 m/s vs. 0.17 ± 0.06 m/s during IC, $P < 0.0001$). Accordingly, peak CFV was higher during LV pre-activation as compared to the other pacing modes (0.32 ± 0.06 m/s vs. 0.23 ± 0.07 m/s during IC, $P < 0.0001$). LAD flow VTI improved only during BIV LV 40 ms (10.5 ± 3.4 cm vs. 8.7 ± 4.1 cm during IC, $P < 0.05$). No significant changes in LAD flow slope and time of CBF were observed between different pacing modes.

Conclusion: Significant changes in LAD flow echocardiographic parameters were observed during different CRT programming modalities. Biventricular pacing with LV pre-activation provided the highest increase in LAD flow compared to the other pacing modes.

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Assessment of left ventricular coronary sinus lead implant position by intracardiac impedance

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Introduction: Pacing site of the left ventricular (LV) lead for cardiac resynchronization therapy (CRT) can be optimized by measuring dP/dtmax or stroke volume (SV) by an additional catheter, which increases complexity and costs. Since intracardiac impedance (Z) reflects LV volume changes well in animal models, Z measured between the right ventricular (RV) and LV leads of a CRT device might be used to guide LV lead positioning. This study compares the LV implantation sites selected by Z and by dP/dtmax.

Methods: Six CHF patients with dilative cardiomyopathy have been included to date (4 male, age 71 ± 6 years). Two LV lead positions were pre-selected in each patient, that were deemed suitable for LV lead implantation. Following atrial, RV, and LV catheter positioning, a dual sensor micromanometer catheter was placed in the LV to measure aortic and LV pressure. Surface ECG, Z, LV and aortic pressure were recorded during repeated alternating intervals of intrinsic rhythm (15 beats) and VDD biventricular (BiV) stimulation (5 beats). DDD pacing was then performed at four rates, up to 140 ppm, in order to test the correlation of stroke impedance (SZ) with SV. The same measurements were repeated for the second LV lead site. The optimal lead site for either method was considered to be the one yielding maximum incremental benefit in LV dP/dtmax or SZ, respectively, for BiV pacing versus intrinsic rhythm. The parameters dP/dtmax and SV were compared for the optimal sites selected by dP/dtmax and by SZ. In the rate tests, the linear correlation between SZ and SV was evaluated.

Results: In all but one patient, the optimal site according to SZ was the same as that for dP/dtmax. In this patient both sites were hemodynamically nearly equivalent. The hemodynamically superior sites provided a mean benefit of $19 \pm 16\%$ (dP/dtmax) and $2 \pm 5\%$ (SV), and the inferior sites: $8 \pm 11\%$ (dP/dtmax) and $-4 \pm 2\%$ (SV). The differences between the better and the worse sites were significant ($p < 0.05$). The SZ-guided site selection offered a benefit of $19 \pm 16\%$ (dP/dtmax) and $1 \pm 5\%$ (SV), which did not differ significantly from the site chosen by dP/dtmax. In the rate tests, correlation coefficients of 0.76 ± 0.21 (better sites) and 0.83 ± 0.08 (worse sites) did not differ significantly.

Conclusion: LV lead site selection guided by intracardiac impedance provided hemodynamic benefit which was not significantly different from that for dP/dtmax-based site selection. The assessment of LV lead positions by intracardiac impedance during lead implantation appears feasible. During the rate test, SZ and SV exhibited a strong correlation for both sites.

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Optimal pacing site in cardiac resynchronisation therapy: evaluation of multiple epicardial left ventricular pacing sites with simultaneous contractility index measurement

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Background: Cardiac resynchronisation therapy (CRT) is an emerging treatment for patients with advanced heart failure and left ventricular (LV) asynchrony. The LV lead is usually positioned transvenously in a posterior branch of the coronary venous system. However, anatomical obstacles, the absence of a suitable vessel or phrenic nerve stimulation can render this approach impractical. Epicardial lead positioning with video-assisted thoracic surgery (VATS) is an alternative approach and allows evaluation of stimulation at multiple sites. The aim of this study was to assess the optimal pacing site by measuring the maximal rate of

LV pressure rise (dp/dt_{max}) as an index of cardiac contractility at different pacing sites.

Method: Five patients underwent minimal invasive surgery using the VATS technique to insert an epicardial LV lead after a failed transvenous approach. A Radi pressure wire was inserted into the LV for measuring the maximal rate of pressure rise in the LV (dp/dt_{max}) and calculating the contractility index (CI). With a roving electrode multiple sites were assessed during biventricular pacing. The epicardial electrode was fixed at the position where the best dp/dt_{max} was measured. Subsequently, atrioventricular delay and VV timing were optimized.

Results: In two patients the best pacing site was found mid posterior. In the three other patients the optimal sites were mid anterior, mid lateral and basal postero-lateral. Remarkably, spatial differences of only 1–2 cm could translate in relatively large differences in LV dp/dt_{max}. The baseline LV dp/dt_{max} was 720±215 mmHg/s (mean±std) during intrinsic rhythm and increased up to 1190±275 mmHg/s during optimal biventricular pacing. This means an increase factor of 1.7±0.5. During short-term follow up, all patients clinically responded to CRT. No procedural complications occurred.

Conclusion: In CRT, epicardial lead placement using the VATS technique allows the identification of the optimal pacing site where the highest CI can be achieved. Small differences in pacing position could cause substantial differences in LV pressure rise. Subsequent optimization of biventricular pacing parameters lead to an increase factor of 1.7±0.5.

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Lead position influences response to cardiac resynchronization therapy

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Introduction: Cardiac resynchronization therapy (CRT) is an established treatment for patients with advanced chronic heart failure (CHF) with electrical and/or mechanical dyssynchrony. Even with stringent criteria at least 30% of patients do not respond to CRT.

Aims: To investigate whether lead localization is of influence on response to CRT.

Methods: 81 consecutive patients were included. Response to CRT was defined as a decrease in echocardiographically determined left ventricular end systolic volume (LVESV) of ≥10% at 6 months follow up.

Results: At 6 months of follow up 43 patients were responders (53%) and 38 non responders to CRT (47%). Responders significantly more frequently were females (16 [37%] versus 6 [16%], p=0.03), had non ischemic cardiomyopathy (29 [67%] versus 16 [42%], p=0.02), a septal to lateral delay of ≥60 ms (16 [37%] versus 6 [16%], p=0.02), an apical right ventricular (RV) lead position (40 [93%] versus 30 [79%], p=0.02), and a posterolateral position of the left ventricular (LV) lead (32 [74%] versus 19 [50%], p=0.04). Multivariate logistic regression analysis revealed a posterolateral LV lead localization and septal to lateral delay ≥60 ms as independent predictors for successful CRT therapy (see table).

Conclusion: Posterolateral placing of the LV lead offers an advantage over both anterolateral and inferolateral positioning. This advantage is independent of mechanical dyssynchrony. Positioning of the RV lead in the apex seems to be better than a septal position.

logistic regression analysis

Variable	Univariate analysis		Multivariate analysis			
	Odds ratio (95% CI)	Wald	P-value	Odds ratio (95% CI)	Wald	P-value
LV lead localization				1		
Inferior	1					
Posterolateral	5.053 (0.925–27.603)	3.496	0.06	11.936 (1.537–92.678)	5.622	0.02
Anterolateral	1.750 (0.275–11.152)	0.351	0.55	3.069 (0.342–27.550)	1.003	0.32
SL delay > 60 ms	3.765 (1.222–11.60)	5.331	0.02	8.145 (1.751–30.926)	7.425	0.006

LV = left ventricular, SL = septal to lateral

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Cardiac resynchronization therapy with triple-site pacing is superior to bi-site pacing in improving left ventricular function and dyssynchrony

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Purpose: To examine the impact of cardiac resynchronization therapy (CRT) using equilateral triangle ventricular pacing (Tri-V) on left ventricular (LV) function and dyssynchrony.

Methods: Twenty-eight patients with NYHA class III (n=19) and IV (n=7) heart failure were studied. For the Tri-V, the right ventricular (RV) lead was separated into two leads, and one lead was anchored at the RV apex and the other in the RV outflow tract. The LV lead was positioned in the postero-lateral or lateral cardiac vein. CRT with standard biventricular pacing (Bi-V) was performed with RV apical and LV leads. The LV function was assessed by LV positive dp/dt (+dp/dt max) and cardiac output (CO). The LV dyssynchrony was assessed, based on the time to peak velocity (Ts) using tissue velocity imaging. The standard deviation of Ts in 12 LV segments (Ts-SD) was computed.

Results: Tri-V has greater acute effects on LV function and dyssynchrony than Bi-V.

Conclusion: Tri-V may be a treatment option in patients who do not respond to Bi-V.

Bi-V vs Tri-V

	Baseline	Bi-ven	Tri-ven
QRS, ms	196±38	157±30 ^b	139±19 ^{b,c}
Systolic BP, mmHg	101±19	105±19	107±20 ^a
+dp/dt max, mmHg/s	749±167	920±188 ^b	972±195 ^{b,c}
Cardiac output, l/min	3.1±0.9	3.4±1.1 ^a	3.7±1.2 ^{b,c}
Ejection fraction, %	25.4±6.3	27.6±7.2 ^a	28.1±7.2 ^a
Ts-SD	58.1±36.8	34.9±15.2 ^b	22.1±7.9 ^{b,c}

^ap < 0.05 vs. baseline, ^bp < 0.01 vs. baseline, ^cp < 0.05 vs. Bi-V.

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Improved mechanical resynchronization using echocardiography for CRT implantation assistance: a pilot experience

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In 65 NYHA Class III patients, 73±10 years, 42 M, 46 sinus rhythm, 19 atrial fibrillation, mean LVEF 30±10%, candidates for CRT, peroperative echo (Vivid 7.4D-General Electric) was used to improve mechanical resynchronization by monitoring parameters of dyssynchrony (D) and mitral regurgitation (MVR%). Left ventricular filling time was expressed as cardiac cycle percentage (LVFT%). Left prejection period (LPEP) was measured between onset of QRS and Aortic flow. Intraventricular D was evaluated both spatially by the delay between septal and lateral contractions (Sept-Lat) and temporally as the duration of diastolic contraction after aortic valve closure of the septum (DC sept) and the lateral wall (DC lat), persisting after mitral valve opening (Op sept). There were 30 first implants, 23 DDD and 12 BiV upgradings. After LV lead implant, RV lead was positioned according to usual practice and Standard BiV was tested. If LPEP was not reduced or remained >130 ms, RV lead was moved to a location providing the best BiV configuration according to LPEP reduction. In case of insufficient reduction Triple ventricular pacing was systematically tested. The procedure was stopped when exceeded 2 hours. Provided resynchronization using echo assistance was compared to D at Entry and Standard BiV. All pts could be tested without adverse events. 17% pts ended with Standard BiV, 25% with optimized BiV, and 58% in Triple ventricular pacing.

All data in Final configuration showed significant improvement compared not only to baseline but also to Standard BiV (p < 0.01 for all variables except the sept-lat delay)

Conclusions: (1) Optimization of RV lead(s) placement and number using echo assistance is feasible, appears to be safe, and improves

effective delivery of mechanical resynchronization compared to Standard BiV. (2) Majority of the pts required a Triple ventricular configuration, (3) Long-term study is necessary to evaluate the potential clinical benefit of this new mechanical approach

	LVFT%	LPEP	DC sept	Op sept	DC lat	Sept-Lat	MVR%
Entry	43±8	160±40	148±92	78±99	57±79	91±112	28±18
BiV standard	45±8	161±38	107±98†	30±98†	54±94	54±125*	26±19
Final config	48±7‡	136±31‡	75±99‡	4±113‡	37±90	38±117‡	20±16‡

P values refer to comparison with baseline. *p < 0.05, †p < 0.01, ‡p < 0.001

MONDAY, 25 JUNE 2007, 14:00–15:30

Evora

Remodelling, stunning and metabolism in atrial fibrillation

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Impact of pulmonary veins isolation on parasympathetic nerve and atrial remodelling in dogs

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Objective: The aim of this study is to investigate the impact of pulmonary vein isolation (PVI) on vagal modulation to the atria and atrial remodeling.

Methods: 18 adult mongrel dogs under general anesthesia were randomized into A group and B group. Bilateral cervical sympathovagal trunks were decentralized. Metoprolol was administered to block sympathetic effects. Atrial remodeling was performed by 600 bpm pacing for 30 minutes through right atrial catheter after PVI performed via trans-septal procedure guided by Lasso catheter in A group. Atrial remodeling was performed after trans-septal procedure in B group. Atrial effective refractory period (ERP), vulnerability window (VW) of AF, and sinus rhythm cycle length (SCL) were measured at baseline and during vagal stimulation before and after PVI at RAA, left atrial appendage (LAA), distal coronary sinus (CSd) and proximal coronary sinus (CSp).

Results: (1) Effects of PVI on vagal modulation: After PVI in A group, the shortened SCL during vagal stimulation attenuated significantly compared with that before PVI (P ＜ 0.001), the decreased ERP during vagal stimulation attenuated significantly compared with that before PVI (P ＜ 0.005 at RAA; P ＜ 0.05 at LAA; P ＜ 0.05 at CSd; P ＜ 0.001 at CSp), VW of AF to vagal stimulation significantly decreased after PVI (P ＜ 0.05 at RA; P ＜ 0.01 at LAA; P ＜ 0.05 at CSd; P ＜ 0.05 at CSp). (2) Effects of PVI on atria remodeling: In A group, ERP remained unchanged at baseline and during vagal stimulation before and after remodeling (P > 0.05). Atrial fibrillation was rarely induced both at baseline and vagal stimulation before and after atrial remodeling (VW close to 0). In B group, ERP decreased at baseline and vagal stimulation after atrial remodeling (P < 0.05). VW during vagal stimulation increased significantly after atrial remodeling (P < 0.05 at LAA; P < 0.01 at RAA). After remodeling, shortenings of ERP were increased significantly in B group compared with that in A group (P < 0.05 at LAA, P < 0.005 at RAA at baseline; P < 0.01 at LAA, P < 0.05 at RAA during vagal stimulation). **Conclusions:** PVI attenuates the vagal modulation to the atria, thereby decreases the susceptibility to atrial fibrillation triggered by vagus. PVI releases the atrial remodeling, which maybe contributes to the vagal denervation.

Key words: atrial fibrillation ； pulmonary vein ； vagus

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Impact of vagal activity on atrial remodelling in dogs

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Purpose: To investigate the impact of vagal activity on atrial remodeling in dogs.

Methods: Twenty four adult mongrel dogs under general anesthesia were randomized into 3 groups. The changes of vagal modulation to atria during atrial remodeling was observed in 10 dogs with administration of metoprolol in A group. The effects of vagal intervention on atrial remodeling was observed in 8 dogs with administration of metoprolol and atropine in B group. The impact of vagal stimulation on atrial remodeling was observed in 6 dogs with administration of metoprolol in C group. Bilateral cervical sympathovagal trunks were decentralized. Multipolar catheters were placed into right atria (RA), coronary sinus (CS) and right ventricle (RV). Atrial remodeling was performed by 600 bpm pacing through RA catheter for 30 minutes. Atrial effective refractory period (ERP) and vulnerability window (VW) of atrial fibrillation were measured with and without vagal stimulation before and after atrial remodeling.

Results: In A group, ERP decreased significantly at baseline and vagal stimulation after atrial remodeling compared with that before atrial remodeling (all p < 0.05). In B group, ERP remained unchanged at baseline and vagal stimulation after atrial remodeling compared with that before atrial remodeling (all p > 0.05). In C group, ERP shortened significantly at baseline and vagal stimulation after atrial remodeling compared with that before atrial remodeling (all p < 0.05). ERP shortening after atrial remodeling in A group and C group increased significantly than that in B group (all p < 0.05). Atrial fibrillation could not be induced at baseline (VW close to 0) before and after atrial remodeling in 3 groups. VW widened significantly during vagal stimulation after atrial remodeling compared with that before atrial remodeling in A group and C group (all p < 0.05), while VW remained unchanged in B group (VW close to 0).

Conclusions: Short-term atrial remodeling results in the decrease of ERP. Atrial remodeling companys with the increases of vagal modulation to atria. The increased vagal activity and vagal stimulation promote the atrial remodeling, thereby increase the susceptibility to atrial fibrillation. Key words: Atrial fibrillation; Vagus; Atrial remodeling

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Study on morphology and ultra structure of pulmonary veins, nodal or node-like cells? Factors influencing various mechanisms of atrial fibrillation

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Considerable number of studies has been conducted in the field of Atrial Fibrillation (AF), anatomy and electrophysiology of pulmonary veins (PV). However, the morphological substrate and mechanism of this arrhythmia is still insufficiently explored.

Methods and Results: Twenty human autopsy hearts were studied: 10 with cardio-vascular disease (8 male, age 56.3±5.4 year, AF in four cases) and 10 without cardio-vascular disease (7-male, age 62.9±4.7). Moreover, in five patients with rheumatic mitral valve disease and atrial fibrillation and five patients with atrial septal defect without arrhythmia biopsies have been taken from the right superior pulmonary vein and left atrium.

Macroscopic, light microscopy and electron microscopy analysis of PV and myocardial sleeves indicated the following: 86% of PV contained the myocardial sleeves. Additional right middle pulmonary vein was found out in 15%. In 25% of cases collector of left superior and inferior PV have been found. No statistically significant difference between the PV diameters in group with and without cardiovascular disease was observed. Diameters of Superior PV's significantly exceeded the diameters of Inferior PV's: Left Superior PV = 19.2±2.2 mm; Right Superior

PV = 18.1±1.5 mm; Left Inferior PV = 16.7±1.9 mm; Right Inferior PV = 16.9±1.9 mm.

Myocardial sleeves are positioned on the adventitial side of the pulmonary vein. Along the whole length of the PV the myocyte groups of sleeves are running in various directions. In PV muscle sleeves of patients with atrial fibrillation were found the local changes like lymphocyte infiltration and fibrosis. Moreover in two patients we have found also fibro-lyphomathosis reminiscent picture of arrhythmogenic displasia in right ventricle. The results of electron microscopy investigation indicated that the cells of PV muscle sleeves conditionally can be divided in to two groups: The first group cells were similar to cardiomyocytes of left atrium, with the exception of atrial granules, in second group we have found the cells with several ultra structural characteristics similar to the nodal cells i.e. node-like cells, but we did not find the P cells and Purkinje fibers.

Conclusion: The changes in myocardial sleeves of PV observed in our research can cause atrial fibrillation by means of trigger activity and/or re-entry mechanism. On the assumption of our ultra structural study we can not strengthen the theory of nodal cells in PV, however node-like cells are proved to exist.

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Cardiac electrical stunning: experimental study on atrial electrical remodelling and reverse electrical remodelling in canine model of slow-fast syndrome

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Purpose: Atrial electrophysiological characteristics were evaluated to study electrical remodeling (ER) and reverse electrical remodeling (RER) in sinus node dysfunction and after rapid atrial pacing.

Methods: Model of sinus node dysfunction (SND) was established by contact cotton with formaldehyde to surface area of sinus node in 12 dogs. Atrial effective refractory period (AERP) and dispersion of AERP, inducible rate of AF, and recovery of shortened AERP were observed in 7 epicardial sites in left and right atrium before and after rapid atrial pacing.

Results: AERPs at 7 sites were shortened markedly ($P < 0.05$), but the dispersions of AERP at different pacing cycle length (PCL) were increased obviously ($P < 0.05$) after SND and 2-hour stimulation. Further analysis showed that there were no significant differences of dispersion of AERPs between PCL350 and PCL250 (29.25 ± 4.43 ms vs 30.76 ± 3.06 ms, $P = 0.861$), and between PCL350 and PCL200 (29.25 ± 4.43 ms vs 30.76 ± 3.06 ms, $P = 0.861$). There was significant difference of dispersion of AERPs between PCL250 and PCL200 (30.76 ± 3.06 ms vs 25.12 ± 3.62 ms, $P = 0.014$). 7 sites were used to induce AF in each dog (56 sites). Averaged probability and duration of inducible AF was increased after 2-hour stimulation (33.6 ± 16.1 s vs 16.5 ± 4.7 s), and the longest duration of AF was prolonged significantly (117.3 ± 44.2 s vs 45.2 ± 19.8 s) ($P < 0.05$). In PCL350 and PCL250, AERP at HRA in 10 min and 100 min after 2-hour stimulation was recovered to that before stimulation, but AERP at HLA in 140 min after 2-hour stimulation could reconstitute to that before stimulation. In PCL200, AERP at HRA in 60 min after 2-hour stimulation was changed to that before stimulation, while AERP at HLA in 100 min after 2-hour stimulation did reconstitute to that before stimulation. So, the recovery of AERPs (RER) in left and right atrium in different PCLs was not simultaneously. Comparison with right atrium, the recovery of AERP in left atrium was late significantly.

Conclusions: SND could produce the shortening of AERP in atrium, suggesting SND may be substrate in precipitating AF. The simplest example of ER and RER might be sinus node depression due to atrial overdrive pacing and its recovery. Rapid atrial pacing obviously induced ER in SND, and ER could recover simultaneously, which is defined as RER. ER and RER do like myocardial stunning due to ischemia-reperfusion injury. So, we forward a new concept defined as cardiac electrical stunning, and hypothesized Cardiac electrical stunning (CES) is an important electrophysiological characteristic of the heart.

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The role of epicardium-derived-cells (EPDCs) in atrio-ventricular (AV)-isolation: implications for AV-reentrant tachycardias

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Background: During embryonic heart development, the ventricular activation sequence changes from a base-to-apex to an apex-to-base pattern, which reflects maturation of the His-Purkinje system and concurrent formation of the annulus fibrosus. The aim of this study was to investigate the role of Epicardium-Derived-Cells (EPDCs) in formation of the isolating annulus fibrosus.

Methods: In quail embryos, EPDC migration was mechanically inhibited by in-ovo microsurgery on the 3rd day of incubation (HH15–18). Ventricular activation patterns were analyzed by extracellular recordings in 40 wild-type (group A, HH38–41) and 8 EPDC-inhibited (group B, HH38–41) post-septated hearts. Electrodes were positioned on the left atrium, right ventricular base, left ventricular base and left ventricular apex. Additionally, in-ovo 'surface'-ECGs were recorded in 6 wild-type and 6 EPDC-inhibited post-septated hearts. Electrophysiological data was correlated with morphology (MLC2a).

Results: While the ventricular apex was the location of earliest ventricular activation in 22/40 (55%) of wild-type embryonic hearts from group A (heart rate 110 ± 18 bpm, AV-interval 77 ± 25 ms), only 2/8 (25%) of EPDC-inhibited hearts from group B (heart rate 140 ± 36 bpm, AV-interval 73 ± 26 ms) showed an apex-first ventricular activation pattern ($p = 0.039$). The vast majority (6/8; 75%) of these EPDC-inhibited embryonic hearts showed that the right or left ventricular base was the location of earliest ventricular activation. Moreover, the PR-interval in the in-ovo 'surface'-ECG recordings was significantly shorter in EPDC-inhibited (53 ± 11 ms) versus wild-type (62 ± 11 ms) post-septated embryonic hearts ($p = 0.003$). Morphologically, EPDC inhibition was related to marked isolation defects of the annulus fibrosus. Although several small persistent accessory myocardial AV-connections can still be found in wild-type hearts, these persistent AV-connections were much broader in EPDC-inhibited embryos.

Conclusion: Although AV-conduction through small remnants of myocardial AV-connections remains possible in post-septated embryonic wild-type quail hearts at near-hatching (HH44) stages of embryonic development, inhibition of EPDC-migration results in marked defects in the annulus fibrosus. These persistent broad accessory myocardial AV-connections were related to premature activation of the ventricular base and may provide a substrate for persistent reentrant arrhythmias in later postnatal life.

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Acute electrophysiological effects of omega-3 fatty acids in human atrial myocardium

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Purpose: Little is known about the relationship of nutritional factors with atrial fibrillation (AF). The purpose of the present study was to evaluate the acute effects of omega-3 fatty acids on atrial electrophysiological properties in humans.

Methods: In 6 patients with paroxysmal atrial fibrillation, two electrophysiological studies were performed – before and immediately after the infusion of 3.8 g, n-3 polyunsaturated fatty acids, (100 ml of omega-3 marine triglycerides, Omegaven, Fresenius-Kabi, Germany). Patients were free of antiarrhythmic drugs for five half-lives before their entry into the study.

Before and after infusion of n-3 polyunsaturated fatty acids, we measured AH and HV intervals, corrected sinus node recovery time (SNRT) and the Wenckebach point. Effective refractory period (ERP) at 3 cycle lengths (CL: 600, 500, 400 ms) were evaluated in right atrial appendage and in

right atrial low lateral wall. During the ERP evaluation the presence or absence of AF induced as a response to the shortest extrastimuli resulted in atrial capture was recorded.

Results: After the infusion of n-3 polyunsaturated fatty acids, corrected SNRT, AH, HV interval and Wenckebach point were not affected.

ERP in atrial myocardium increased significantly (right atrial appendage ERP at CL 500 ms, increased from 189 ± 9 to 202 ± 11 ms, $p < 0.05$ and right atrial low lateral wall ERP at CL 500 ms, increased from 198 ± 12 to 209 ± 14 ms, $p < 0.05$).

AF was induced in 5 of the patients during baseline atrial ERP determination. After the administration of n-3 fatty acids AF was inducible in only 3 patients. In these patients the duration of AF induced after the infusion of n-3 fatty acids was significantly shorter and the mean fibrillatory cycle length interval was prolonged (156 ± 9 ms compared to 134 ± 15 ms, $p < 0.05$).

Conclusions: N-3 polyunsaturated fatty acids exert important electrophysiological effects on atrial myocardium. The increase in atrial refractoriness, the reduction of AF inducibility and the prolongation of fibrillatory cycle length interval may explain the correlation of fish intake with the reduction in the risk of AF observed in epidemiological studies.

MONDAY, 25 JUNE 2007, 14:00–15:30

Guarda

Clinical aspects of cardiac pacing

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Pacing-induced cardiac memory in the human ventricle: rapid and potentially deleterious electrophysiological remodeling

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Purpose: Cardiac memory (CM) is induced by periods of altered ventricular activation following e.g. ventricular pacing. The development of CM and its electrophysiological consequences were studied with electro-ECG and vectorcardiography (VCG).

Methods: Twenty patients with symptomatic sinus bradycardia and normal intraventricular conduction received a DDD-R pacemaker and were paced from the right ventricular endocardium at physiologic rates. A short AV-delay was programmed to achieve maximum ventricular pacing. ECG and VCG were recorded prior to and one day post-implantation, and then daily within the first week ($n=6$) or weekly for 5–8 weeks ($n=14$), during normal ventricular activation (temporary AAI-programming). The temporal and pathophysiological aspects of altered repolarization was compared for several ECG and VCG parameters; the latter characterizing the maximum T vector and T vector loop morphology.

Results: Maximum T vector amplitude and the loop parameter Tarea were the first to react and both decreased within one day after the initiation of pacing. Prolonged repolarization during normal activation (QTc 429 ± 33 vs. 454 ± 46 ms, $p < 0.05$) and signs of increased repolarization heterogeneity, as reflected by the loop parameters Tegen and Tavplan, may imply deleterious repolarization changes when abruptly switching from ventricular pacing to normal conduction. During ventricular pacing on the other hand, a gradual shortening of the repolarization time was observed over weeks (QTc 518 ± 20 vs. 469 ± 26 ms, $p < 0.01$), suggesting an adaptive process.

Conclusion: In sick sinus syndrome patients ventricular pacing should be avoided, but if indicated switches between normal conduction and ventricular pacing should be minimized to avoid periods of repolarization instability.

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Comparison of final results of two registries evaluating the use of therapy advisor in c-series pacemakers

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Background: The VIBRANT Registry conducted in the U.S. and the C-STAR Registry conducted in Europe were designed to evaluate the overall utility of the Therapy Advisor (TA) feature in general pacing populations. TA is designed to analyze all diagnostic data during pacemaker (PM) interrogation, alert the physician to areas of clinical concern and provide programming suggestions to optimize patient therapy. This abstract compares the US and European experiences regarding TA's usefulness and efficiency.

Methods: VIBRANT enrolled 298 patients (pts) with C-Series PMs; mean age 75.6 years; 49% male. The primary indication was Sinus Node Dysfunction (SND) 66%; AV Block (AVB) 27%. C-STAR enrolled 990 pts; mean age 73.4 years; 58% male. The Primary indication was SND 37.2%; AVB 53.1%.

Results: VIBRANT included 884 follow up (FU) visits; at 90% of visits TA was reported to be helpful in assessing the pt's condition and at 91% of visits it was reported that TA made for more efficient PM FU. When the reason for therapy change was specified, the advanced diagnostics including TA contributed to or were the sole driver of PM programming changes at 73% (334/459) of visits and of medication changes at 29% (85/294) of visits.

C-STAR included 1196 FU visits; at 64% of visits TA was reported to be helpful in assessing the pt's condition and at 69% of visits it was reported that TA made for more efficient PM FU.

Table 1 compares results reported in 2005 to the final results.

Conclusions: In the final VIBRANT experience, physicians continued to report a very high level of confidence in TA's impact on patient management. C-STAR reported TA to be more helpful than in the preliminary report, but did not reach the levels reported by VIBRANT. This may be attributable to different pt populations and differences in PM programming preferences between US and European physicians.

Table 1: Comparison of Results

	Interim/Final			
	Total FU Visits	% SND Implants	% TA Helpful	% TA Efficient
VIBRANT	319/884	66/66	91/90	92/91
C-STAR	121/1196	46/37	55/64	54/69

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The real world of dual-chamber pacemaker patients: use and performances of dedicated modes to minimize ventricular pacing

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Purpose: Randomized trials in selected pacemaker (PM) patients (pts) have highlighted the need to reduce the cumulative ventricular pacing (%Vp). Our goal was to determine, in the routine follow-up (f-up) of unselected dual-chamber (DC) paced pts, the use (and related performances) of dedicated pacing modes routinely programmed to minimize %Vp after first DC PM implant.

Methods: To date 187 pts have been consecutively enrolled in 13 Centres. Implant indications (% of pts) were: sinus node disease (SND) 39.5%; paroxysmal atrioventricular block (AVB) 33.9%; SND and AVB 14.5%; permanent AVB 12.1%. The choice of pacing mode was left at investigators' discretion, among SafeR, DDD/AMC, DDD + long AVD, DDD + free AVD. Pts were classified according to the programmed pacing mode,

then followed every 6 months. PM memories were interrogated at each f-up, to retrieve information about %Vp.

Results: Data on 124 pts have been to date analyzed. Pacing modes dedicated to Vp reduction (SafeR or DDD/AMC) were chosen in 68 out of 109 pts without permanent AVB (63.2% in SND pts, 66.6% in SND+AVB pts, 59.5% in paroxysmal AVB pts), and in 1/15 (6.6%) of permanent AVB pts. In the subgroup of pts with %Vp=0, we determined (first part of the table) the programmed pacing mode allowing to achieve that result at 2 and 8 months (M2-M8) f-ups. Moreover, analyzing the subgroup of pts with PM programmed in SafeR mode, the %Vp at M2 and M8 f-ups were measured (second part of the table).

Conclusions: This preliminary analysis in an unselected DC PM population, shows that: (1) in 62.4% of pts without permanent AVB a dedicated mode to reduce %Vp was programmed; (2) pacing modes only dedicated to %Vp reduction were able to achieve %Vp=0 in a consistent number of pts; (3) SafeR mode programming allowed to obtain %Vp < 5 in 73% and 76% of unselected pts at M2 and M8 respectively.

Pts with %Vp=0%	SafeR	DDD/AMC	DDD + long AVD	DDD + free AVD
M2 (n=32 pts)	75%	19%	6%	0%
M8 (n=19 pts)	84%	11%	5%	0%
SafeR mode only	%Vp=0	0 < %Vp < 5	%Vp ≥ 5 (no MS*)	%Vp ≥ 5 (MS**)
M2 (n=34 pts)	70%	3%	6%	21%
M8 (n=25 pts)	64%	12%	12%	12%

*no MS, pts without Mode Switching episodes; MS, pts with Mode Switching episodes.

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Improving DDD systems by optimizing atrioventricular (AV) delay

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Purpose of the study: To study usefulness of echocardiography to determine hemodynamic AV 1 block meaning and to define an optimal AV delay for DDD patients.

Methods: 20 patients (M 58%, 64±5 years) with hypertension and coronary artery disease were enrolled in the study. Indications for pacemaker implantation were sick sinus syndrome and transient complete AV block. DDDR systems were implanted to all patients. Sinus rhythm with permanent AV 1 block was dominated. All patients had rigid mitral flow type and diastolic heart failure (mean EF = 54±5%). We tried to improve LV diastolic filling time and optimize AV delay with Echo.

Echo examination was performed at baseline and after operation. Modes with AV delay from 80 to 200ms were programmed step-by-step. We measured mitral inflow and velocity time integral (VTI). We defined an optimal AV delay as a period of time with adequate left ventricle (LV) filling and maximal VTI. There are 3 LV filling types, which depend on duration and hemodynamic meaning of AV interval. There are too short, too long and optimal AV delays.

Results: Patients were divided into 2 groups. Group 1 included 12 patients. Optimal Echo parameters were registered with sinus rhythm. Intrinsic AV interval <250ms. Group 2 included 8 patients. Optimal Echo parameters were registered with RV pacing. Intrinsic AV interval > 250ms.

Optimization of AV delay results are in the table.

There was no hemodynamic meaning of AV 1 block in Group 1. Programming of maximal AV delay helped to decrease RV pacing percent. AV 1 block made hemodynamic worse in Group 2. Best clinical and Echo results were registered with short AV delay.

Conclusions:

1. Selection of AV delay with Echo is effective method for optimizing DDD systems.
2. Optimizing AV interval increase VTI in patients with LV filling delay.
3. Programming maximal AV delay and ADI mode are indicated to patients with intrinsic AV interval 250 ms.
4. DDD mode with short AV delay are indicated to patients with intrinsic AV interval >250 ms.

5. It is necessary to avoid permanent RV pacing in DDD patients if possible.

Optimization of AV delay results

AV delay	Group 1 (<250 ms)		Group 2 (>250 ms)	
	VTI	6 min. walk test	VTI	6 min. walk test
Intrinsic	17.9±0.8	410±15	14.1±1.1	349±10
Short	14.5±0.9*	361±13*	17.1±0.5*	391±11*

*P < 0.001 (intrinsic-short).

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Pacemaker and implantable cardioverter defibrillator procedures can be performed safely in anticoagulated patients

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Anticoagulation with warfarin is frequent in patients presenting for pacemaker or cardioverter defibrillator (ICD) procedures. We assessed the impact of various levels of anticoagulation at the time of the procedure on complication rates at our institute. A total of 1240 pacing or ICD procedures were performed between November 2000 and March 2006. Baseline demographics and procedural variables as well as in-hospital, 30 day and 6 month outcomes were collected in 198 of these patients who were anticoagulated with warfarin. A minor pocket haematoma was defined as swelling of the pacemaker pocket exceeding the size of the generator, whilst a major pocket haematoma was defined as a haematoma requiring re-operation or prolonged hospitalization. The mean patient age was 68±14.3 years, with 71% being male. The main indications for anticoagulation were atrial fibrillation (59%), prosthetic valves (29%), LV dysfunction (7.1%) and other (5.1%). The majority of procedures involved pacemaker implantation (63.6%) or revision (18.2%) with the remaining procedures being ICD insertion (14.1%) or revision (4%). To evaluate the impact of INR at the time of the procedure on complication rates patients were divided into 3 groups: group 1 INR < 1.5 (42.4%), group 2 INR 1.5–1.9 (34.3%) and group 3 INR ≥ 2.0 (23.2%). Baseline demographic and procedural variables including age, aspirin use, procedure type, vascular access and pocket location (prepectoral or submuscular) were similar between the 3 groups. Periprocedural heparin use was as follows: group 1 (9.5%), group 2 (8.8%) and group 3 (2.2%). At 30 day follow-up minor haematomas occurred in 1 (1.3%), 2 (2.9%) and 2 (4.3%) of groups 1, 2 and 3 respectively (p=0.53). One major haematoma requiring evacuation occurred in group 2 following an ICD implantation and treatment with heparin periprocedurally. There were no pocket infections at 30 days. At 6 months follow up only one additional complication occurred which was a pocket infection in group 2. Combined complication rates (haematoma or infection) at 6 months were similar between the 3 groups (p=0.16). Pacemaker and ICD procedures can be performed in patients with therapeutic INR levels with a low risk of complications.

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Influence of perioperative antithrombotic therapy on occurrence of bleeding events in elective pacemaker implantations

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Background: According to literature pacemaker implantation shows a risk of bleeding in 0.5–0.7% of procedures. Preoperative discontinuation of acetylsalicylic acid (ASA), clopidogrel (clop) and oral anticoagulants (OAC) is routinely performed to reduce the risk of bleeding, although withdrawal of antithrombotic medication elevates the risk of thromboembolic events especially in patients (pts) at high risk.

In this retrospective analysis we investigated 376 pts undergoing pacemaker implantation (PI) or device replacement (PR) from January 2005 till the end of October 2006. We documented perioperative antithrombotic therapy, bleeding events, major hematomas and the intraoperatively use of a hemostyptic agent, when diffuse bleeding was overt.

Methods: In the study period 376 procedures were performed at our center (273 PI and 103 PR). Mean age was 78 years, 53% were male. The indication was high degree av-block in 140 pts, sick sinus syndrome in 107 pts, brady/tachy syndrome in 99 pts and 30 pts had a bifascicular block.

Peri-operative antithrombotic therapy, severe hematomas as well as bleeding complications are listed in table 1.

Results:

1. In 61 patients (16.2%) antithrombotic therapy was continued despite of pacemaker implantation.
2. In 34 pts (9%) a specific hemostyptic agent was used by decision of the operator according to intraoperative bleeding status.
3. There were no significant bleeding complications requiring re-operation.
4. In 4 pts (1.06%) significant hematomas were noted.

Conclusion: In a high risk population discontinuation of antithrombotic therapy for pacemaker implantation or replacement may be harmful and is no longer necessary as shown in our investigation. There were no major bleeding complications requiring re-operation or prolonging hospital stay. Precisely coagulation and the intraoperative use of hemostyptic agents and even accurate postoperative care may be helpfull to avoid bleeding complications.

Table 1

	Hemostyptic	Bleeding	Hematoma
ASA and Clopidogrel n=6	1	0	0
ASA or Clopidogrel n=48	7	0	1
OAC INR > 1.5 n=7	3	0	0
OAC INR < 1.5 n=66	8	0	0
No therapy n=249	15	0	3

Monday, 25 June 2007

Poster Session 2

MONDAY, 25 JUNE 2007, 15:30–16:30

Poster Area

Moderated Posters II – Major issues in cardiac resynchronisation therapy

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Vectorcardiographic measures of cardiac asynchrony

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One of the main challenges in cardiac resynchronization therapy (CRT) is identification of responders. The most widely used marker to identify patients with cardiac asynchrony has been a widened QRS complex on the surface electrocardiogram. However, the relation between pre-implant QRS duration and mechanical improvement displays considerable scatter. The aim of this study therefore was to find better correlate measures of mechanical asynchrony in the electrocardiogram of heart failure patients who are eligible for cardiac resynchronisation therapy. First, we simulated cardiac asynchrony using software based on the equivalent double layer model (ECGSim, University of Nijmegen, The Netherlands). Depolarization delays were introduced on different segments of the left ventricular wall and the effect of these delays on the surface ECG were studied. Subsequently, standard echocardiography with Tissue Doppler Imaging was performed and a 2-minute ECG was recorded in 22 candidates for CRT. After the device had been implanted, atrioventricular and interventricular timing of the pacemaker was optimized based on Tissue Velocity Imaging. At least 4 weeks after optimization (mean follow-up 67 days), another 2-minute ECG was recorded and echocardiographic measurements were repeated. ECG data were averaged, filtered and converted into orthogonal vector components for further analysis, using Matlab R13. 18 out of 22 patients improved haemodynamically during CRT (stroke volume 83 vs. 72 ml, $p < 0.02$; mean dp/dt 1026 vs. 585 mmHg/s, $p < 0.001$). QRS duration on the surface ECG, the most widely used marker to identify patients with cardiac asynchrony, did not differ significantly before and after implant (132 vs. 131 ms, ns). However, we found that QRS area, QRS vector magnitude and pathlength of the QRS vector loop decreased significantly ($p < 0.005$) during biventricular pacing, where the strongest decrease was usually found at the optimized V-V timing of the pacemaker. These findings corresponded well with the results of our simulations. The results of this study indicate that QRS area, and vectorcardiographic markers such as vector magnitude and vector loop pathlength are associated with cardiac asynchrony and with haemodynamic improvement after CRT. These measures may provide better markers for asynchrony than QRS duration. The mechanisms relating these electrocardiographic measures to cardiac asynchrony and their possible role in optimization of V-V timing and more adequate identification of responders to CRT need to be further investigated.

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Comparison of different methods of TDI in identification of intraventricular dyssynchrony after CRT

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Purpose: compare different methods of TDI to identify the degree of LV synchronism obtained after CRT.

A group of 45 patients with heart failure received a biventricular device and TDI was performed at least 3 months after CRT. With a Vivid 7 General Electric TDI was acquired as digital loops in the apical four and two-chambers. During off line analysis the time to peak systolic velocity was measured in 8 segments of the LV. We have compared (1) an

analysis performed on 2 basal segments (septal and lateral) with 60 ms of difference among the 2 times as index of intraventricular dyssynchrony with (2) an evaluation on 4 segments (basal and middle septal and lateral walls) with a cut off of 65 ms and with (3) an analysis performed on 8 segments (basal and middle septal, lateral, inferior and anterior walls) with a cut off of 100 ms of difference among 2 any times. Only in 22 patients (48.9%) the methods gave homogeneous results showing absence of LV dyssynchrony. With the method of 2 segment (1) it was synchronous the 75.6% of the patients, appraising 4 segments (2) it was synchronous the 60% and with the analysis of 8 segments (3) was synchronous 57.8% ($p = \text{NS}$). The feasibility of the analysis and the reliability of the curves was different among the three methods for the presence of not optimal visualization especially of the middle anterior wall. In the analysis of 8 segments good curves are obtained only in 77.8% of the patients while in the analysis of 2 segments we obtained reliable curves in 95.6% ($p = 0.03$).

Conclusion: different methods of analysis with TDI can show not univocal results. Greater the numbers of segments considered and smaller can be the degree of feasibility and accuracy of the examination.

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Additional value of 3-dimensional echocardiographic dyssynchrony to conventional 2-dimensional dyssynchrony in predicting the response after cardiac resynchronization therapy

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Introduction: Real-time-3-dimensional (3D) echocardiography has shown great promise for imaging ventricular dyssynchrony (VD). We investigated whether the additional 3D morphologic assessment of VD has any significant impact on the response after cardiac resynchronization therapy (CRT).

Methods: 41 patients with a QRS > 120 ms, class III or IV NYHA and an ejection fraction $< 35\%$ were implanted with a CRT device and underwent a 2D (time dispersion of 12 electromechanical delays) and 3D echocardiographic assessment of VD (dispersion of time to minimum regional volume for 16 left ventricular segments) (1) before implantation; (2) 3 days after implantation with optimization of the pacing interventricular delay with a pre-excitation of the right or left ventricular pacing lead of 20, 40, 60 ms. The changes of 2D and 3D dyssynchrony were correlated with those of cardiac output and ejection fraction; (3) 6 months after implantation.

Results: (1) During the different configurations of sequential CRT, the changes in 3D VD were highly correlated with those of cardiac output ($r = -0.67$, $p < 0.001$) and ejection fraction ($r = -0.68$, $p < 0.001$). The correlation between 2D VD and cardiac output and ejection fraction were significant but less ($r = -0.60$ and $r = -0.56$ respectively; $p < 0.01$). (2) After 6 month of CRT, 76% of the patients were considered as responders (10% decrease in end-systolic volume). Before implantation, we observed a significant difference between responders and non responders in terms of 3D VD ($p < 0.05$) but not in terms of 2D VD ($p = \text{ns}$).

Conclusion: This prospective echocardiographic study demonstrated an additional value of 3D assessment of ventricular dyssynchrony in predicting the response after cardiac resynchronization therapy and in optimizing the pacing configuration.

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Repercussion of functional mitral regurgitation on reverse remodelling in cardiac resynchronization therapy

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Introduction and Aim: Cardiac resynchronization therapy (CRT) reduces the degree of functional mitral regurgitation (FMR). However, FMR has also been associated with a lack of clinical response to CRT. We undertook this study to determine whether the presence of FMR influences the reverse remodelling induced by CRT.

Methods: We used Doppler echocardiography to assess 20 patients with dilated cardiomyopathy before and six months after undergoing CRT. We evaluated the effect of reverse remodelling (reduction $\geq 10\%$ in end-systolic volume) according to the presence or absence of important FMR, defined as a regurgitant orifice area of (ROA) ≥ 0.20 cm².

Results: Of the 20 patients (mean age, 64.7 \pm 8.2 years, eight women), nine had marked FMR (ROA 0.40 \pm 0.12 cm²), six mild or trivial FMR (ROA 0.15 \pm 0.02 cm²) and five had no FMR. CRT reduced the presence of mitral regurgitation by 33.3% and induced reverse remodelling in 60% of the patients. A ROA ≥ 0.20 cm² was associated with a lack of reverse remodelling, despite presenting similar baseline characteristics and a reduction in asynchrony to the other patients. Reverse remodelling was produced in all the other patients, with a significant reduction in end-systolic volume (41.7 \pm 21%; p=0.003), accompanied by improvement in the ejection fraction (p=0.003) and myocardial performance index (p=0.027).

Conclusions: CRT improved FMR, although the baseline presence of important mitral regurgitation, with a ROA ≥ 0.20 cm², in patients undergoing CRT was associated with a lack of response in reverse remodelling.

Echocardiographic effects of CRT

	SMR (n=9)		No SMR(n=11)	
	Baseline	Follow-up	Baseline	Follow-up
EDV (ml)	238.1 \pm 64.3	250.3 \pm 88.7	188.7 \pm 53.9	141.3 \pm 52.2S ^{†‡}
ESV (ml)	181.0 \pm 53.1	191.4 \pm 81.6	143.9 \pm 43.7	84.5 \pm 44.0 ^{†‡}
EF (%)	22.6 \pm 6.4	24.2 \pm 8.8	22.7 \pm 6.7	41.0 \pm 11.0 ^{†‡}
ROA (cm ²)	0.40 \pm 0.12	0.23 \pm 0.19 [†]	0.08 \pm 0.08*	0.03 \pm 0.04 [†]
SSI	0.89 \pm 0.24	0.81 \pm 0.30	1.00 \pm 0.34	0.47 \pm 0.23 ^{†‡}
Bax index (ms)	86.2 \pm 18.1	15.2 \pm 58.1 [†]	91.2 \pm 22.5	25.8 \pm 14.7 [†]
ESVr (%)	-	4.3 \pm 26.1	-	-41.7 \pm 21 [‡]

SSI: systolic sphericity index; ESVr: reduction in ESV.

*p<0.05 vs. baseline significant mitral regurgitation (SMR); [†]p<0.05 vs. Baseline study; [‡]p<0.05 vs. Follow-up SMR.

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Validation of a new noninvasive haemodynamic monitor. Implications for optimization of the ventricular pacing sites

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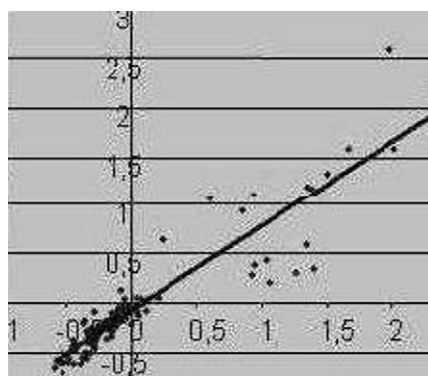
Background: The peak of myocardial vibrations (PEA 1, peak endocardial acceleration) occurring during isovolumic systole is an index of myocardial contractility and can be measured with an accelerometer.

Aims: (1) to demonstrate that the PEA 1 during isovolumic systole measured by the non invasive cutaneous precordial application of the accelerometer sensor is related to positive peak left ventricular (LV) dP/dt; (2) to assess the usefulness of the PEA monitoring during different pacing configurations.

Methods and Results: Measurements of left ventricular positive peak LV dP/dt with a Millar catheter were compared with measurements of transcatheter PEA in 7 pigs at baseline and during acute haemodynamic interventions: Dobutamine and Beta-blocker infusion (close-chest), right, left, biventricular and sequential biventricular pacing before and after

graded ischemia of the left anterior descending coronary artery (open-chest). A consistent PEA signal was obtained in all animals. PEA 1 changes were highly related to positive peak LVdP/dt changes in close + open-chest conditions (r=0.94; p<0.001, Picture 1). The changes of LV contractility induced by the different pacing configurations were detected by PEA analysis in absence of ischemia (r=0.93; p<0.001) and in presence of ischemic LV dysfunction (r=0.92; p<0.001).

Conclusion: Non invasive PEA 1 measurement allows monitoring of left ventricular contractility in pigs with normal and depressed ischemic left ventricular function and may be used to optimize the choice of the pacing site and configuration.



Correlation changes in dP/dt pos and PEA

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Usefulness of intrathoracic fluids accumulation monitoring with an implantable biventricular defibrillator in reducing hospitalizations in patients with heart failure: a case control study

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Background: Patients (pts) with advanced heart failure (HF) are frequently hospitalized for fluid overload. In some of them, the implantation of biventricular pacing device with back-up ventricular defibrillator (B-ICD) is indicated. In a new available B-ICD model (InSync SentryTM, Medtronic Inc), measurement of intrathoracic impedance recently has been integrated. This parameter is strictly related, with an inverse linear correlation, to the pulmonary fluid overload. Purpose of our work is to evaluate the clinical usefulness of this device in the reduction of hospitalization rates for HF.

Methods: in a case-control study, we have compared the number of hospital admissions for congestive HF during same follow-up period in two homogeneous groups of pts, each (one) composed of 27 consecutive pts undergoing B-ICD device implantation in our center. The first group of pts was implanted with a B-ICD device with OptiVol system for monitoring the intrathoracic fluid accumulation with activated acoustic alarm (Group I Optivol) and the second group was implanted with B-ICD device (InSync III Marquis, Medtronic, Inc.), with similar features except for the absence of OptiVol monitoring system (Group II No Optivol). Follow-up visits and device controls were periodically performed at 3 months interval or in case of acoustic alarm or hospitalization for congestive HF.

Results: The clinical characteristics of the two groups of pts were not statistically different. In 12 of the 27 pts with B-ICD Optivol+ device, in a follow-up of 359 \pm 98 days, 18 Optivol alarms were observed and only one hospital admission for congestive HF occurred in a pt ignoring the device alarm for 13 days. In the B-ICD Optivol-group pts, 8 hospitalizations (in 7 pts) for HF decompensation were observed (p<0.05).

Conclusions: InSync Sentry device is as a useful tool for the clinical management of HF pts., it can result in early treatment during the pre-clinic stage of HF decompensation and in a significant reduction of hospital admissions for congestive HF.

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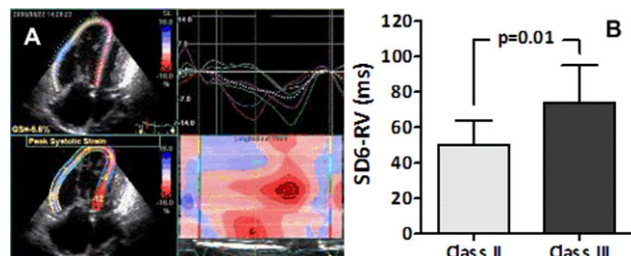
Evaluation and clinical utility of right intraventricular dyssynchrony in patients with pulmonary hypertension: insights from two-dimensional strain echocardiography

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Background: Little is known on both the presence and clinical importance of right intraventricular dyssynchrony in patients with right ventricular (RV) dysfunction secondary to pulmonary hypertension (PHT). Two-dimensional strain (2DS) echocardiography is a newer modality that provides for a comprehensive evaluation of segmental contractile patterns. **Methods:** We evaluated 21 patients with severe primary PHT (16 female, 48±17 yrs, 7 class II, 14 class III, RV systolic pressure 83±21 mmHg, HR 78±15 bpm, QRS 102±17 ms) and 29 healthy controls (19 female, 49±15 yrs, HR 66±10 bpm, QRS 89±12 ms) by means of standard and 2DS echocardiography. We recorded: (a) global and segmental longitudinal strain of the RV from 4-chamber views using a 6-segment model (Figure A); (b) the interval from QRS onset to peak strain for each segment. All intervals were corrected for heart rate [corrected=raw/(RR)^{1/2}]. We used the standard deviation of the 6 segmental intervals (SD6-RV) as a global index of RV dyssynchrony.

Results: SD6-RV was significantly higher in PHT patients compared to controls (65±21 ms vs. 28±14 ms, $p < 0.001$). In addition, peak global RV strain was both lower (-15.7±4.3% vs. -22.2±2.6%, $p < 0.001$) and delayed (408±36 ms vs. 375±31 ms, $p = 0.002$) in PHT patients compared to controls. Among standard and 2DS indices of RV function, only SD6-RV was found to entail discriminative value regarding functional class in the PHT population (Figure, B). No correlation was found between SD6-RV and QRS duration in these patients ($\rho = -0.1$, $p > 0.5$).

Conclusion: Comprehensive evaluation of RV function by 2DS reveals the presence of significant right intraventricular dyssynchrony in patients with PHT and RV dysfunction. Importantly, this dyssynchrony appears to exert a pivotal effect on the functional capacity of these patients.



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Does cardiac resynchronization therapy improve right ventricular ejection fraction?

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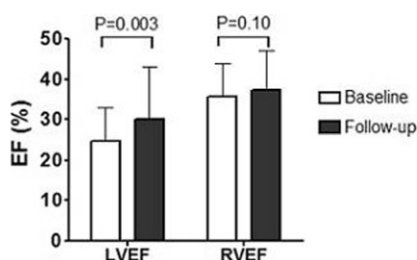
Background: It is now well established that cardiac resynchronization therapy (CRT) improves left ventricular ejection fraction (LVEF) in patients with heart failure. However, the effect of CRT on right ventricular function has not been well studied.

Methods: Twenty-eight patients (23 men, age 71±9 years) with a standard indication for CRT (LVEF < 0.35, QRS width > 120 ms, NYHA III-IV) underwent radionuclide angiography just after device implantation and after at least 6 months' follow-up. LVEF and RVEF were measured using gated equilibrium radionuclide angiography by a single observer.

Results: After a mean follow-up of 10±5 months, LVEF improved significantly (mean improvement 5.3±8.5% in absolute terms, $P = 0.003$). However, RVEF was not significantly improved (mean improvement 1.6±4.7% in absolute terms, $P = 0.10$, see figure below). Results did

not differ when patients were divided into subgroups with RVEF < 0.35 ($n = 12$) or > 0.35 ($n = 16$) at baseline.

Conclusion: As opposed to improving LVEF, CRT does not improve RVEF, irrespective of baseline right ventricular function.



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Assessment of the profile of superresponders to cardiac resynchronization

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Introduction: Cardiac resynchronization therapy (CRT) is now an established treatment in patients with heart failure refractory to medical treatment and cardiac dyssynchrony. The rate of non responders is variable but remains relatively high reaching 30%.

Aim: The aim of this study was to compare the clinical, electrical and echocardiographic characteristics of super responders to CRT to non super responders.

Methods: 24 patients with a mean age of 63.4±11 years followed up for heart failure NYHA III-IV with cardiac asynchronism refractory to medical treatment underwent biventricular pacing. Patients were grouped according to their LVEF response to CRT. Super responders were those who increased LVEF ≥ 15%, and non super responders had a LVEF response < 15%.

Results: After 6 months of CRT, we noticed a significant improvement of the functional status and a significant increase in the left ventricular ejection fraction. Four patients (21%) were considered as super responders. There was no difference between super responders and non superresponders regarding age, aetiology of HF, NYHA class, QRS width and LVEF at baseline. Non super responders had baseline left ventricular end diastolic and systolic diameters significantly higher than super responders. The inter-ventricular delay was significantly higher in super responders. The lateral wall was the latest wall in all super responders and in 77% of the non super responders.

Conclusion: A better selection of patients for CRT may increase the rate of patients responders to this therapy. In our study patients having less dilated left ventricles had a better response to CRT. This result emphasizes that CRT should be indicated before irreversible myocardial damage. Lateral wall asynchrony seems to be a good predictive factor of super responders. This underlines the importance of stimulating the latest wall. Further studies are needed to determine preimplant and perprocedure parameters allowing better selection of short and midterm responders to CRT.

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Clinical benefit of Cardiac Resynchronization Therapy with Cardioverter-Defibrillator function

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Background: Cardiac resynchronization therapy (CRT) has been shown to improve symptoms and quality of life as well as survival in patients

with chronic heart failure (CHF). The use of implantable cardioverter-defibrillators (ICD) resulted in a significant reduction of sudden cardiac death in this patient collective. Thus, we aimed to evaluate the clinical benefit of CRT with ICD function (CRT-D) for primary prevention of sudden cardiac death in patients with CHF.

Methods: Since January 1999, overall 242 CRT systems were implanted in our institution, of which 70 included ICD function. In the CRT-D collective, 41 suffered from ischemic CHF (59%) and 29 from non-ischemic CHF (41%), and 22 patients (31%) had documented atrial fibrillation (9 permanent and 13 paroxysmal). In this analysis concerning primary prevention in CHF, we excluded all sudden death survivors (11 patients). In the remaining 59 patients with CRT-D, ventricular arrhythmias were documented in 10 patients (17%) and inducible in further 14 patients (24%).

Results: Within a follow-up period of 2.0 ± 1.3 years, 31 patients with singular CRT died, whereas only 3 patients with CRT-D died within a follow-up period of 1.7 ± 1.4 years (18% versus 5%, $p < 0.01$). One year mortality was 8% versus 3% ($p = \text{NS}$). Anti-tachycardic pacing for ventricular arrhythmias was found in 22 patients (37%). Appropriate defibrillation was recorded for 14 patients (23%); of which 9 also underwent inappropriate shocks, whereas 1 patient underwent inappropriate defibrillator discharges only. Thus, inappropriate shocks were found in 10 patients (17%).

Conclusions: Patients with chronic heart failure benefit from CRT with ICD function, and therefore may be considered for all patients targeted for CRT. Nevertheless, the problem of inappropriate defibrillator discharges is still of concern.

MONDAY, 25 JUNE 2007, 15:30–16:30

Poster Area

New indication for cardiac resynchronisation therapy and prediction of response

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Long-term effects of cardiac resynchronization therapy in patients with narrow QRS: the InSync/InSync ICD Italian Registry

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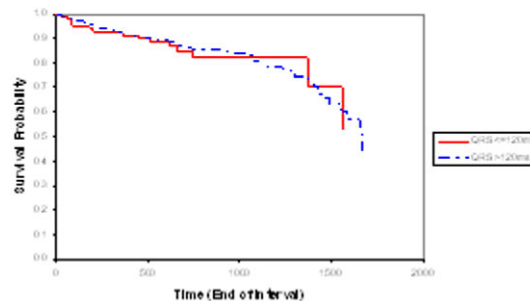
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Background: Cardiac resynchronization therapy (CRT) is recommended for patients with symptomatic heart failure presenting QRS >120 ms, as marker of ventricular dyssynchrony. The effects of CRT in narrow QRS patients (QRS ≤ 120 ms) are still controversial. Aim of this study was to evaluate the effects of CRT in patients with QRS ≤ 120 ms (nQRS) with respect to patients with QRS >120 ms (IQRS).

Methods: The study population consisted of 1971 patients (217 nQRS) consecutively implanted with biventricular devices. They were enrolled in the InSync/InSync ICD Italian Registry and underwent baseline evaluation and periodical follow-up visits. We estimated the clinical outcome after 12-month of CRT, and the mortality data.

Results: After 12 months of CRT, NYHA Class significantly improved in both groups (IQRS: from 2.9 ± 0.6 to 2.1 ± 0.7 ; nQRS: from 2.9 ± 0.6 to 2.0 ± 0.7), ejection fraction increased (IQRS: from $26 \pm 8\%$ to $34 \pm 11\%$; nQRS: from $28 \pm 8\%$ to $37 \pm 11\%$), left ventricular end-diastolic diameter decreased (IQRS: from 69 ± 9 mm to 66 ± 10 mm; nQRS: from 68 ± 9 mm to 66 ± 9 mm), as well as left ventricular end-systolic diameter (IQRS: from 59 ± 11 mm to 54 ± 12 mm; nQRS: from 57 ± 8 mm to 54 ± 10 mm). At a median follow-up of 16 months, the all-cause mortality resulted similar in the two groups (log-rank test $p = 0.678$).

Conclusions: Our results indicate that CRT induced similar benefits in both groups at long-term follow-up, resulting in comparable effects on mortality.



Kaplan-Meier

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Cardiac resynchronization therapy and chronic atrial fibrillation: a single center experience over a long-term follow up

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Background: Cardiac resynchronization therapy (CRT) is an effective treatment in patients (pts) with refractory heart failure (HF), ventricular dyssynchrony and sinus rhythm. The role of this therapy in pts with chronic atrial fibrillation (AF) remains controversial. The purpose of our study was to assess long-term clinical and hemodynamic effects of CRT in pts with refractory HF and chronic AF.

Methods: In a population of 105 pts treated with CRT, since 2003 18 pts (14 males, mean age 68 ± 8 yrs) with NYHA class III and IV, prolonged QRS complexes (either spontaneous or pacing-induced) and chronic AF were successfully implanted with biventricular devices (15 ICDs and 3 PMs). HF etiology was ischemic in 33% and non ischemic in 67% of pts. In 44% of cases CRT was a de-novo implant; in 56% it was an upgrading from pre-existing pacing devices.

Results: During a mean follow up of 16 ± 13 months (range 2–40), a significant improvement of NYHA class (from 3.2 at baseline to 1.9; $p < 0.05$), of quality of life, assessed by the Minnesota Living with Heart Failure Questionnaire (mean score from 49.7 to 27.1; $p < 0.005$) and of 6 minute hallwalk distance (from 290 to 325 metres; $p < 0.05$) was observed. QRS width decreased as well (from 171.2 ms at baseline to 136.5 ms; $p < 0.01$). Transthoracic echocardiography showed an improvement of left ventricular ejection fraction (from 24.5 to 30.2%; $p = 0.005$), of mitral and tricuspid regurgitation (respectively from semiquantitative mean score of 2.1 to 1.5, $p = 0.02$; and from mean score of 1.6 to 1.3; $p = 0.05$) and a significant decrease of left ventricular end-diastolic and end-systolic volumes (respectively from 198 to 162 ml and from 149 to 112 ml; $p < 0.02$). In 6 pts sinus rhythm was restored after defibrillation at the implant test; in 5 of them AF recurred during the first month of follow up. The percentage of “responders” (pts that improved at least 1 level of NYHA class after 6 months of CRT) was 78%; 2 pts died, 1 after stroke during the first year of follow up, and 1 for refractory HF during the second year of follow up.

Conclusions: Our data suggest that CRT improves functional class, exercise tolerance and left ventricular function also in HF pts with chronic AF, even during relatively long-term follow ups.

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Bundle branch block patterns and mortality in hospitalized patients with heart failure

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Background: Widened QRS interval is associated with increased mortality in patients with heart failure (HF). However, the prognostic signifi-

cance of the type of bundle branch block (BBB) pattern in these patients is unclear.

Objectives: To examine the relationship between outcome and type of BBB pattern in hospitalized HF patients.

Methods: We analyzed the data of 4102 patients with HF hospitalized during a prospective national survey. The current study investigated the association between BBB type and 1-year mortality in 3737 patients without a pacemaker.

Results: Right BBB (RBBB) was present in 381 (10.2%) and left BBB (LBBB) in 504 (13.5%) patients. Both RBBB and LBBB were associated with increased 1-year mortality by univariate analysis. [Odds ratio (OR) 1.44, 95% confidence interval (CI) 1.15–1.81, and 1.20 (0.97–1.47), respectively]. However, after adjusting for multiple variables there was a trend for increased mortality in the RBBB group only (adjusted OR 1.21, 95% CI 0.94–1.56, $p=0.14$). RBBB was an independent predictor of mortality (adjusted OR 1.62, 95% CI 1.12–2.33) in patients with systolic HF. This correlation was stronger in patients with lower left ventricular ejection fraction, and was also maintained in patients without acute MI. LBBB was not related to mortality in patients with either systolic HF or preserved systolic function.

Conclusions: In hospitalized patients with systolic HF, RBBB but not LBBB is an independent predictor of mortality. Further studies are needed to explore the potential role of cardiac resynchronization therapy in patients with HF and RBBB.

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Invasive measurements of electrical asynchrony induced by right ventricular stimulation in dilated and in normal hearts

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Objective: To measure the interventricular conduction delay in patients with structurally normal hearts and in patients with dilated cardiomyopathy (DCM).

Methods: 43 patients were admitted for an electrophysiological study. Six with DCM (ischemic and idiopathic) and 37 with structurally normal hearts and QRS below 120 ms were analyzed. Intracardiac electrograms were recorded from the bundle of His (H), the right ventricular apex (RV), and the ventricular signal of the coronary sinus at the posterolateral wall (LV). The following conduction times were measured: from H to the first ventricular signal (H-V), from H to LV, from RV to LV, from the initial surface QRS deflection to LV (QRS-LV), and from the stimulus artifact during RV pacing to LV (S-LV).

Results: See table. The baseline QRS duration and paced QRS were significantly longer in DCM vs. normal hearts. All invasive measurements except for the H-V were significantly longer in the DCM group. In the structurally normal heart group, the stimulation from the RV apex produced a wide range of delays to the LV, with some patients showing delays similar to those with DCM.

Conclusions: Invasive measurements of conduction times to the left ventricle and QRS duration are significantly longer in patients with DCM. Stimulation from the RV apex in patients without structural abnormalities may induce a conduction delay similar to that observed in patients with DCM. This substantial effect of RV stimulation could explain the adverse outcomes of permanent pacing in the RV in some patients with previously normal hearts and may be used to identify a subgroup of patients for whom RV pacing could be harmful.

	Basal QRS	Paced QRS	H-V	H-LV	RV-LV	QRS-LV	S-LV
Normal	84±15	152±17	50±9	95±23	21±20	44±23	111±19
DCM	112±34	173±20	56±9	129±16	68±48	92±35	140±30
p value	0.002	0.007	0.2	0.001	0.000	0.000	0.001

Time values expressed as mean±SD in milliseconds.

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Right ventricular apical pacing can induce left ventricular dyssynchrony: a “Speckle Tracking” echocardiography study

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Background: The detrimental effects of permanent right ventricular (RV) apical pacing may be related to the induction of left ventricular (LV) dyssynchrony. The purpose of the present study was to assess the effects of permanent RV pacing on LV function and LV dyssynchrony, as assessed with ‘speckle tracking’ strain analysis.

Methods: Fifty-eight patients (33 men, age 61 ± 11 years), treated with His bundle ablation and pacemaker implantation, were studied. At baseline and after a minimum of 1 year RV apical pacing, NYHA functional class was assessed and an echocardiogram was obtained. Novel ‘speckle tracking’ radial strain analysis was applied to standard LV short-axis images, to assess the effect of RV pacing on time-to-peak radial strain of 6 standard LV segments. LV dyssynchrony was defined as a time difference ≥ 130 ms between time-to-peak radial strain of the anteroseptal and posterolateral segments.

Results: At baseline, similar time-to-peak strain for each of the 6 segments was observed (mean 371 ± 114 ms). In contrast, after a mean of 3.8 ± 2.0 years of RV apical pacing, there was a marked heterogeneity in time-to-peak radial strain of the 6 segments. In 33 patients (57%) LV dyssynchrony was present after long-term RV apical pacing. In these patients, a deterioration of LV systolic function (LVEF from $48 \pm 5\%$ to $39 \pm 10\%$, $p < 0.01$) and NYHA class (from 1.8 ± 0.7 to 2.4 ± 0.7 , $p < 0.01$) was observed. In 11 patients “upgrade” of the conventional pacemaker to a biventricular pacemaker resulted in partial reversal of the detrimental effects of permanent RV pacing.

Conclusion: Speckle tracking radial strain revealed that permanent RV pacing induces heterogeneity in time-to-peak strain within the left ventricle, resulting in LV dyssynchrony in 57% of patients. LV dyssynchrony was associated with deterioration in LV systolic function and NYHA functional class. Biventricular pacing may reverse the adverse effects of RV pacing.

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Effect of different right ventricle pacing places on left ventricular electro-mechanical time

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Cardiac stimulation is a primary electrophysiological process that causes mechanical changes. Previously, the effect of different RV pacing places on LV lateral wall activation was shown measured by coronary sinus registry (CSR). The aim of the present study is the comparison between electrical and mechanical changes measured by both CSR and ultrasound tissue doppler (UTD).

Methods: A total of eighty four consecutive patients, 62 with narrow QRS (nQRS) and intraventricular conduction disturbances (13 with LBBB and 9 with RBBB) referred for electrophysiologic evaluation (EP) were analyzed. Patients were paced from RV apex (RVA p), His zone (HIS p), and right ventricular outflow tract (RVOT p), at 600 ms pacing rate with double threshold. In all of them we measured QRS duration, R-wave to LV time (R-LV) from the beginning of surface QRS to distal ventricular deflection which was recorded from coronary sinus. UTD was also recorded in 20 patients (8 with narrow QRS, 8 with LBBB and 4 with RBBB) to evaluate time between septum and left ventricle lateral wall (TIV). Both methods were compared. Correlaton coefficient: 0.84.

Conclusion: (1) Electrical measurement by CSR has an excellent correlation with mechanical measurement by UTD; (2) CSR during EP study is a simple method to evaluate candidates for resynchronization therapy or to test alternative pacing places. (3) His pacing zone has the lowest

electromechanical activation time, in patients without intraventricular conduction disturbances.

	84 R-LV by CSR (ms) (p<0.01)				20 R-LV vs TIV (ms)							
	SR	RVA P	RVOT P	HIS p	SR	RVA p	RVOT p	HIS p				
	R-LV	R-LV	R-LV	R-LV	R-LV	TIV	R-LV	TIV				
nQRS (n=62)	50.7±6.7	110±17.7	113±17.8	58±11	57.25	153.1	117	201.8	113.8	203.3	57.5	147.5
LBBB (n=13)	121±30	133±30	125±27	70±14	128	262.5	140.1	266.8	125	268.3	73	189.4
RBBB (n=9)	60.8±15	120±12.1	114±20	68±19	70.2	152.5	65	223.7	122.2	228.7	83	144.2

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Biventricular pacing in right bundle-branch block

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Introduction: Biventricular pacing improves systolic function and symptoms in patients with heart failure, systolic dysfunction and left bundle-branch block. However its value in right bundle-branch block patients (RBBB) is still unknown.

Patients and Methods: We analyzed 180 patients who had a cardiac resynchronization implanted. RBBB was observed in 20 of these patients. All of them had indication for pacemaker or ICD, functional class (NYHA) II to IV, LVEF <40%, left ventricular end-diastolic volume (LVEDV) >55 mm and QRS >140 ms. The average patient age was 71.3±5.8 years, 5 patients (25%) were in NYHA II and 15 (75%) in NYHA III. 9 patients (45%) had ischemic cardiomyopathy and 11 (55%) dilated cardiomyopathy. 7 patients (35%) underwent implantation of a pacemaker and 13 (65%) an ICD. 8 patients (40%) showed RBBB and 12 (60%) RBBB and left anterior hemi-block. One patient needed heart transplantation due to heart failure during follow-up.

Conclusions: Biventricular pacing improves ventricular function and symptoms in systolic dysfunction and right bundle-branch block population.

Results

	Baseline	6 months	p
NYHA	2.74±0.45	1.6±0.32	0.028
LVEF	34±7.6	37.1±5.6	0.12
LVEDV	64.7±11	61±8.8	0.047
6-min walk	265±22	315±45	0.022
QOL score	44.3±8.5	11±11	0.02

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Improvement of congestive heart failure by upgrading of permanent right ventricular apical pacing (DDD) to cardiac resynchronization therapy

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Right ventricular apical (RVA) pacing induces chronic LV remodeling, including asymmetric hypertrophy and redistribution of cardiac mass, mitral regurgitation, increased left atrial diameter, reduced EF, and may explain the increased risk for heart failure (HF) hospitalization.

Aims: To evaluate the clinical response of patients with RVA pacing upgraded to cardiac resynchronization therapy (CRT).

Methods: Twenty-eight consecutive patients (mean age 68, mean EF 0.28) with RVA pacing (DDD) and a very high-risk substrate (low EF, MI, a history of symptomatic HF) were upgraded to CRT-D. Eighteen patients (64.3%) had DDD/Cum%VP ≥40 and 10 patients (35.7%) had DDD/Cum%VP ≤40. All patients had a wide paced QRS (226±34 ms). Clinical and echocardiographic parameters were recorded prior to, at 3 and at 6 months after CRT upgrading.

Results: Upgrading of RVA pacing to CRT resulted in a significant improvement in EF, mitral regurgitation degree, and in measures of electrical and mechanical synchrony. NYHA functional class was also significantly

improved (from 3.1±0.7 at 2.3±0.6, p<0.0001). The 6-minute walking distance increased from 202±107 m to 354±115 m (P<0.005). No fatal event (death due to MI or HF, and SCD) occurred during the follow-up. 9 patients (32.2%) received an appropriate treatment for SVT, no ventricular fibrillation was documented.

Conclusions: CRT has become a routine option for patients with drug refractory HF and intraventricular conduction delay. Patients with prior RVA pacing (DDD) and a very high-risk substrate had a dramatically increased risk of HF hospitalization that could be attributed to ventricular and AV desynchronization. Upgrading to CRT by the addition of a coronary sinus lead is now considered a valid option for patients with intractable HF and wide QRS with permanent RVA pacing.

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Can cardiac resynchronization therapy defer or prevent heart transplantation?

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Background: Heart transplantation (HT) is the gold standard therapy for end-stage chronic heart failure (CHF). Recently, cardiac resynchronization therapy (CRT) has become an additional therapy, on top of an optimized medication, for selected patients (pts) with severe CHF and a widened QRS interval.

Aim: To evaluate the impact of CRT in pts with severe and advanced CHF, regarding the quality of life and the need for HT.

Methods: Retrospective analysis of a database containing 30 pts with severe CHF, who underwent CRT between June/2000 and November/2004 at our institution. Pts were mainly of male gender (73%), with mean age of 54.1±10.0 years. Most of the pts had idiopathic dilated cardiomyopathy (80%). All of them had QRS durations wither than 120 ms on the baseline ECG and were under optimized medical therapy. They all met the accepted criteria for potential cardiac transplant candidates [age <65 years old, left ventricular ejection fraction (LVEF) < 35%, NYHA functional class III or IV, maximum peak VO₂ <14 ml/Kg/min, more than two hospitalizations due to decompensated CHF] at the time of biventricular pacing implant. We evaluated the NYHA class, the Minnesota living with heart failure questionnaire (MLWHFQ) score and the LVEF, both at the baseline and during the follow-up period.

Results: Mean follow-up time was 25.5±10.7 months (M). Twenty pts (67%) had a sustained clinical and echocardiographic improvement (MLWHFQ score 57.0±19.2 at baseline vs 27.5±15.1 at 12 M, p=0.01; NYHA class 3.0±0.4 at baseline vs 1.2±0.5 at 12 M, p=0.002; LVEF 22.1±3.0% at baseline vs 44.0±10.0% at 12 M, p=0.003), which removed them from the transplantation list. Six pts (20%) underwent HT and 4 pts (13%) died. These two last groups of pts experienced a mild improvement from baseline until 6 M (MLWHFQ score 72.0±9.9 at baseline vs 63.7±13.8 at 6 M, p=n.s.; NYHA class 3.2±0.4 at baseline vs 2.1±0.7 at 6 M, p=0.02; LVEF 20.8±11.7% at baseline vs 26.0±7.0% at 6 M, p=n.s.). Then, at 12 M, they maintained mild clinical improvement (MLWHFQ score 56.2±24.0 and NYHA class 1.7±0.9) but the LVEF had a progressive decline (24.0±4.0%).

Conclusions: In our study, CRT showed a beneficial effect in pts with severe CHF, which allowed the prevention or deferment of heart transplantation. This suggests that pts with CHF and a widened QRS should be evaluated for CRT before being listed for heart transplantation.

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Predictors of a positive response to biventricular pacing in patients with severe heart failure and ventricular conduction delay

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Introduction: Cardiac resynchronization therapy (CRT) is now recommended in patients with ejection fraction < 35%, QRS width > 120 ms and NYHA functional class III or IV despite optimal medical therapy. We

aimed to define demographic, clinical and electrocardiographic predictors of a positive clinical response to CRT.

Methods: This prospective study included 100 consecutive patients (mean age: 66 ± 11.7 years, 78% men) fulfilling the recommended criteria. They were implanted with a CRT device. Demographic, clinical, 2-dimensional echocardiographic and electrographic parameters were measured at baseline and after 6 months of simultaneous biventricular pacing. A positive clinical response to CRT included: alive status, no hospitalisation for decompensated heart failure, improvement of at least one NYHA functional class.

Results: At the end of follow-up, 12 patients were dead (1 sudden death, 3 non cardiovascular deaths, 8 deaths for end-stage heart failure). In the survivors ($n=88$), there was a significant improvement in NYHA class (3.1 ± 0.3 versus 2.2 ± 0.4 ; $p < 0.01$) and left ventricular ejection fraction (26.77 ± 5.79 versus $32.75 \pm 8.64\%$; $p < 0.05$). 71% of the patients were classified as responders to the therapy. After 6 months of biventricular pacing, the ejection fraction was significantly higher ($p=0.035$) in the responders versus the non responders. Multivariate analysis identified 3 independent predictors of a positive response to CRT: the origin of the cardiomyopathy (more non responders in patients with ischemic heart disease; $p=0.043$), the presence of a wider QRS before implantation ($p=0.017$) and the narrowing of the QRS width after implantation ($p=0.037$).

Conclusions: 71% of patients had a positive clinical response following 6 months of biventricular pacing. The origin of the cardiomyopathy, the pre-implantation QRS width, and narrowing of the QRS width after implantation were identified as independent predictive factors of positive response.

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Six minutes walking test predicts long-term cardiac death in patients referred to cardiac resynchronization therapy for chronic heart failure

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Background: Cardiac resynchronization therapy (CRT) has been proven efficient in patients with chronic heart failure (CHF) associated to electrical dyssynchrony. CRT reduces mortality in patients with advanced symptoms of CHF, but long-term predictors of mortality remain poorly investigated.

Objective: The aim of this study was to determine basal long-term predictors of mortality in patients with CHF treated with CRT.

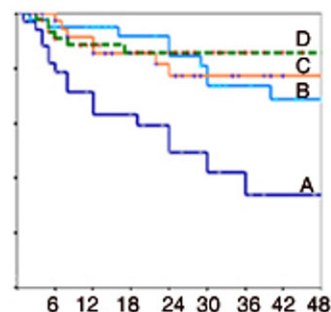


Figure 1

Methods and Results: A total of 155 consecutive patients with moderate to severe CHF (82% men, mean age 69 ± 8 years, NYHA class: II 22%, III 73.5%, IV 4.5%) referred to CRT were included. The baseline evaluation included clinical history, performance of the 6 minutes walking test (6MWT) and echocardiographic study. Patients with cardiac or noncardiac diseases limiting the ability to perform a 6MWT were excluded. A total of twenty four patients (15.5%) died of cardiovascular causes, and 1 patient underwent heart transplantation during a mean follow-up of 24.4 ± 18.1 months. Univariable analysis showed NYHA functional class, distance walked in 6MWT, male gender, left ventricle (LV) end-diastolic

diameter and LV ejection fraction were significantly related to mortality. Multivariable Cox regression showed that LV ejection fraction (OR 0.91 (95% CI: 0.84–0.98) $p=0.008$) and walked distance in 6MWT < 225 m (OR 5.6 (95% CI: 1.2–25.3) $p=0.026$) were independent predictors of mortality. Figure 1: Kaplan–Meier showing accumulated survival to cardiovascular death according to 6MWT quartiles: < 225 m (a), 225–310 (b), 310–400 m (c) and > 400 m (d); Log-rank test $p < 0.001$.

Conclusions: Basal functional capacity measured through 6WT and the LV ejection fraction were predictors of mortality in moderate to severe CHF patients despite being submitted to CRT.

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Role of tissue doppler in the selection of patients with standard indication to CRT

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Purpose: utility of tissue Doppler imaging (TDI) to select patients who could benefit of CRT.

Two-dimensional color TDI in 20 patients with heart failure (middle age 68.4 ± 8.3 years, 95% males, 55% ischemic, 2 with permanent atrial fibrillation, 18 with left bundle branch block, 2 with pacemaker) and standard indication to CRT (ejection fraction EF $> 35\%$, QRS > 120 ms, NYHA functional class 3–4) was performed. Traditional evaluation with physical examination, ECG and standard echocardiography was done. With a Vivid 7 General Electric TDI was acquired as digital loops in the apical four-chambers view. During off-line analysis a time to peak systolic velocity was measured in 8 segments (basal and medial septal, lateral, inferior and anterior walls). A difference among any times > 100 ms was considered index of intraventricular dyssynchrony. The atrioventricular interval was optimized using Doppler echocardiography on the first day after implantation of the biventricular device. At least 3 months after CRT new clinical evaluation and color TDI were performed. In the whole group of patients after CRT an improvement of the mean NYHA functional class (from 3 ± 0.4 to 1.9 ± 0.4 $p < 0.001$) and of EF (from 26.1 ± 5.5 to 35.8 ± 8.1 $p < 0.001$) was observed. The index of intraventricular dyssynchrony varied from 115.6 ± 38.8 to 85.4 ± 39.5 $p < 0.05$. The mean duration of the QRS varied from 169.1 ± 28.1 to 145 ± 22.9 ms ($p < 0.05$). In 5 patients (25%) an improvement of at least 5 percentage points of the EF was not observed (not responder). Age, etiology, NYHA functional class, EF, mean QRS of these patients before CRT didn't differ from responders. Only the degree of intraventricular dyssynchrony measured with TDI was different among the 2 groups (103.4 ± 38.8 ms responder vs 42 ± 41.1 ms not responder $p < 0.05$). 4 of the 5 patients not responder had not intraventricular dyssynchrony.

Conclusion: TDI is able to select patients with marked intraventricular dyssynchrony that can benefit of CRT.

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Myocardial performance index and left ventricular dyssynchrony

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Introduction: In spite of the widespread use of cardiac resynchronization therapy (CRT), up to 30% of patients do not respond to it, therefore the criteria to identify which patients (P) with heart failure (HF) would benefit more from CRT, is continuously being reviewed.

Objective: To analyze what proportion of P those qualify for CRT, do not present echocardiographic criteria of dyssynchrony, but constitute a population with different characteristics; as well as to analyze the response after CRT.

Methods: Prospective study of patients with HF who met CRT criteria according to clinical practice guidelines (QRS > 120 ms + NYHA III-IV + left ventricular ejection fraction LVEF < 0.35) sent for echocardiogram during the selection process for CRT. Echocardiographic, morphologic

and functional characteristics were analyzed, to define which parameters would be related to the presence of intraventricular (DTI septum-lateral wall delay >60 ms), interventricular (aorto-pulmonary delay >40 ms) and atrio-ventricular (diastolic filling/R-R' <40%) dyssynchrony. Echocardiographic response after CRT was also analyzed.

Results: 45 P were included (26.7% women, 62±11 years). 31.1% showed ischemic etiology. The average QRS was 165±18 ms. All patients were on ACE inhibitor/ angiotensin II receptor blocker treatment, 95% received beta-blockers and 90% spironolactone. 31 P (68.9%) presented intraventricular, 29 (64.4%) interventricular and 11 (24.4%) atrio-ventricular dyssynchrony. P with intraventricular and interventricular dyssynchrony displayed a worse Myocardial Performance Index (MPI) (1.12±0.18 vs. 0.88±0.11; $p < 0.001$; and 1.12±0.18 vs. 0.91±0.14, $p = 0.003$). No differences were found in the rest of the clinical and echocardiographic parameters analyzed (diameters, volumes, ejection fraction, left ventricular size, mitral regurgitation, pulmonary pressure, and transmitral filling pattern), neither when analyzing atrio-ventricular dyssynchrony. CRT was performed in 30 patients. Significant improvement was observed of the MPI (0.78±0.13 vs. 1.11±0.18; $p = 0.037$), end-systolic left ventricular volume (ESV) (77.5±39.9 vs. 102.0±42.4 ml/m²; $p = 0.021$) and EF (30.4±8.0 vs. 21.7±6.6%; $p = 0.050$).

Conclusions: (1) More than 30% of patients, who met criteria for CRT according to the clinical guidelines, do not present echocardiographic parameters of dyssynchrony. (2) The echocardiographic parameters of dyssynchrony identified patients with worse MPI. (3) CRT is associated to improvement of the MPI, ESV and EF.

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Endocardial electric parameters of cardiac resynchronization therapy in normal hearts and dilated cardiopathy

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Aim: To compare the electrical conduction differences between a group of heart failure patients candidate to CRT and a group of patients with standard indication for ventricular pacing in normal hearts.

Methods: Group 1 was composed by 76 patients (23 female, mean age 69±9 years) undergoing CRT therapy for advanced heart failure. Control group was composed by 13 patients without cardiomyopathy and with standard indication for ventricular pacing implanted with biventricular devices following Biopace (SJM) Study randomization's criteria. We measured the interval between spontaneous electrical signal obtained by RV and LV, between spike and opposite ventricular signal (Rp-Ls and Lp-Rs), and 12 leads QRS width.

	Group 1 – CMP	Group 2 – Controls	P
LVEF (%)	27.2±5.6	58.4±10	0.0001
LVEDVi (ml/mq)	103.9±30.1	56.3±21.4	0.0001
QRS (ms)	161.3±26.5	120±35	0.0001
IEGM Rsen–Lsen (ms)	87±44	26.7±13	0.0001
QRS left paced (ms)	191.7±40	200.8±43.6	0.582
IEGM Lpac–Rsen (ms)	123.8±33.9	93.8±23.1	0.005
QRS right paced (ms)	203±35	198±36	0.577
IEGM Rpac–Lsen (ms)	130.2±38.0	101.3±22.2	0.013
QRS biventricular (ms)	140.7±23.9	137.2±18.4	0.591
Q–Po (ms)	94.0±43.0	68.2±15.8	0.196
Q–Ao (ms)	131±41	78.4±23.6	0.007
Q–Ao – Q–Po (ms)	37.5±38	10.2±8.7	0.121
Q–PL (ms)	179.3±53.7	72.0±12.1	0.0001
Q–Siv (ms)	121±59.5	72.6±24.2	0.087
Q–PL – Q–Siv (ms)	58.4±51.8	0.6±12.6	0.018

IEGM, intraventricular electrocardiogram; Rpac/Rsen, pacing or sensing from RV lead, Lpac/Lsen, pacing or sensing from LV lead.

Results: See the table.

Conclusions: Patients affected by symptomatic DCMP, with severe impaired left ventricular systolic function, intraventricular and interventricular desynchronization with prolonged QRS duration, present a significant prolongation of spontaneous intraventricular conduction time

measured with endocardial leads, and a significant prolongation of paced conduction time not revealed by surface QRS.

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Electrophysiology study before cardiac resynchronization device implantation: Pre-implantation coronary sinus cannulation offers advantages for cardiac resynchronization procedural outcome

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Background: Routine electrophysiology study (EPS) is no longer required before every cardiac resynchronization device (CRT) implantation, although its role in risk stratification still can be important in selected cases. On the other hand, failure of cannulation of the coronary sinus (CS) during CRT implantations is the major obstacle for procedural success.

Objectives: In this study we tested the hypothesis that EPS conducted from the right jugular vein allowing cannulation of the CS (CSC) before CRT implantation has positive impact on acute CRT procedural outcome.

Methods: 112 consecutive patients (median age: 54 years; range: 20 to 79 years) who received CRT (n=45) or CRT-D (n=67) with symptomatic (NYHA II–IV) dilated (n=57) or ischemic (n=55) cardiomyopathy were enrolled into this study and were divided into two groups. 45 patients were enrolled into group I (CRT n=11, CRT-D n=25) in whom pre-implantation EPS was not performed. The remaining 67 patients (CRT n=30, CRT-D n=37) underwent CSC (2–5 days before the implantation) from the right jugular vein were in group II. As part of the EPS cannulation of the CS was attempted with standard EP catheters for a maximum of 20 minutes. Patients with unsuccessful pre-implantation CSC were referred directly for epicardial left ventricular lead implantation via mini-thoracotomy. CRT implantation success rate, need for epicardial lead placement (EPIEP), procedure time (PT) and fluoroscopy time (FT) were compared between groups.

Results: The overall percutaneous implantation success rate was higher in group II (group I: 89.4%, group II: 98.5%; $p < 0.001$). Patients who received EPIEP were equally distributed in the two groups (group I: 4 patients (8.8%); group II 4 patients (5.9%); $p = \text{NS}$). In group I. PT and FT were significantly longer than in group II (119.5±43.77 min. vs. 77.79±26.44 min, $p = 0.001$ and 36.18±19.05 min vs. 17.46±10.23 min; $p < 0.001$, respectively).

Conclusions: (1) Pre-implantation EPS with CSC has a significant impact on procedural outcome. (2) CSC during the pre-implantation EPS results in a shorter procedure and fluoroscopy time and higher implantation success rate.

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Vector-Cardiography predicts haemodynamic improvement by cardiac resynchronizations therapy

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Cardiac resynchronization therapy (CRT) is an accepted treatment for congestive heart failure (NYHA III–IV), but a substantial number of patients does not respond to therapy. LBB, QRS width and echo-cardiographic measurements are parameters for indication, but are not consistent with hemodynamic response. A new method, based on Vector-Cardiogram (VCG)-Analysis can deliver additional information on areas with late excitation, with slow or fast depolarization speed, to identify responder. The aim of this study is to validate the effectiveness of VCG-based analysis in predicting the CRT Responders and compare the results with hemodynamic data.

Methods: 91 pts (67 male, 62.06 years, QRS width 158±21.5 ms, EF 23.5%, LVEDD 72.1 mm) received a CRT pacing system. The VCG was obtained at baseline (CRT off) and the evaluation of the VCG were blinded and performed offline. Hemodynamic parameters such as pulse pressure (PP) and contractility (dp/dt) were intraoperative measured.

Hemodynamic improvement was measured after CRT therapy was initiated and the patients were subsequently divided into two responder groups (RG) and one non-responder group (NR). RG 1: PP > 10%, dp/dt > 20%, RG 2: PP 5–10%, dp/dt 10–20%, NR: PP < 5%, dp/dt < 10%.

Results: In all 91 pts we were able to perform the VCG analyses. In 77 out of 91 pts (84.6%) we found a good correlation between the hemodynamic improvement and the predicted classification drawn from the VECG. 16 pts did not respond to therapy, 13 pts out of this 16 were identified by VCG analyses.

Conclusions: Preliminary results of the VECG show a good correlation with the invasive hemodynamic parameter in 84.6% of pts. A further improvement and automation of the algorithm could help to make the VCG-method a standard procedure.

MONDAY, 25 JUNE 2007, 15:30–16:30

Poster Area

Technical aspects of cardiac resynchronisation therapy device implantation

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Balloon angioplasty of hypoplastic coronary veins allows the implant of the left ventricular electrode for cardiac resynchronization therapy

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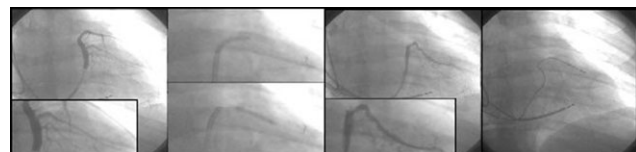
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Introduction and Aim: Cardiac resynchronization therapy (CRT) has demonstrated to reduce morbimortality in patients (p) with heart failure. For this purpose, it is necessary to implant an electrode in a vein of the lateral region of the left ventricle (LV), which may have a borderline diameter to allow its placement. The use of a balloon catheter has proven to be useful in dilation of a focal stenosis at the target vein. The aim was to analyze our experience with balloon angioplasty of hypoplastic coronary veins.

Methods: In 14 (8%) out of 170 p to whom we implanted a CRT device, the veins in the LV free wall were hypoplastic and, thus, unsuitable for the implant. In 6 of these, a coronary balloon catheter was used to dilate the vein, as there was no suitable antero-lateral one and surgical implantation had been discarded. Veins with a diameter < 2 mm were considered hypoplastic. Successful venoplasty was defined as stable placement of the lead in the target vein.

Results: The diameter of the target vein was 1.7 ± 0.14 mm (1.5–1.8). In all cases, a 3 mm coronary balloon-catheter was used with an inflation pressure of 9.4 ± 0.9 atmospheres (8–10). After dilatation, angiography showed a blurred shape of the vessel but no contrast tattoo was observed. In 5 p (83%), the electrode was successfully positioned with a stimulation threshold of 1.8 ± 1.7 V, an impedance of 939 ± 258 and local electrogram amplitude of 11 ± 7 mV. There were no acute complications but 1p with oral anticoagulation for atrial fibrillation, showed hemopericardium 24 h after the procedure, which was solved by drainage and transient discontinuation of anticoagulation.

Conclusion: Balloon angioplasty of a hypoplastic target vein is effective and it may allow the implant of the LV electrode for CRT in patients with no other alternative.



Angioplasty of hypoplastic coronary vein

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Mechanisms of dislodgement of the LV electrode in cardiac resynchronization therapy

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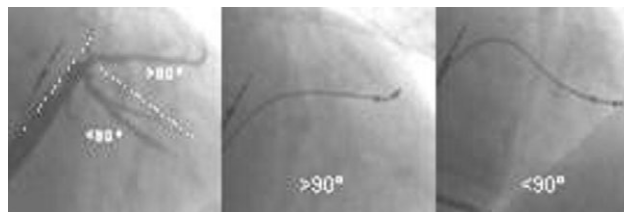
Introduction: The displacement of the left ventricular (LV) electrode is a problem that can occur up to a 10% of the cases. The identification of factors associated with the dislodgement of the LV lead may, thus, be useful.

Aim: To study factors potentially associated to the migration of the LV electrode.

Methods: 15 (8.8%) out of 170 patients (p) to whom we implanted a CRT device, experienced displacement of the LV electrode. The lead was placed in a lateral vein in 11 p, postero-lateral one in 2 p and anterolateral in 1 p. Chest X-rays prior and after dislodgement and anatomical and technical aspects were analyzed.

Results: In 4 p, migration of the device and traction of the lead was seen. 9 p had a marked atrial enlargement, 6 of which had atrial fibrillation. In 11 p, the lead did not lean on the right atrial wall and in 7, its tip was implanted in the basal portion of the vein. The angle of the vein at its drainage was >90° in 10 p (fig). When comparing this group of p with the one with stable electrode position, statistically significant differences were found in terms of BMI (p=0.03), size of Thebesian valve (p=0.04), apposition of the LV lead to the RA wall (p < 0.001), final position of the tip of the electrode (p=0.004) and angle of the vein at its drainage (p=0.026). There were no differences in terms of aetiology, gender, rhythm, lifetime presence of atrial fibrillation, atrial enlargement, LV dimensions, EF, diameter of the coronary sinus, nor diameter of the target vein. The use of a catheter balloon or other manoeuvres during the implant did not influence the stability, either.

Conclusion: There are several anatomical and technical factors that may explain the displacement of the LV electrode that should be taken into account when implanting the lead at the target vein.



Angle at the drainage of the target vein

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Temporary pacing of the right ventricle using a standard guidewire: a useful trick in the advent of complete heart block during coronary sinus lead implantation

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Background: During implantation of biventricular pacemakers and defibrillators, manipulation of the guiding-catheter during localisation of the coronary sinus (CS) os may result in traumatism to the right bundle with complete heart block. A preventive measure is to implant the right ventricular lead first, but this may interfere with guiding-catheter manipulation and may result in lead dislodgement. Many implanting physicians use a 0.35" guidewire within the guiding catheter during CS localisation. The guidewire is insulated by the guiding sheath, and may serve for unipolar backup pacing of the right ventricle in the advent of traumatic complete heart block. Whether this is feasible has not yet been tested systematically.

Methods: 54 consecutive patients (38 males, age 69 ± 11 years) undergoing biventricular device implantation were studied. A standard 0.35"

uncoated J-tipped guidewire was advanced within the guiding-catheter into the right ventricle, and pacing thresholds, R-wave sensing amplitudes and pacing impedances measured in the unipolar mode using the guidewire.

Results: Right ventricular pacing was successful in all patients. Capture threshold was 4.0 ± 2.1 V/0.5 ms, R-waves sensing was 5.1 ± 4.5 mV, and pacing impedance 223 ± 56 Ohms. No arrhythmias were noted during the tests. One patient developed complete heart block during the implant procedure, and was successfully paced temporarily using the 0.35" guidewire.

Conclusion: Temporary pacing of the right ventricle using a standard 0.35" guidewire within the guiding catheter is a reliable and safe method to ensure backup pacing. This may be a simple bailout solution in the advent of traumatic complete heart block during biventricular device implantation.

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Late failure of left ventricular lead stabilized by the use of the retained guide-wire technique

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Introduction: A technique using a retained coronary guide-wire in patients (p) with repetitive intraoperative dislocation of the left ventricular (LV) lead has been described in order to stabilize the coronary lead in its final position [1].

Aim: To describe the long-term follow-up of 3p in whom the retained wire technique was used.

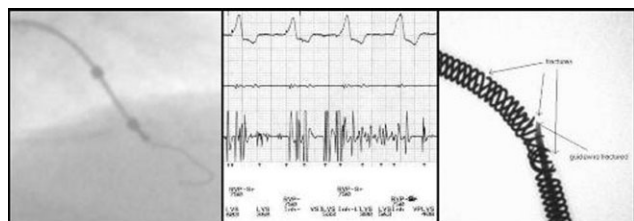
Methods: From 170p treated with cardiac resynchronization we analyzed 3 who required the retained wire technique. They were all male, aged 72, 65 and 64 years-old, respectively, in functional class III, with an EF <35% and a QRS <135 ms. The retained guide-wire technique was used to stabilize the lead after repetitive dislocation. In all p, a polymer-coated wire was used.

Results: The implant LV lead threshold was 2.3, 3.5 and 1.4 V, the local electrogram amplitude 5.5–14.3 mV and the pacing impedance 899, 1001 and 988 Ohms, respectively. Although no fluoroscopic dislocation was detected, alterations of the sensing and stimulating parameters were observed 6 months (1p) and 1 year later (2p) (3/3p). The figure shows noise in the LV electrogram. Coincidentally, a marked elevation of impedance (>2000 Ohms) was seen. In 1p the damaged lead and guidewire were explanted, showing macroscopic evidence of fracture (fig.). The laboratory analysis showed that the conductor coils were deformed and fractured. Besides, the inner and outer insulation were damaged as well as the segment of guide-wire inside the lead.

Conclusion: Our experience shows that the retained wire technique should not be used because the wire damages the lead in the mid and long-term follow-up.

References

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Retained wire technique late failure

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Radiation burden and associated risks in patients undergoing fluoroscopically guided implantation of cardiac resynchronization devices

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Purpose: Cardiac resynchronization therapy (CRT) may be associated with extended fluoroscopic exposure. We evaluated radiation risks for patients undergoing fluoroscopically-guided cardiac resynchronization device implantation.

Methods: The fluoroscopy time, dose-area product (DAP), exposure parameters, and percentage contribution of the fluoroscopic projections commonly used were recorded in a series of 14 consecutive patients referred for cardiac resynchronization device implantation and compared to corresponding data obtained from a control group of 20 patients who underwent a conventional rhythm device implantation operation. The DAP to peak skin dose, DAP to effective dose and DAP to gonadal dose conversion factors were determined for biventricular pacing and conventional rhythm device implantation using a humanoid phantom and thermoluminescence dosimetry.

Results: The mean total fluoroscopy time and DAP values were 35.2 min and 4,765 cGy cm², respectively, for biventricular pacing and 8.2 min and 1,106 cGy cm², respectively, for conventional rhythm device implantation. Patient skin dose from biventricular pacing procedures requiring extended fluoroscopic exposure may exceed threshold dose for the induction of skin effects only if X-ray source-to-skin distance is kept low. The risk values for fatal cancer and severe hereditary disorders, respectively, associated with a typical CRT procedure were 273 per million and 0.2 per million treated patients.

Conclusions: Radiation risks associated with fluoroscopically guided CRT procedures may be considerable. Present data may be used for the estimation of patient radiation risks from CRT procedures performed in other institutions.

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Comparison of RV, LV, and BiV pacing assisted or not by echocardiography at implant in narrow QRS patients

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According to recommendations CRT implant may be proposed in CHF patients with QRS width >120 ms although little is known about mechanical effects of device implantation in "narrow" QRS patients. In order to check and eventually improve optimal delivery of CRT, a group of 14 NYHA class III narrow QRS pts (118±18 ms) was implanted under echo monitoring of dyssynchrony (D) parameters in order to optimize pacing configuration.

Left Ventricular filling time reported to cardiac cycle (LVFT%), Left Preejection Period (LPEP), DTI measurement of septal to lateral contraction delay (sept-lat), duration of diastolic contraction of the septum after aortic valve closure (DC sept) and eventually after opening of mitral valve (Op sept) and mitral regurgitation area reported to left atria surface were recorded. After LV lead implant (lateral position), RV lead was implanted in a location according to physician choice (4 apex, 10 septal) and Initial BiVentricular pacing was tested. If LPEP was not reduced or remained >130 ms, RV electrode was moved searching for the maximal reduction of LPEP during BiV pacing. In absence of significant shortening, a second RV lead was inserted, and LPEP was measured under triple ventricular pacing. Final configuration was the one providing the shortest LPEP.

Results: 7 patients ended in Triple V, 5 in BiV with optimized positioning of RV and 2 in Initial BiV configuration. QRS increased to 136±18 ms (p < 0.001). Echo data in all configurations are reported and compared to baseline.

Conclusions: (1) In Narrow QRS patients, standard pacing configurations including BiV did not improve filling duration, neither reduced D,

(2) deterioration of LPEP/LVET ratio under standard BiV may contribute to predict non-response of CRT, (3) Tailored configuration was necessary in 12/14 pts. (4) Pursuing shortening of the LPEP allowed improvement of other D parameters.

Table 1

	LVFT%	LPEP	DC sept	Ov sept	LPEP/LVET	Sept-lat	MVR%
Baseline	41±7	125±32	152±75	108±93	0.45±0.19	99±88	23±17
RV pacing	38±10	181±29 [‡]	122±106	74±117	0.72±0.20 [‡]	83±102	25±24
LV pacing	39±7	168±30 [‡]	125±75	36±70*	0.69±0.18 [‡]	45±90	21±17
BiV initial	42±8	148±41 [†]	113±93	37±75*	0.56±0.19*	65±127	23±21
Final config	45±7*	124±31	54±59 [‡]	1±40 [‡]	0.43±0.16	27±95*	15±16

P values refer to comparison with baseline. *p < 0.05, [†]p < 0.01, [‡]p < 0.001.

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Biventricular VDD pacing versus biventricular DDD pacing

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Purpose: To compare the feasibility and efficacy of biventricular VDD pacing with DDD biventricular pacing in chronic heart failure (CHF) pts refractory to standard therapy, preserved RA contraction, sinus rhythm, and indication for cardiac resynchronization therapy (CRT).

Methods: Between 2003–2005 25 pts.=group A, (17 males, mean age=66±11) III NYHA class, QRS duration ≥150ms, left atrial diameter >5 cm, normal RA volume, no history of atrial tachyarrhythmias, planimetric LV ejection fraction (LVEF) ≤35%, were implanted with biventricular pacemaker (PM) connected at only 2 leads: a coronary sinus lead (left ventricular channel-LV), and a VDD single pass lead (right ventricular-RV and right atrium-RA channel). The PM was programmed in VDD mode, LV+RV configuration, with V-V and A-V delays corresponding to the best echocardiographic Doppler profile. In the same period, 23 pts. = group B, (18 males, mean age=62±9) with similar clinical and laboratory conditions were implanted with biventricular PM connected at 3 leads, one for every channel RA, LV and RV, with an adequate programming of PM in the DDD mode.

Results: The results obtained from two groups are shown in Table 1.

Conclusions: Biventricular VDD pacing is an effective simplified feasible technique in pts with CHF and preserved atrial function due to shortness of radiological exposure time, decreased risk of leads dislodgements and cost effective. One year follow up relieve no significant differences in improvement of left ventricular function and in incidence of atrial fibrillation between VDD and DDD systems.

Table 1

	Group A (25 pts)			Group B (23 pts)			P
Fluoroscopy time, mean±SD	21±12			32±11			p < 0.001
Procedure time, mean±SD	54±10			80±25			p < 0.01
LVEF at discharge, mean±SD	32±6			30±5			p=0.36
LVEF at 12 months, mean±SD	37±5			35±4			p=0.24
Acute complications							
1. Lead dislodgments (RA, RV, LV)	RA	RV	LV (SC)	RA	RV	LV (SC)	p=NS
	0	0	1	1	0	4	
2. Sinus perforation	0			1			p=NS
Chronic complication							
1. Skin lesion	0			2			p=NS
Permanent atrial fibrillation at 12 month	2			3			P=NS

SD, standard deviation; CS, coronary sinus; NS, not significant.

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Treatment alternative for Dilated Cardiomyopathy: Resynchronization Therapy and Stem Cells Therapy. Preliminary results

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Introduction: Cardiac Resynchronization Therapy (CRT) improves quality of life, functional capacity and reduces the risk of mortality. However; the progress of myocardiopathy leads, in a long term follow-up, to the return of symptoms of Heart Failure (HF) besides synchronization, also there are 20 to 30% of non-responders. The Stem Cells Therapy (SCT) seems to be a feasible and good alternative to the treatment of HF, particularly, using Mononuclear Bone Marrow Stem Cells (CD34+/CD133+). These treatments for HF could be associated with optimized pharmacological therapy. The SCT results (6 months follow-up) show a rapid recuperation of patient, time to develop the myocytes in the ventricles walls new vessels or angiogenesis, and promote a kind of recovery of cardiac function.

Aim: To characterize the early term results of CRT combined with SCT in patients under optimized pharmacological therapy, with HF (NYHA Class III and IV), and intraventricular dyssynchronization, Ejection Fraction (EF) <35%, and without severe mitral regurgitation.

Method: The Iliac posterior crests were punctured under peridural anesthesia to obtain 40 or 50 ml of bone marrow cells. The blood was filtered and speared by centrifugation in Ficoll, and more than 1 to 2×10⁸ mononuclear cells were obtained.

Four hours after, the patient went thru a CRT procedure under peridural anesthesia. The left ventricle stimulation was achieved with an epicardial lead (left minitoracotomy), and under the same approach were injected with 0.2 cc of mononuclear cells in each puncture (total 10 ml, directly in ventricle muscle, in all epicardial faces).

The control parameters are – functional class, BNP level (EF), echocardiography study, performed by Nuclear Medicine (MIBG, Gated and Scintigraphy), Coronaryarteriography (wall motion and collateral vessels growing).

Results: Since April 2005, 10 patients received CRT and SCT by epicardial minithoraco tomy implantation.

The mean age was 65.8 years. The etiology of the dilated cardiomyopathy were, 2 pts Idiopathic, in 3 pts Ischemic and 5 pts Chagas disease. Three pts. with A-V block and 7 with LBBB. The mean pre-op EF was 19% and in 6 pts with more than 9 months follow-up, were 31%. The mean BNP level pre op was 430 pg/mL, changed for near the normal levels.

After 12 months follow-up all patients increased quality of life and exercise capacity. The cintigraphy studies made in 6pts that had more than 9 months of follow-up, showed the improvement of EF and Sympatic cardiac activity.

Conclusions: CRT and SCT seem to be a good alternative to treat HF. Procedures made at the same time are safe and feasible.

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Poster Area

Optimization of cardiac resynchronisation therapy after implant

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Is right ventricular pacing necessary for the hemodynamic benefit in CRT? An investigation of the Ventricular Sense Response algorithm (VSR)

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Objective: The positive effect of the resynchronisation therapy (CRT) in patients with symptomatic chronic heart failure, ejection fraction < 35% and an intra ventricular conduction delay (QRS >150ms) is well proven. Most of the patients are paced simultaneously in the right apex and in an epicardial vein. Pacing in the right apex produces an abnormal pattern of ventricular depolarization and therefore it is associated with adverse functional effects and structural changes of the left ventricle. A combination of intrinsic RV conduction with LV-only pacing could be a physiological way of improving the ventricular conduction. One possibility of biventricular stimulation without RV pacing is the Ventricular Sense Response algorithm (VSR). VSR allows the device to maintain cardiac resynchronization delivery when ventricular sensing occurs. Each right ventricular sensed event triggers a stimulus in one or both ventricles. The first chamber is paced at 1.25 ms after the ventricular sensed event. The purpose of this study was to evaluate the hemodynamic effect of VSR compared to BIV pacing.

Methods: After implantation of a Medtronic CRT-D device a RADI pressure wire 5F (0.014") was positioned catheter in the left ventricle. The LVP was measured beat to beat over a period of 15 seconds and LV+ dP/dt was calculated online. Hemodynamic data were measured stepwise during intrinsic conduction, intrinsic conduction with VSR and BIV pacing.

Results: All patients benefit from biventricular pacing. 20 patients (17 male, 3 female, age 67±6 years, 16 with CAD, 4 with DCM) were investigated. They had standard indication for CRT implantation. The LVEF was 24.5±5%, the QRS width was 173±27 ms. In 15 of 20 patients the RV lead was implanted in the high septal area of the right ventricle, in 5 patients in the right apex. Compared with intrinsic conduction the LV+ dP/dt increased during VSR stimulation by 4.55±4.9% (p=0.03 (paired T-Test)). With standard setting of BIV pacing (sensed av delay 120 ms and vv delay 0 ms) the LV+ dP/dt increased by 10.63±14.4% (p=0.005 (paired T-Test)). In this small patient group, no significant differences were observed between patients with RV apex pacing and RV high septal pacing.

Conclusion: VSR showed in this patient population a significant increase in LV+ dP/dt, however the increase is low compared to BIV pacing. Based on the hemodynamic criterion at present it is not useful to stimulate a patient permanently with VSR only, but VSR is helpful as back up algorithm during biventricular stimulation in case of intrinsic conduction.

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Left ventricular free-wall electrical activation time: an electrophysiological parameter correlated with improvement in intraventricular dyssynchrony after cardiac resynchronization therapy

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Background: it has been suggested that lack of responsiveness to cardiac resynchronization therapy (CRT) can be related to placement of the left ventricular (LV) lead in a unfavourable pacing site. Aim of this study was to determine whether electrophysiological parameters, calculated at time

of pacemaker (PM) implantation, can predict improvement in synchrony and in LV function after CRT and so be useful in choosing the optimal pacing site.

Methods: 27 pts with dilated cardiomyopathy (7 ischemic, 20 idiopathic; NYHA class 2.7±0.5, LVEF 25±5%, QRS 159±26 ms) were implanted with a biventricular PM. Conventional and tissue Doppler echocardiography (TDI) were performed at baseline and 1 month after CRT to evaluate intraventricular synchrony, and at 3 months to assess the presence of reverse remodeling (reduction in end systolic volume ≥15%). At baseline all pts showed interventricular and intraventricular dyssynchrony, the latter defined as septal to lateral delay in peak velocity at TDI ≥ 65 ms. During implantation right and left ventricular lead electrograms and surface ECGs in sinus rhythm were recorded and the following parameters calculated: ECG-LV (time of LV wall electrical activation from QRS onset); ECG-LV ratio (ECG-LV time as a percentage of QRS duration); LV-RV delay (difference between LV and RV activation times from QRS onset); RVP-LV (LV wall activation time measured from spike during RV pacing).

Results: ECG-LV and ECG-LV ratio showed a linear correlation with reduction of intraventricular dyssynchrony after CRT (R=0.45, P=0.04 and R=0.47, P=0.03, respectively). The population was divided into two groups according to the median value of ECG-LV ratio (group A ECG-LV > 90%, group B ECG-LV ≤ 90%). The two groups had similar baseline characteristics. At 1 month group A showed a larger reduction in intraventricular dyssynchrony as compared to B (-66±20 ms vs -19±17 ms, P=0.04). After CRT septal to lateral delay was shorter in A (32±27 ms vs 63±17 ms, P=0.01) and a septal to lateral delay <65 ms was found in 83% of pts in A vs 25% of pts in B (P=0.008). At 3 months pts in group A were more likely to show LV reverse remodeling as compared to pts in group B even if the difference was not statistically significant (70% vs 37%). Similar results were found when the population was stratified according to the median value of ECG-LV (160 ms).

Conclusions: the timing of LV free-wall electrical activation correlates with reduction in intraventricular dyssynchrony after CRT. This marker should be considered in order to select an optimal pacing site at time of PM implantation.

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Optimization of CRT-Devices – in comparison impedancecardiography with invasive measurement and echocardiography

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Background: Cardiac resynchronization therapy (CRT) is well established as a treatment option in patients (P) with severe heart failure under special conditions. For optimization of biventricular stimulation patient individual timing of AV- and VV-delay is necessary. Usually this spent on time.

Method: Patients with classic indication for CRT-therapy (LBB>120 ms, ejection fraction (EF) <35%, NYHA III, Sinusrhythm) were included. In a first period P received impedancecardiographic measurements of cardiac output (CO) with different VV- (-40 to +40) and AV-delays (60–150 ms). Additional an invasive optimization using a micro tip pressure catheter (Millar, SPC790), which was placed in the left ventricle to figure out dp/dt, was performed. In a second period instead of invasive measurement an echocardiography assessment of inter- or intraventricular dyssynchrony (Delta PEP, TDI) following the same protocol was done.

Aim of study was an optimization of biventricular devices with impedancecardiography in comparison with invasive measurement (Millar) and echocardiography.

Results: 11 P (age: 67±7.4 years; EF 22±7%, 9 P with DCM) were compared invasive with Millarcatheter and 6 P ((age: 66±6.8 years; EF 24±5%, 5 P with DCM) with echocardiography. In the invasive group without stimulation we measured CO of 4.2±1.3 l/min with a dp/dt_{max} of 835±184 mmHg/s. With simultaneous biventricular stimulation and optimized AV-delay the CO increased to 5.3±1.5 l/min with a dp/dt_{max}.

of 1021 ± 214.4 mmHg/s ($p < 0.01$). After optimization of the VV-time the dp/dt_{max} increased additionally to 1090 ± 127.8 mmHg/s with a CO of 5.9 ± 1.8 l/min ($p < 0.01$). In 90% we have seen corresponding results for the optimal programmed VV- or AV-delay in comparison to impedance-cardiography.

In the Echocardiography group increased the CO from 3.7 ± 0.7 l/min up to 4.8 ± 1.1 l/min during optimal biventricular stimulation. Optimized biventricular stimulation resulted in improvement of inter- and intra-ventricular synchrony (without stimulation Delta PEP 52 ± 10 ms/TDI 100 ± 16 ms/ with stimulation Delta PEP 36 ± 21 ms/TDI 4 ± 16 ms). For all P the echocardiography confirmed the optimal VV- or AV-delay based on impedance-cardiography.

Conclusion: Impedance-cardiography is an easy tool for optimization of CRT-devices. The measured values were in the most cases confirmed using invasive measurement and echocardiography.

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ECG guided optimization of left ventricular pacing in patients with heart failure, left bundle branch block and sinus rhythm

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Our hypothesis is that electrical fusion between left ventricular (LV) pacing alone and spontaneous right ventricular activation, evaluated through ECG, leads to resynchronization of myocardial contraction. In patients with heart failure, left bundle branch block (LBBB) and sinus rhythm (SR), LV pacing promotes different degrees of fusion as programmable AV delay changes. This can be easily detected through surface ECG.

Methods: We enrolled 12 patients (7 males, 63 ± 12 yrs) treated with cardiac resynchronization therapy. We recorded 12 lead ECG with LV pacing alone at each programmable AV delay starting from the one at which pacing was inhibited (native LBBB morphology). Shortening programmable AV intervals 10 by 10 ms, we obtained a series of ECG showing progressive transition in morphology from LBBB to a completely left pre-excited right BBB (RBBB), passing through intermediate QRS of fusion. The transition was more easily detected in V1 lead. The "fusion band" was defined as the range of AV intervals at which surface ECG shows an intermediate morphology between the native LBBB pattern and the fully paced RBBB pattern.

The upper limit of the band was set 40 ms shorter than the interval between atrial and ventricular sensing. The lower limit was set at the AV interval leading to a RBBB-like morphology. Two intermediate AV intervals, inside the fusion band, were also evaluated. At each selected AV interval ($n=4$), we measured, through echocardiography, diastolic filling time, Tei index, indexes of asynchrony by Tissue Doppler Imaging (Ts-12-ejection, Ts-SD-ejection) and interventricular delay.

Results: The data referred as "fusion band" (see Tab) correspond to the average of data at the 2 intermediate AV intervals.

Conclusions: Resynchronization therapy based on LV pacing alone can be optimized through morphologic ECG criteria in SR patients. The "fusion band" method seems feasible, effective, easy and time-saving.

	LBBB	Fusion band	P
Tei index	0.81 ± 0.19	0.53 ± 0.11	0.006
Ts-12-ejection (ms)	166 ± 36	88 ± 22	0.037
Ts-SD-ejection (ms)	66 ± 17	29 ± 8	0.046
Interventricular delay (ms)	42 ± 11	13 ± 8	0.017
Filling time (ms)	413 ± 55	471 ± 63	0.062

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6-month evaluation of IEGM predicted optimal PV and VV delays

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Purpose: Cardiac resynchronization therapy (CRT) has been widely and clinically validated as an efficient therapy for patients with heart failure. However, 30% of patients do not directly respond to this therapy. Echocardiographic optimization of PV and VV delays has been shown to improve cardiac performance and might decrease the non-responder rate, but remains time- and resource-intensive. Recently, a fast intracardiac electrogram (IEGM)-based method (QuickOpt, St. Jude Medical) has been shown to produce hemodynamic performance similar to that obtained by the maximal aortic VTI (AVTI) optimization method. The objective of this study is to evaluate if optimized values for PV and VV delays as determined by the IEGM method would change over the first 6-month follow-up period.

Methods: Ten patients [63 ± 5 years; LVEF = $17 \pm 6.1\%$ (inclusion criterion $\leq 35\%$); QRS= 153 ± 15 ms (≥ 120 ms); 30% NYHA III and 70% NYHA IV] were implanted with an ATLAS+HF device. IEGM PV/VV optimization was conducted at pre-hospital discharge (PHD) and compared to tests done at 3- and 6-month visits. Maximal AVTI PV/VV optimization was also done at pre-discharge visit and compared to the QuickOpt method.

Results: At the 6-month visit, all patients responded to CRT both on 6-minute walk test (improvement: 264 ± 174 m) and NYHA class (improvement: 2 ± 0.8). At PHD, AVTI at IEGM PV delays highly correlated with maximal AVTI values (24.2 ± 9 cm v. 24.6 ± 9.5 cm; $R_2 = 0.95$; slope = 1.03), and AVTI at IEGM VV delays also had good correlation with the maximal AVTI values (26.3 ± 8.8 cm v. 24.9 ± 10.1 cm; $R_2 = 0.98$; slope = 1.1). IEGM PV and VV delays obtained during the 6-month follow-up were compared within patients to those at PHD (Table 1). PV delays decreased at 3 month visits and changed little (within 10 ms) from 3 month to 6 month visits.

Conclusions: Good correlation was achieved between AVTI at IEGM PV and VV delays and the maximum AVTI values at PHD. IEGM PV and VV delays varied within patients during the first 6-month follow-up which provides rationale for a frequent routine optimization of PV and VV delays using the fast QuickOpt method during follow-up visits.

Table 1: Variations of IEGM delays

Follow-Up	Change in IEGM PV = PV(PHD) - PV(Follow-Up), ms, mean \pm SD (range)	Change in IEGM VV = VV(PHD) - VV(Follow-Up), ms, mean \pm SD (range)
3 Months	6 ± 14 (-20 to 20)	-2 ± 15 (-20 to 20)
6 Months	6 ± 20 (-30 to 30)	0 ± 20.0 (-30 to 35)

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Comparing echo aortic VTI (AVTI) at the IEGM-suggested VV delay and with simultaneous biventricular pacing

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The new IEGM method offers physicians to estimate optimal VV delays in less than one minute. Published studies showed strong agreement when comparing AVTI at the IEGM-suggested VV delay to maximum AVTI at echo-optimal VV. In this study, the ACUTE IEGM-CRT VV and RHYTHM VV data were retrospectively analyzed for: impact of

the IEGM-optimized VV intervals vs. simultaneous biventricular (SIM) pacing on AVTI; and comparisons to the inpatient range of AVTI at a range of VV values.

Methods: The data from CRT-D patients in the ACUTE IEGM-CRT VV study (n: 57; age: 71±10 years; 75% NYHA Class III; 71% ischemic; mean LVEF: 24±9%; mean QRS width: 148±24ms) and the RHYTHM VV study (n: 61 pts; age: 65±11 years; 91% NYHA class III; 75% ischemic; mean LVEF: 21.1±6.9%; mean QRS width: 171±18ms) were included for the analysis. The conduction delays to RV and LV leads were used to determine the IEGM VV and in ACUTE IEGM-CRT, the correction term by using paced inter-ventricular conduction delays was added but it was small in most patients. The echo-optimal VV was determined by the maximum AVTI obtained over pre-selected VV delays of 20, 40, 60 and 80 ms with both RV and LV lead pre-activated, and with SIM. The difference between AVTI at the IEGM VV and the maximum AVTI (d_IEGM) was compared with the difference between AVTI with SIM and at maximum AVTI (d_SIM), and with the range of AVTI within patients by a Student's t-test (two-tailed) for paired data.

Results: In RHYTHM VV, d_SIM was significantly greater than d_IEGM (1.87±1.45 cm vs. 1.1±1.3 cm, p=0.0001). d_IEGM was significantly smaller than the range of AVTI at 7 VV delays (1.1±1.3 cm vs. 4.6±2.0 cm, p<0.0001). d_SIM was also significantly smaller than the range (1.87±1.45 cm vs. 4.3±1.7 cm, p<0.0001). Similar results were found from ACUTE IEGM-CRT VV data. d_IEGM was significantly smaller than the range of AVTI at 8 VV delays (1.64±1.73 cm vs. 4.3±1.7 cm, p<0.0001). d_SIM was also significantly smaller than the range of AVTI (2.1±1.7 cm vs. 4.3±1.7 cm, p<0.0001). d_SIM tended to be greater than d_IEGM (2.1±1.7 cm vs. 1.64±1.73 cm, p=0.14).

Conclusions: The IEGM-suggested VV delays tended to produce greater mean AVTI values than those with simultaneous biventricular pacing in the ACUTE IEGM-CRT VV and the RHYTHM VV patients. The difference in AVTI values between maximum AVTI and AVTI at the IEGM was significantly smaller than the variations in AVTI within patients over a range of VV delays, implying that optimizing VV delay by the IEGM confers short-term hemodynamic benefit.

MONDAY, 25 JUNE 2007, 15:30–16:30

Poster Area

Haemodynamic assessment of cardiac resynchronisation therapy

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Evaluation of exercise tolerance by cardiopulmonary exercise test in patients with heart failure after cardiac resynchronisation therapy

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Background: Cardiac resynchronisation therapy (CRT) using biventricular pacing improves hemodynamics and symptoms in patients with heart failure. However, their effects on oxygen uptake (VO₂) kinetics at the exercise have not been elucidated. The aim of the present study was to examine the mid-term effects of the ventilatory response to exercise after CRT.

Methods: A prospective analysis was performed on 42 patients with chronic heart failure (mean age 68±6 years, 28 males, NYHA class ≥3, with left ventricular ejection fraction <35%, on conventional medical therapy) in stable clinical conditions. All patients performed cardiopulmonary exercise test (CPET) up to the limitation of symptom on a cycle ergometer. We assessed the change during 6 months by NYHA class and parameters obtained by CPET; peak oxygen consumption (pVO₂), slope relating ventilation to carbon dioxide output (VE/VCO₂ slope), the time constant of VO₂ (TC) during the onset of exercise and anaerobic threshold (AT). At the 6-month follow-up, responder after CRT defined as a relative increase in pVO₂ ≥10%.

Results: Follow-up at 6 month was completed in 37 patients (NYHA class 3.1±0.4, left ventricular ejection fraction 29±7%, left ventricular end-diastolic diameter 63.6±4.4mm, QRS duration 154±26ms and Ischemic heart disease 57%). The severe incidence in symptom-limited exercise test was none. Compared to baseline, pVO₂ and AT significantly increased during follow-up period. NYHA class significantly decreased and VE/VCO₂ slope and TC significantly reduced. Responders were 27 patients (64%) at 6 months after CRT.

Conclusion: Exercise tolerance, ventilatory response and subjective symptoms in patients with chronic heart failure have improved significantly during 6 months after CRT.

	Baseline	3 months	6 months	P (B-3)	P (B-6)
NYHA class	3.2±0.4	2.1±0.4	1.9±0.3	<0.0001	<0.0001
PeakVO ₂ (ml/kg/m)	13.1±3.1	14.6±2.4	15.7±2.7	0.006	0.0001
AT (ml/kg/m)	10.2±1.9	10.7±1.6	11.0±1.6	0.2	0.03
VE/VCO ₂ slope	36.1±3.3	36.0±3.8	31.2±3.4	0.04	<0.0001
TC (sec)	26.5±18.9	22.0±10.6	19.0±8.1	0.2	0.05

NYHA class: New York Heart Association functional classification, P (B-3): Baseline and 3 months after the CRT, P (B-6): Baseline and 6 months after the CRT

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Relation between subjective and objective response to cardiac resynchronization therapy

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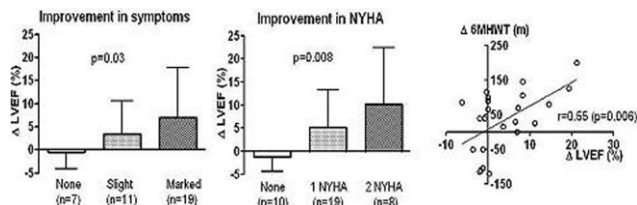
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Background: Some patients with cardiac resynchronization therapy (CRT) may show a dramatic improvement in symptoms and in functional capacity, although on average, left ventricular ejection fraction (LVEF) is only modestly improved by this therapy. The relationship between improvement in functional parameters and increase in LVEF and has not yet been well studied.

Methods: We included 37 patients (30 males, age 71±9 yrs) implanted with a biventricular device for refractory heart failure. LVEF was measured by nuclear ventriculography directly after implantation and after 9±5 months' follow-up along with different clinical parameters.

Results: LVEF showed a modest increase for the group as a whole (24±7% at baseline vs 29±13% at follow-up, p=0.005). Improvement in symptoms were noted in 30/37 (81%) patients. NYHA improved by >1 class in 27/37 (73%) patients. For both parameters, degree of improvement was significantly associated with absolute increase in LVEF (see figure). Improvement in 6-minute hall-walk test (6-MHWT) showed a moderate but significant correlation with improvement in LVEF. There was a significant association between improvement in NYHA class and 6-MHWT (p=0.002).

Conclusion: Clinical outcome is significantly related to improvement in LVEF in patients with CRT.



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Efficacy of cardiac resynchronization therapy on Japanese ischaemic-cardiomyopathy patients is similar with non-ischaemic cardiomyopathy

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Background: It is reported that CRT on ischaemic cardiomyopathy (ICM) is less effective compared to non-ischaemic cardiomyopathy (NICM). However, there is no data about CRT effectiveness on Japanese ICM patients (pts) and the purpose of this study is to evaluate the efficacy of CRT on Japanese ICM pts.

Methods: We investigated 110 pts received CRT at our institution (age 71±10 years, NYHA class 3.1±0.5, LVEF 26±7 ％, LVEDD 61±7 mm, pre QRS duration 178±29 ms) and divided into two groups, 47 (43%) ICM pts (ICM group) and 63 (57%) NICM pts (NICM group). Long-term echocardiographic and clinical data were obtained.

Results: ICM group consisted of more male gender (81% vs. 49%, $p=0.0007$), hypertension (48% vs.13%, $p<0.0001$) and less upgrading from RV pacing (30% vs. 49%, $p=0.04$), but another baseline clinical characteristics, echocardiographic parameters, pre and post QRS duration, LV lead locations and medical treatments were similar between two groups. After 3–6 months echocardiographic follow-up, only reduction of LVEDD was significantly smaller in ICM group (−4.1 mm vs.−5.8 mm, $p=0.04$), but improvement of another parameters were similar between two groups (ICM group vs. NICM group: LVEF +8% vs.+10%, LVESD −5.0 mm vs. −5.7 mm, LVEDV −40 ml vs. −44 ml, LVESV −39 ml vs. −43 ml, MR area −2.0 cm² vs. −1.9 cm², all p values were NS). After mean follow-up of 346±251 days, event free survival rates from death were similar between two groups (ICM group vs. NICM group: 88% vs.89% at 1 year, Log-rank $p=NS$) and event free survival rates from combined death and heart failure hospitalization were also similar between two groups (75% vs.75% at 1 year, Log-rank $p=NS$). Even after Adjusted sex, hypertension and upgrading CRT, ICM was not associated with clinical adverse events. Newly occurring ventricular tachyarrhythmias were also similar between two groups during follow-up period (6% vs.5% at 1 year, Log-rank $p=NS$).

Conclusion: Japanese ICM pts received CRT had almost equally effects compared to NICM pts in echocardiographic and clinical outcomes.

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Comparison of the ejection fraction evolution in chagasic and idiopathic cardiomyopathy patients submitted to cardiac resynchronization therapy

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Objectives: To analyze and compare the evolution of the ejection fraction (LVEF) of Chagasic (CC) and Idiopathic Cardiomyopathy (IC) patients (pts) underwent to Cardiac Resynchronization Therapy (CRT), and if only this measure is a good prognosis parameter.

Material and Methods: 135 pts (47 CC and 88 IC) were analyzed. The average age was 53 in CC group and 65 in IC group ($p<0.001$) and the average Ejection Fraction by Echocardiogram (LVEF) was 0.30 in CC group and 0.33 in IC group ($p<0.001$). All of them were in C and D Stage (ACC / AHA) and were submitted to a CRT. The LVEF in these pts were analyzed and compared as an isolated prognosis parameter.

Results: The average Follow Up was 15 months in CC group and 26 months in IC group ($p=0.0013$). There was a significant increase of EF in both groups, mostly in idiopathic ($p=0.0098$), from 0.30 to 0.35 in CC group ($p=0.0034$) and from 0.33 to 0.45 in IC group ($p<0.001$). There was no statistical difference in mortality in both groups, and the LVEF isolated wasn't a good prognosis parameter.

Conclusion: We observed a good evolution in both groups with CRT, mostly in idiopathic group. The LVEF isolated in these patients wasn't a good prognosis parameter.

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Incidence and characteristics of super-responders after cardiac resynchronization therapy

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Background: Cardiac resynchronization therapy (CRT) has been shown to significantly benefit patients (pts) with moderate to severe heart failure and electro-mechanical dyssynchrony. However, clinical and echocardiographic characteristics of super-responders after CRT is not well known.

Methods: We investigated 60 patients received CRT at our institution (age 71±10 years, NYHA class 3.0±0.4, LVEF 24±6 ％, LVEDD 62±7 mm, pre QRS duration 181±29 ms). Super-responder was defined as LVEF became twice or LVEDV became half after 3 to 6 months CRT. Clinical characteristics, QRS pattern, LV lead position and echocardiographic parameters were evaluated to characterize super-responders.

Results: We recognized 12 patients (20%) as super-responders by echocardiographic definitions (pre and post 3–6 months implantation: LVEF 20±5% to 44±5%, LVEDV 172±52 ml to 90±32 ml). Of these, 9 (75%) had non-ischemic cardiomyopathy vs. 58% in the remainder of the cohort. Pre QRS duration was not different between super-responders and reminders (184±31 ms vs. 180±22 ms). QRS pattern of super-responders was 7 LBBB (58%) and 5 RV apex pacing (42%), that of reminders was 38% LBBB, 38% RV apex pacing and 24% IVCD or RBBB. All 12 patients (100%) had an LV lead position on the lateral or posterolateral wall of LV vs. 92% of the remaining cohort. Super-responders had a significantly lower pre LVEF compared to that of reminders (20±5% vs. 25±6%, $p=0.006$). There were no other clinical predictors of super-responders including age, sex, severity of MR, LVEDV and LVESV.

Conclusion: Super-responders was seen in one fifth of patients treated CRT and more frequently seen LBBB or pacing induced cardiomyopathy with lead position on the lateral or psotero-lateral wall of the LV.

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The patient characteristics of responders and non-responders in patients undergoing cardiac resynchronization therapy

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Introduction: A proportion of patients undergoing cardiac resynchronization therapy (CRT) becomes non-responder. The purpose of this study was to evaluate the difference of patient characteristics between acute responders, late responders and non-responders in CRT recipients.

Method: This study consisted of 39 CRT recipients (29 Males, mean age 63.0±15.6 years). Patients were divided to acute-responders (AR; LVESV reduction >15% was confirmed at 1month after implantation), late responders (LR; LVESV reduction >15% was confirmed at 6months after implantation), and non-responders (NR; LVESV reduction was not confirmed until 6 months after implantation). We compared patient characteristics before CRT implantation between 3 groups.

Result: AR had fewer heart failure hospitalizations, and relatively preserved heart function than NR despite there was no significant difference except serum BNP level between LR and NR. Mean age, gender and etiology of heart failure were not significantly different between 3 groups. QRS width was rather wider in LR than NR.

Conclusion: Severity of heart failure and LV remodeling was relatively mild in AR compared to NR and LR. It seemed to be difficult to detect LR prior to CRT procedure. CRT benefit cannot be promising in patients with seriously disturbed and remodeled LV function.

Patient characteristics prior to CRT

	AR (n=15)	LR (n=8)	NR (n=16)
Age (years)	60.0±21.9	66.1±13.9	64.2±8.0
Gender (Male%)	20	37.5	25
Etiology of HF (IHD%)	6.7	12.5	37.5
Number of HF hospitalization	1.7±1.1*	2.6±1.1	3.1±1.2
NYHA class	3.2±0.4	3.3±0.5	3.4±0.5
BNP (pg/ml)	679.0±605.2*	684.7±334.8*	1590.2±1107.0 [#]
QRS width (ms)	171.7±29.4	200.5±42.7*	168.4±31.7 [#]
LVEDD (mm)	57.7±9.3 [#]	70.8±6.2	71.4±8.9
LVESD (mm)	49.1±9.0 [#]	62.3±7.5	61.6±10.0
LVEF (%)	30.2±6.4 [#]	23.1±5.1	23.0±6.9
LAD (mm)	41.8±10.1*	46.6±8.8	49.6±8.6

*p < 0.05 vs NR, [#]p < 0.05 vs LR; HF; heart failure, IHD; ischemic heart disease

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Plasma levels of brain natriuretic peptide and QRS duration in heart failure patients prior and after cardiac resynchronization therapy

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Purpose: Cardiac resynchronization therapy (CRT) is an accepted treatment for patients with heart failure and wide QRS, and can improve their cardiac function and functional class. Plasma levels of Brain Natriuretic Peptide (BNP) are elevated in patients with heart failure and can be used as useful parameter for monitoring the response to CRT. The aim was to estimate the correlation between plasma levels of BNP and QRS duration prior and after CRT.

Methods: A group of 38 patients, with heart failure, mean age 64±13, left bundle branch block, ejection fraction ≤35%, NYHA class II-IV underwent CRT. At the baseline and 18 months after CRT we recorded the plasma levels of BNP (ng/L) and QRS duration. Based on the NYHA class improvement by at least one patients were divided in two groups (responders and non-responders to CRT).

Results: There were 28 responders and 10 non responders to CRT. At the baseline BNP level was 272.81±169.00 in responders group and 322.11±160.65 (p > 0.1) in non responders group. At the follow-up BNP level was 131.70±101.40 for the first group, and 452.20±193.00 for the second group of patients (p0.1). 18 months later in the first group duration of QRS was 129.00±21.40, and 194.10±24.10 for non-responders (p < 0.001). Reduction of plasma level of BNP is highly correlated with reduction of QRS in responders group (r = 0.74).

Conclusion: Patients who were responders to cardiac resynchronization therapy showed both significant decrease of plasma levels of BNP and reduction of QRS. Also, we observed a good agreement between those two parameters. Reduction of QRS after CRT can also be used as parameter of response to CRT.

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Reliability of a new method for identification of long-term responders to the morphology discrimination algorithm in patients with heart failure and CRT-D

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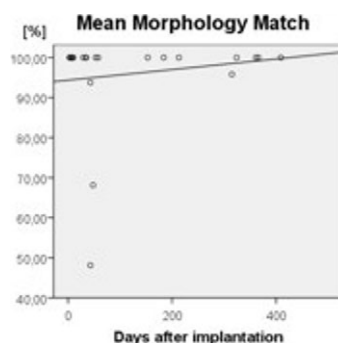
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Background: Modern ICDs use the morphology analysis of ventricular intracardiac signals for the discrimination between VT and SVT. It is not known yet, whether QRS changes during cardiac resynchronization therapy (CRT) have effects on the morphology discrimination (MD) algorithm. We studied the reliability of a new method for the differentiation of responders (MR) and non-responders (non-MR) to the MD-algorithm in CRT-D patients.

Methods: 23 patients (19 m, 60±11 y) with reduced left ventricular function (EF 22±4%) and prolonged QRS duration (162±24 ms) received a CRT-D-system (St. Jude Medical). Follow-up duration was 118±140 days after implantation. The morphology match (MM) of 8 consecutive beats during AAI pacing (rate offset +30 bpm) was compared with reference beats during sinus rhythm. Patients with average MM scores >90% were classified as MR, and positive (PPV) and negative predictive values (NPV) were calculated.

Results: During AAI pacing, the optimal MM cut-off value was >93.7% for the differentiation between MR and nonMR as shown by ROC analysis. Using this cut-off value, 21 patients (91.3%) were identified as MR during AAI pacing. PPV was 81% for the identification of MR and NPV was 100% for the identification of nonMR. The figure shows MM during AAI pacing and long-term CRT.

Conclusions: The presented new method is a simple and reliable tool for the identification of MR and nonMR to the MD algorithm during sinus tachycardia. During long-term CRT there was even an increase in MM, which might further improve discrimination of tachycardia. Thus, this method should be used for individual and optimized SVT discriminator programming in order to reduce inappropriate therapies in CRT-D patients.



Morphology match during AAI pacing & CRT

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Long-term evolution of spontaneous cardiac activation and left ventricular remodeling during cardiac resynchronization therapy and in matched heart failure control patients

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Purpose: Cardiac resynchronization therapy (CRT) in patients with left bundle branch block (LBBB) and severe systolic heart failure results in a decrease of the left ventricular end diastolic diameter (LVEDD). Little is known about the relationship of structural ventricular remodeling and the evolution of spontaneous ventricular activation. The study therefore aims to comparatively characterize changes of LVEDD and spontaneous ventricular activation with CRT and in heart failure controls without LBBB.

Methods: In 42 patients (n=21 with LBBB and CRT indication, n=21 without LBBB) an unpaced 12 lead standard ECG and a transthoracic echocardiogram was obtained at baseline and after 21±14 months. The LBBB patients and controls were matched with regard to age (LBBB 65±9 vs. controls 62±8 years, p=n.s.), left ventricular ejection fraction (23±8% vs. 26±9%, p=n.s.) and underlying heart disease (CAD 8, NICM 13 in each group). Changes of spontaneous cardiac activation (P wave duration, PR interval, QRS width, QRS vector), repolarization (QTc) and LVEDD were analyzed.

Results: The LVEDD was significantly reduced in the CRT group (62±8 vs. 69±10 mm, p=0.002), whereas the controls showed a nonsignificant increase (65±8 vs. 64±9 mm, p=n.s.). Mean QRS duration increased in both groups, but only for the controls the difference was statistically significant (LBBB: 171±20 vs. 165±22 ms, p=0.07; controls: 118±19

vs. 111 ± 17 ms, $p=0.01$). The PR interval increased over time in both groups (LBBB: 188 ± 30 vs 175 ± 29 ms, $p=0.03$; controls: 187 ± 19 vs 177 ± 25 ms, $p=0.2$). QTc and P wave duration showed no significant longitudinal differences in both groups. By univariate and multivariate analyses in both groups no correlation between changes of LVEDD and ECG parameters was found. The results did not differ in patients with CAD and NICM.

Conclusion: Despite a significant reduction of the left ventricular dimension during long-term CRT, spontaneous ventricular activation does not recover, but tends to further worsening. This finding is consistent in CAD and NICM patients. In heart failure control patients without LBBB LVEDD and electrophysiological measurements tend to worsen over time.

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Characteristics of patients with reverse remodelling after cardiac resynchronization therapy

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A subgroup of patients (pts) who underwent cardiac resynchronization therapy (CRT) shows an important clinical improvement and left ventricular reverse remodeling approaching a normal function. However which groups of pts could better benefit from CRT is not known.

Aim of our study was to analyze the characteristics of pts that showed the greater clinical improvement and reverse remodeling after CRT in a large multi-center register.

Methods: After a mean follow-up of 23 ± 17 months, a total of 353 consecutive pts (75 female, 278 male, mean age 70 ± 8 years) that underwent CRT for advanced heart failure (NYHA class III or IV, ejection fraction (EF) $\leq 35\%$, QRS interval of at least 120 ms) were evaluated. Pts who were alive, that showed a functional improvement of at least two NYHA classes, an EF increase of at least 20 percentage points and reached at least EF $\geq 45\%$ during the follow-up, were defined as "super-responders". Clinical, electrocardiographic and echocardiographic characteristics and predictive variables of super-responder patients were analyzed.

Results: 37 pts (10.4%) (15 female, mean age 67 ± 7 years) were identified as super-responders. Nine pts (24%) had coronary artery disease, 7 pts (19%) had atrial fibrillation, 10 pts (33%) were paced for complete AV block. After CRT the EF increased from $28 \pm 6\%$ to $54 \pm 6\%$ and NYHA class decreased from 3.0 ± 0.1 to 0.9 ± 0.4 , mitral insufficiency decreased from 2 ± 1 to 1 ± 0.8 . As compared with other pts, super-responders were more often female (41% vs 19%, $p=0.005$), with not ischemic cardiomyopathy (77% vs 51%, $p=0.005$) and had better baseline EF ($28 \pm 6\%$ vs $26 \pm 6\%$, $p=0.024$). Baseline QRS interval was similar in both group (175 ± 26 ms vs 178 ± 31 ms), however after CRT super-responders showed a shorter QRS interval (145 ± 25 ms vs 162 ± 28 ms, $p=0.001$).

Conclusions: Female affected by less advanced not ischemic cardiomyopathy shows the greater clinical improvement and left ventricular reverse remodeling after CRT. Moreover QRS reduction after CRT seems to be a predictive variable of good outcome. In this subgroup of patient ventricular desynchronization seem the major cause of left ventricular failure and CRT could be a curative treatment.

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Imaging reverse remodelling: multi-slice computed tomography in patients with congestive heart failure receiving cardiac resynchronization therapy

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Introduction: Cardiac resynchronization therapy (CRT) is an effective treatment for selected patients with congestive heart failure (CHF) re-

fractory to medical therapy and ventricular dyssynchrony. Volumetric evaluation of these patients is usually provided by echo, whereas the gold standard, magnetic resonance imaging (MRI), is not suitable. Current studies described multi-slice computed tomography (MSCT) based volumetry correlates to correlate well with MRI data. In this study, we investigated MSCT in CHF patients under CRT.

Patients and Methods: 7 pts (m: 3, f: 4) (NYHA III) with dilated cardiomyopathy and LBBB were evaluated before and after CRT (19.8 ± 11.1 months). Using a 16-slice MSCT (rotation time 420 ms) cardiac enhancement was achieved with 100 mL non-ionic contrast medium (Omnipaque-300; flow rate 4.5 mL/s) during one breath hold (19.5 ± 2 s). After scanning (collimation 16×0.75 mm, 120 KV, 550 mAs), short axis views of the left ventricle were reconstructed from basis to apex in 20 time windows of the RR-interval (0% to 95% in 5% steps). End diastole (ED) and end systole (ES) were identified, left and right ventricular (LV, RV) ED and ES volumes (EDV, ESV) and ejection fraction (EF) were calculated. The volumetric LV-parameters were blindly compared with echoc data. In order to demonstrate reverse remodelling following CRT we performed a MSCT based wall motion analysis utilizing colour coded polar maps after manual myocardium planimetry.

Results: MSCT and echo based volumetric data are given in the table. Echo underestimates cardiac volumes. Colour coded polar maps are suitable to demonstrate CRT induced reverse remodelling.

Conclusion: MSCT provides exact cardiac volumetry, whereas echo underestimates cardiac volumes. MSCT based wall motion analysis utilizing colour coded polar maps in order to demonstrate CRT induced reverse remodelling seems to be suitable, but must be validated via more extensive studies.

	LVEDV (mL)	LVESV (mL)	LVEF (%)	RVEDV (mL)	RVESV (mL)	RVEF (%)
Pre CRT						
MSCT	278.2 ± 75.0	226.7 ± 75.4	20.1 ± 8.8	131.4 ± 51.0	108.5 ± 49.4	22.1 ± 9.5
Echo	274.4 ± 85.6	220.1 ± 74.0	19.9 ± 11.9			
Post CRT						
MSCT	218.9 ± 106.4	145.0 ± 71.5	29.6 ± 11.3	107.1 ± 41.8	68.1 ± 32.1	37.4 ± 11.1
Echo	188.7 ± 93.1	125.6 ± 78.0	38.6 ± 14.5			

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Left ventricular diameter reduction with long-term cardiac resynchronization does not depend on improvement of VE/VCO₂ slope or peak oxygen uptake

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Introduction: To date various definitions of response to cardiac resynchronization therapy (CRT) for severe systolic heart failure and intraventricular conduction delay (IVCD) are applied. Changes of the left ventricular end diastolic diameter (LVEDD) and exercise capacity are frequently used to assess response to CRT as they are accepted surrogate parameters to appraise the prognostic relevance of treatment modalities in heart failure patients. Little is known about the interdependence of LV remodeling and functional improvement. This study aims to characterize the association of changes in LV size and exercise capacity during long-term CRT.

Methods: In 37 patients (66 ± 9 y, QRS 161 ± 27 ms, left ventricular ejection fraction $24 \pm 7\%$, 13 female, 22 coronary artery disease, 15 nonischemic cardiomyopathy) with severe systolic heart failure and IVCD a CRT system was implanted. Transthoracic echocardiography and treadmill cardiopulmonary exercise testing was performed at baseline and after 9.6 ± 5.5 months. Changes of LVEDD, peak oxygen uptake (pVO₂), and VE/VCO₂ slope were comparatively analyzed.

Results: LVEDD was reduced from 66 ± 10 to 61 ± 9 mm ($p=0.001$), pVO₂ rose from 14.2 ± 4.4 to 15.7 ± 3.8 ml/min/kg ($p=0.016$) and VE/VCO₂ improved from 38.1 ± 10.9 to 33.8 ± 10.8 ($p=0.007$). The reduction of LVEDD was not correlated to the increase in pVO₂ ($r=-0.16$, $p=0.35$) or improvement of VE/VCO₂ ($r=-0.17$, $p=0.31$). Changes of

VE/VCO₂ and VO₂max were significantly linked to each other ($r=0.73$, $p<0.0001$).

Conclusion: The significant respective improvements of exercise capacity and respiratory efficiency on the one hand and of LV size on the other hand in patients with severe systolic heart failure under long-term CRT are not significantly correlated. The increase in pVO₂ and VE/VCO₂ nor depends on neither produces reduction of LVEDD. Definitions of response based on echocardiography or cardiopulmonary exercise testing are incongruent and are likely to identify different subpopulations. In this light further investigations to clarify mechanisms of functional and structural improvement with CRT are desirable.

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Left ventricular resynchronization is needed for response to cardiac resynchronization therapy

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Background: Recent studies have demonstrated that a positive response to cardiac resynchronization therapy (CRT) is related to the presence of pre-implantation left ventricular (LV) dyssynchrony. However, the time course and the extent of LV resynchronization following CRT implantation and their relationship to response are currently unknown.

Methods and Results: One hundred consecutive patients scheduled for the implantation of a CRT device were prospectively included, using the following criteria: NYHA class III-IV, LV ejection fraction $\leq 35\%$, QRS duration >120 ms and LV dyssynchrony (≥ 65 ms) on color-coded tissue Doppler imaging (TDI).

Immediately after CRT implantation, LV dyssynchrony was reduced from 114 ± 36 ms to 40 ± 33 ms ($P<0.001$) which persisted at 6 months follow-up (35 ± 31 ms, $P<0.001$ vs baseline, $P=NS$ vs immediately post-implantation). At 6 months follow-up, 85% of patients were classified as responders to CRT (defined as $>10\%$ reduction in LV end-systolic volume). Immediately post-implantation, the responders to CRT demonstrated a significant reduction in LV dyssynchrony from 115 ± 37 ms to 32 ± 23 ms ($P<0.001$). The non-responders however, did not show a significant reduction in LV dyssynchrony (106 ± 29 ms vs 79 ± 44 ms, $P=NS$). If the extent of acute LV resynchronization was $<20\%$, response to CRT at 6 months follow-up was never observed. Conversely, 93% of patients with LV resynchronization $\geq 20\%$ responded to CRT.

Conclusion: LV resynchronization following CRT is an acute phenomenon, and predicts response to CRT at 6 months follow-up.

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Assessment of left ventricular dyssynchrony: Phase analysis of gated myocardial perfusion SPECT compared with tissue Doppler imaging

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Purpose: To compare gated myocardial perfusion SPECT (GMPS) with tissue Doppler imaging (TDI) for the assessment of left ventricular (LV) dyssynchrony.

Methods: Recently, it has been suggested that LV dyssynchrony is an important predictor of response to cardiac resynchronization therapy (CRT); LV dyssynchrony is predominantly assessed by TDI with echocardiography. Information on LV dyssynchrony can also be provided by GMPS with phase analysis of regional LV maximal count changes throughout the cardiac cycle which tracks the onset of LV thickening. In 75 patients with heart failure, depressed LV function and wide QRS complex, GMPS and 2D echocardiography, including TDI, were performed as part of clinical screening for eligibility for CRT. Clinical status was evaluated using NYHA classification, 6-minute walk distance and quality-of-life score.

Different parameters (histogram bandwidth, phase standard deviation (SD), histogram skewness and histogram kurtosis) of LV dyssynchrony

were assessed from GMPS and compared with LV dyssynchrony on TDI using Pearson's correlation analyses.

Results: Histogram bandwidth and phase SD correlated well with LV dyssynchrony assessed with TDI ($r=0.89$, $P<0.0001$ and $r=0.80$, $P<0.0001$ respectively). Histogram skewness and kurtosis correlated less well with LV dyssynchrony on TDI ($r=-0.52$, $P<0.0001$ and $r=-0.45$, $P<0.0001$ respectively).

Conclusion: LV dyssynchrony assessed from GMPS correlated well with dyssynchrony assessed by TDI; histogram bandwidth and phase SD showed the best correlation with LV dyssynchrony on TDI. These parameters appear most optimal for assessment of LV dyssynchrony with gated SPECT. Outcome studies after CRT are needed to further validate the use of GMPS for assessment of LV dyssynchrony.

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Description of mechanical dyssynchrony before and after standard CRT implantation in narrow QRS patients

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In heart failure patients (pts) with $120 < \text{QRS width} < 150$ ms echo evaluation of mechanical dyssynchrony (D) has been proposed for better identification of potential responders. Nevertheless, no data presently describe D in this specific group and its evolution after standard CRT implantation.

Methods: 77 patients candidates for CRT because of heart failure NYHA Class III or IV, 33 of ischemic origin, EF = $28\pm 9\%$ and QRS = 120 ± 18 ms have been successively studied in echocardiography at baseline and before discharge. Left Ventricular filling duration reported to heart rate for normalization (LVFT%) evaluated atrio-ventricular synchrony. Left and Right Preejection periods (LPEP and RPEP) defined the mechanical InterVentricular Delay (IVD) = LPEP - RPEP. Intraventricular D was assessed in both in its spatial dimension by measuring the septal to lateral wall delay (Sept-lat) and when possible in its temporal dimension by measurements of diastolic contraction of the septum (DC sept) and/or the lateral wall (DC lat) after aortic valve closure. DC may overlap or not with the next filling phase (Ov sept, Ov lat). Mitral valve colour flow regurgitation area was reported to left atria area (MVR%). Left ventricular ejection time (LVET) was measured and the LPEP/LVET ratio was calculated.

Results: See Table 1.

Conclusions: (1) This narrow QRS population had no significant Atrioventricular and Interventricular D at baseline. (2) Spatial septum to lateral delay was due to major temporal septal Dyssynchrony. (3) Standard BiV implantation only improved the overlapping between septal contraction and LV filling. (4) All others D parameters were either not modified or deteriorated and QRS width increased. (5) These data rise questions about effective delivery of resynchronization by standard BiV pacing in this specific population

Table 1

	Baseline	BiV pacing
LVFT%	46±9	46±13
LPEP ms	133±26	159±38***
RPEP ms	112±24	150±30***
IVD ms	25±32	15±23 ns
Sept-lat ms	99±88	64±127 ns
MVR %	23±17	23±21 ns
DC sept ms	152±75	113±94 ns
DC lat ms	37±59	31±82 ns
Ov sept ms	108±94	37±74*
Ov lat ms	-60±101	-75±87 ns
LPEP/LVET	0.53±0.15	0.64±0.27**
QRS ms	120±18	139±26***

P values refer to comparison with baseline. * $p<0.05$, ** $p<0.01$, *** $p<0.001$

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Systolic asynchrony reduction and sleep disordered breathing in patients with chronic heart failure treated with cardiac resynchronization therapy

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Introduction: It is known, that cardiac resynchronization therapy (CRT) reduces the systolic asynchrony and the incidence of sleep disordered breathing (SDB). However, it has not been yet investigated, if there is a relation between these changes.

Aim of the study: To assess the influence of inter- and intraventricular asynchrony' reduction on the incidence of SDB in patients (pts) with chronic heart failure (CHF) during CRT in 6 months (6m) follow-up.

Methods: The study group consisted of 40 pts (30M; aged 54.8±9) with CHF at NYHA 3.2, LVEF – 24.2±8%, with BMI 26.9±4.1 kg/m² – before CRT. Pts were examined echocardiographically and monitored by ECG Holter 24 h – before and at 6m of CRT. We evaluated intraventricular asynchrony (tissue Doppler imaging) by measuring times to onset of systolic velocity in ejection period: (a) for LV: septum – lateral wall (SL), posterior – anteroseptal wall (PAs) in 4Ch and 3Ch apical view respectively, (b) for RV: RV laterall wall – septum (RVS) – in 4Ch apical view, and interventricular asynchrony – preejection period for LV (LVPEP) and the difference between LVPEP and RVPEP (LV-RV). SDB for 7 hours sleep period was assessed based on digital Holter monitoring – using Lifescreen Apnea software Del Mar Reynolds Medical which determines the Estimated Apnea-Hypopnea Index (AHI). The calculation were made on the changes of AHI (ΔAHI) and SL (ΔSL), PAs (ΔPAs), RVS (ΔRVS), LVPEP (ΔLVPEP) and LV-RV (ΔLV-RV) – parameters before CRT were subtracted from those at 6m.

Results: are presented in table.

Conclusion: The improvement of SDB corresponds with the reduction of interventricular, intraRV and intraLV asynchrony. The resynchronization of ventricular systole could be related to the decrease of SDB incidence.

Table. Asynchrony and SDB reductions.

	Δ LVPEP	Δ LV-RV	Δ SL	Δ PAs	Δ RVS
Δ AHI	p=0.0024	p=0.0017	p=0.0076	p=0.0017	p=0.0369

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The interdependence of mitral valve regurgitation and sleep disordered breathing in patients with chronic heart failure treated with cardiac resynchronization therapy

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Introduction: Cardiac resynchronization therapy (CRT) has proved to diminish the mitral regurgitation (MVR) and the incidence of sleep disordered breathing (SDB). – It has not been yet investigated, whether these changes correspond one with each other.

Aim of the study: To assess the influence of MVR changes and left atrial remodeling on the incidence of SDB in patients (pts) with chronic heart failure (CHF) during CRT in 6 months (6m) follow-up.

Methods: The study group consisted of 40 pts (30M; aged 54.8±9) with CHF at NYHA 3.2, LVEF – 24.2±8%, with BMI 26.9±4.1 kg/m² – before CRT. Pts were examined with echocardiography and monitored by ECG 24 hours Holter – before and at 6 months of CRT. MVR as MVR 'jet area and left atrial area' ratio (JA/LAA) in 2D echocardiography – 4Ch apical view were measured.

SDB for 7 hours sleep period was assessed based on digital Holter monitoring – using Lifescreen Apnea software Del Mar Reynolds Medical which determines the Estimated Apnea-Hypopnea Index (AHI).

The calculation were made on the changes of AHI (ΔAHI), JA/LAA (ΔJA/LAA) and LAA (ΔLAA) – parameters before CRT were subtracted from those at 6m.

Results: LAA diminished from 28.14±7.7 to 25±6.5cm² (p=0.024886), JA/LAA diminished from 0.26±0.16 to 0.15±0.12 (from 26% to 15% of LAA) (p=0.000054), AHI diminished from 17.22±16.35 to 5.24±4.65 (p=0.000016). Main results are presented in table.

Conclusion: The improvement of SDB correspond with the reduction of MVR. The changes of MVR could be responsible for the decrease of SDB incidence.

Table. SDB and MVR

	Δ LAA	Δ JA/LAA
Δ AHI	p=0.000263	p=0.000028

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Poster Area

Atrial fibrillation and cardiac resynchronisation therapy

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Effects of cardiac resynchronization therapy on left atrial remodeling and the incidence of atrial fibrillation in heart failure patients with implantable defibrillators

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Introduction: Cardiac resynchronization therapy (CRT) is beneficial for patients with heart failure. The mechanism of CRT benefit is an improved left ventricular (LV) systolic function and reverse LV remodeling. The effect of CRT on left atrial (LA) remodeling is unknown. Accordingly, the purpose of this study was to evaluate LA remodeling and the incidence of AF after 3 months of CRT.

Methods: 83 consecutive patients with heart failure (71% NYHA III), LV ejection fraction (LVEF) <35%, QRS duration >120ms were included. Clinical parameters, LV dimensions and volumes, LVEF, and LA size were assessed at baseline and after 3 months of CRT. The presence of AF was determined by use of ECG's, monitoring, and stored electrograms of the defibrillator.

Results: Clinical parameters improved significantly; NYHA class decreased from 2.7±0.5 to 2.2±0.5 (p<0.01) and six minute walk distance increased from 330±119 m to 395±111 m (p<0.001). LVEF improved significantly from 21±5 to 30±8% (p<0.001), LV end-diastolic volume decreased from 228±84 ml to 206±86 ml (p<0.001), and LV end-systolic volume decreased from 181±66 to 146±66 ml (p<0.001). Significant reduction in mitral regurgitation was observed. Left atrial diameter decreased from 46±7 mm to 42±7 mm (p<0.001), and LA volume decreased from 67±21 ml to 57±19 ml (p<0.001). During follow-up, 22% of patients had documented AF. Left ventricular and LA remodeling was not significantly different between patients with and without AF during follow-up.

Conclusion: Cardiac resynchronization therapy results in significant LV and LA remodeling after 3 months of CRT. Despite these beneficial effects, the incidence of atrial fibrillation was not affected by LA remodeling.

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Cardiac resynchronization therapy in patients with atrial fibrillation without AV-nodal ablation compared to sinus rhythm: long term outcome

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Introduction: Cardiac resynchronization therapy (CRT) and optimized medical therapy are the treatment of first choice for patients (pts.) with congestive heart failure (CHF), NYHA > II-III, EF 150 ms. There are only few data for pts. with CHF and atrial fibrillation (AF) receiving CRT. The aim of our study was to compare CRT-pts. with AF to pts. with sinus rhythm (SR) during a follow up (FU) period of 1 year. AV-nodal ablation was not performed on AF-pts., but they received optimized rate controlled medication to avoid intrinsic conduction.

Methods and Results: 519 pts. (SR: n=450; AF: n=69) received CRT following acute testing prior implant. FU was 23±19.5 months. Epidemiologic data at baseline showed no significant differences between pts. with SR vs. AF: age 62±11, 62±10 years; female 107 vs. 15; dilated cardiomyopathy 56 vs. 43%; coronary artery disease 36 vs. 33%; EF 24±7 vs. 25±8%, QRS-width 183±29 vs. 181±37 ms. NYHA, VO2 peak and 6 minute walk improved significantly in both groups without significant difference between them. Left ventricular enddiastolic diameter (LVEDD) showed a significant decrease only in SR-pts.. No significant difference was observed for severe cardiac events, i.e. death, transplant (SR 15.3 vs. AF 20%).

Conclusion: Long term outcome of CRT-pts. with AF on rate controlled medication demonstrates similar improvement in functional tests and no significant difference in severe cardiac events. CRT-pts. with AF improve without AV-nodal ablation, which appears to be avoidable and furthermore, the best region(s) of ventricular stimulation after AV-nodal ablation have still to be determined.

	baseline		1-year FU	
	AF	SR	AF	SR
n	69	450	29	236
NYHA	3.1±0.4	3.0±0.4*	2.4±0.8	2.1±0.6*
VO2peak [ml/kg BW/min]	12.3±2.4	13.0±3.2°	13.9±5.1	15.5±3.8°
6-min walk [m]	341±139	325±107°	406±91	424±96*
LVEDD [mm]	76±9	78±11°	76±9	71±14*

*p < 0.05, °non significant: SR vs. AF

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Is necessary to ablate de A-V junction to assess a positive response to CRT in patients with permanent AF ?

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The need for AV node ablation in patients with permanent atrial fibrillation (AF) who underwent cardiac resynchronization (CRT) is still under debate.

The aim of the study was to compare the results of CRT in a group of patients with AF depending on whether or not they were submitted to AV node ablation.

Methods and Results: A group of 126 consecutive patients with permanent AF treated with CRT due to refractory heart failure were included in the study. A total of 19 patients undertook AV node ablation due to poor rate control (group A). Group B had a good rate control with drugs (> 85% pacing) (n=107). There were no differences in basal characteristics (age, NYHA class, drug therapy, EF, ventricular diameters, 6-minutes walk test 6MWD). Patients in group A had 100% pacing as compared

to 93±10 in group B (p < 0.01) At 12 months There was no difference in the % of responders (alive, not transplanted and that increased >10% at the 6 min walk test) (58% group A vs. 67% group B). Table 1 show the response and the reverse remodelling obtained in survivors in both groups.

Conclusion: In patients in AF who underwent CRT, AV node ablation is only necessary when a satisfactory rate control is not achieved with drug therapy.

Table 1. Improvement at 12 months follow-up

Variation in survivors	Improvement ^a		p
	Group A	Group B	
6MWD	99±200	75±155	n.s.
LVEDD	-3±6	-1±7	n.s.
LVESD	-2±8	-3±9	n.s.
LVEF	6±6	7±9	n.s.

^aDifference between value at 12 months and value at baseline. 6MWD: 6 minutes walking distance test; LVEDD: Left ventricular end diastolic diameter; LVESD: Left ventricular end systolic diameter; LVEF: Left ventricular ejection fraction.

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Cardiac resynchronization therapy combined by atrioventricular junction ablation could have beneficial effects in advanced heart failure patients with permanent atrial fibrillation

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Cardiac resynchronization therapy (CRT) reduces morbidity and mortality in patients with heart failure, sinus rhythm and left bundle branch block. The effects of CRT in advanced HF patients with permanent atrial fibrillation and the role of atrioventricular junction ablation has, thus far, not been investigated in detail.

Methods: We did a prospective study in which AVJ ablation was performed in AF patients the same day with CRT implantation. Thereafter, detailed follow up of clinical, functional and echocardiographic parameters was carried out.

Results: A total of 65 patients were consecutively implanted with CRT at two Greek Centers. Twenty-nine patients were in AF. In all AF-patients ventricular rate was not adequately controlled by controlling anti-arrhythmic drugs and AVJ ablation was consequently performed, ensuring 100% effective CRT delivery. Both sinus rhythm group and AF patients with AVJ ablation showed significant and permanent (up to 28 months) improvements of all estimated parameters (p value for all parameters < 0.002). However, the AF group with AVJ ablation showed a more significant increase of ejection fraction (EF) (P < 0.01) and also a more significant increase in peak exercise oxygen consumption (pVO2) (p < 0.01) compared to the sinus rhythm group.

Conclusions: The cardiac resynchronization therapy (CRT) on Heart failure (HF) patients with permanent AF showed large and sustained long-term improvements if atrioventricular junction ablation (AVJ) was performed simultaneously with CRT implantation.

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Incidence of atrial fibrillation in patients with cardiac resynchronization therapy, a case control study

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Purpose: Prevalence of Atrial Fibrillation (AF) in patients with Heart Failure (HF) in NYHA class IV is about 50%. Cardiac Resynchronization Therapy (CRT) produces beneficial effects in the ventricular remodelling. The aim of this study was to determine the effects of CRT in the incidence of AF.

Methods: We studied two groups of 28 and 29 patients with similar characteristics, without previous AF neither antiarrhythmic drug therapy,

treated with CRT without anti-tachycardia algorithm or Implantable Cardioverter Defibrillator (ICD). The mean follow-up period for arrhythmic events was 8.5 months.

Results: In the CRT group, 57.6% of all patients presented idiopathic Dilated Cardiomyopathy and 42.2% presented ischemic aetiology. 2 patients died during follow-up (one cardiovascular death). 3 patients (11.5%) were readmitted because of HF symptoms. 4 patients presented AF during follow-up (15.4%) but only one episode of AF longer than 12 hours. In the ICD group, 5 patients died during follow-up (3 cardiovascular death) and 4 patients were readmitted because of HF. 8 patients presented AF (23.2%) and there were 6 episodes longer than 12 hours ($p < 0.05$). (See Cox regression graphic). Regarding echocardiographics data, in the CRT group the atrial diameter remained unchanged. The mean ejection fraction raised from 22.8 ± 8.8 to 32.5 ± 13.3 ($p < 0.001$). In the ICD there were no differences.

Conclusions: CRT was associated to lower AF rate (hours at AF and AF episodes longer than 12 hours). Based on the lack of significant changes in the atrial dimensions observed in this study, our data support a beneficial effect in the atrial electric remodelling in patients with CRT respecting to those with ICD.

Echocardiographics data

Data	ICD (n=29)	CRT (n=27)	p
Baseline ejection fraction	31.7±7.6	22.8±8.8	<0.05
Follow-up ejection fraction	30.15±6.8	32.50±13.3	0.306
Baseline left atrial diameter (mm)	38.9±5.41	43.19±8.12	0.034
Follow-up left atrial diameter (mm)	39±4.14	43±8.54	0.064
Baseline left ventricular diameter (mm)	46.6±9.07	56.07±9.61	0.001
Follow-up left ventricular diameter (mm)	48.54±6.4	50.65±13.9	0.533

On the CRT group the atrial diameter remained unchanged.

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Does cardiac resynchronisation therapy facilitate spontaneous conversion to sinus rhythm?

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Background and Aim: Recent studies have demonstrated that positive hemodynamic effects of cardiac resynchronisation therapy (CRT) apply to patients with atrial fibrillation in similar as to patients with preserved sinus rhythm. Furthermore, case reports suggest that CRT may facilitate the spontaneous conversion to sinus rhythm in patients with persistent or permanent atrial fibrillation. Aim of the study was to assess the conversion rate to sinus rhythm in a cohort of patients who were in chronic atrial fibrillation at the time of implantation of a CRT system.

Methods: Patients with optimal pharmacological heart failure therapy, left ventricular ejection fraction $< 35\%$, NYHA functional class III or IV, left bundle branch block and atrial fibrillation for at least 3 months were included in the study. The implantation of an atrial lead was left upon the discretion of the implanter. Spontaneous conversion to sinus rhythm was assumed if patients presented at follow-up with sinus rhythm (patients without an implanted atrial lead) or if the modeswitch burden was $< 98\%$ according to the Holter of the device (patients with atrial lead).

Results: 25 patients (23 male, 24 NYHA III, 23 with the implantation of a cardioverter defibrillator) were included in the study. Age at implantation was 70 ± 8 years, the left ventricular ejection fraction was $22 \pm 7\%$, the left atrial diameter was 57 ± 9 mm, and the left ventricular enddiastolic diameter was 71 ± 9 mm. In 15 patients a coronary artery disease and in 10 patients a dilated cardiomyopathy was diagnosed. The patients were followed for a mean of 11 months (range 1–48 months). Five patients converted to sinus rhythm on the occasion of defibrillation threshold testing during the implantation of a cardioverter defibrillator. All these patients received an atrial lead. Modeswitch burden was between 0 and 80% during follow-up for these patients. Among the other patients (10 patients with the implantation of an atrial lead and 10 without an atrial lead), none converted spontaneously to sinus rhythm during follow-up.

Conclusion: In patients with atrial fibrillation who receive a CRT system the implantation of an atrial lead is recommended when “accidental”

cardioversion occurs during defibrillation threshold testing. In all others the implantation of an atrial lead seems dispensable because spontaneous conversion to sinus rhythm is infrequent.

MONDAY, 25 JUNE 2007, 15:30–16:30

Poster Area

Arrhythmic risk and mortality factors in cardiac resynchronisation therapy patients

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Effects of cardiac resynchronization therapy on premature ventricular contractions and life-threatening ventricular tachyarrhythmias in patients with chronic heart failure

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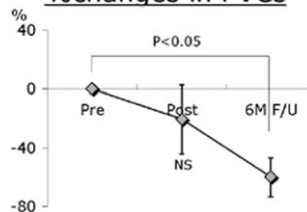
Backgrounds: It still is controversial whether cardiac resynchronization therapy (CRT) is effective to reduce ventricular arrhythmias in patients with chronic heart failure (CHF).

Methods: In 13 consecutive CHF patients with CRT (4 with a combined defibrillator, CRT-D), a 24-hour Holter ECG was serially examined before and 2 weeks and 6 months after CRT to evaluate the frequency of premature ventricular contractions (PVCs) and non-sustained ventricular tachycardia (NSVT, ≥ 3 consecutive PVCs). The event of sustained VT was followed for 19 ± 3 (mean \pm SE) months after CRT.

Results: Patients included 10 males and 3 females and were averagely 63 ± 2 (52–77) years old. The NYHA class improved from 3.2 ± 0.2 to 2.2 ± 0.1 ($p < 0.05$) and the plasma BNP level decreased from 578 ± 140 to 303 ± 74 pg/ml ($p < 0.05$) 6 months after CRT. Analysis of Holter ECGs showed that frequency of PVCs before CRT was $4.9 \pm 1.8\%$ per day (5139 \pm 1941 beats). Among the 10 patients (71%) who showed frequent PVCs ($\geq 1\%$ of total beats) before CRT, PVCs were decreased in 9 patients at 2 weeks ($-20 \pm 24\%$) and in all at 6 months ($-60 \pm 13\%$) ($P < 0.05$; Figure). Although the frequency of NSVT also was decreased in 7 patients at 2 weeks after CRT, the exacerbation of NSVT (≥ 10 consecutive PVCs) was noted in other 3 patients who had no exacerbated NSVT before CRT. During the follow-up period, VT occurred in 3 patients with a CRT-D device. There was no relationship between the occurrence of VT and that of PVCs or NSVT.

Conclusions: Although CRT decreases the frequency of PVCs and NSVT, the therapy may not affect the occurrence of exacerbated NSVT or sustained VT in patients with CHF.

%changes in PVCs



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Sudden Cardiac Death in patients undergoing Cardiac Resynchronization Therapy (differences between etiologies)

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Objective: Analyze sudden cardiac death (SCD) in relation to total mortality (TM) in different etiologies of dilated cardiomyopathies in patients (pts) undergoing cardiac resynchronization therapy (CRT).

Material and Methods: Between June/99 and August/06, 257 patients (pts) were submitted to CRT in our service, 39 of them receiving CRT associated to ICD (excluded from this sample). This study evaluated 207 pts in follow-up. Mean age was 61.7 ± 11.9 years and 135 pts were male (65.2%). Cardiopathy etiologies were: idiopathic = 88 pts (42.5%), ischemic = 52 pts (25.1%), chagasic = 44 pts (21.3%) and other = 23 pts (11.1%).

Results: During a mean follow-up of 23.0 ± 20.1 mo., total mortality was 37.7% (78 pts). Cause of death was: SCD = 37 pts (47.4%), CHF = 21 pts (26.9%) and other = 20 pts (25.6%). Mortality in the chagasic group was 52.2% (47.8% due to SCD), idiopathic = 34% (46.6% due to SCD), ischemic = 28.8% (33.3% due to SCD) and other etiologies = 43.4% (70% due to SCD). Among deaths, 71.7% (56 pts) occurred the first year after CRT. From SCD 78.3% occurred the first year after CRT being 51.7% during the first month. Between different etiologies there was no significant difference in number of deaths or causes of death.

Conclusions: These results allow us to conclude that: (1) After CRT, TM is significantly higher the first year than later. (2) SCD was the main cause of death in this group of pts, occurring more frequently during the first year and mainly during the first month. There is no difference in TM or SCD between different etiologies.

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Is cardiac resynchronization proarrhythmic?

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Purpose: Cardiac resynchronization therapy (CRT) reduces mortality in selected patients with impaired left ventricular systolic function. CRT induced proarrhythmia has been raised as a potential drawback. We assessed the impact of CRT on the incidence of ventricular tachyarrhythmias in patients who underwent an upgrade of their conventional implantable cardioverter-defibrillator (ICD) system to a CRT-ICD system.

Methods: Patients undergoing upgrade to CRT-ICD between September 2003 and February 2006 were included in this study. After the upgrade the patients were followed in the ICD clinic at least every 3 months. Data were analyzed for episodes of ventricular tachycardia (VT) and ventricular fibrillation (VF) requiring therapy.

Results: The study population included 59 patients (47 men and 12 women; 33 with single chamber ICD and 26 with dual chamber ICD). Forty nine patients (83%) had ischemic cardiomyopathy and 10 (17%) had non-ischemic cardiomyopathy. The follow-up period was 58 ± 35 months before and 10 ± 6 months after the upgrade. At time of upgrade, the patient age was 70 ± 9 years and the ejection fraction was $22 \pm 8\%$. Before upgrade to CRT-ICD, the frequency of combined VT and VF events was 1.58 events/year/patient versus 13.85 events/year/patient after upgrade ($P = 0.003$).

Conclusion: Although CRT improves mortality and symptoms in patients with advanced heart failure, our study showed an increase in ICD therapy after upgrade to CRT-ICD, suggesting a proarrhythmic effect.

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Does cardiac resynchronization therapy prevent ventricular arrhythmias?

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Background: Cardiac resynchronization therapy (CRT) has been shown to improve prognosis, quality of life and exercise tolerance in patients with chronic heart failure (HF). Ventricular arrhythmias are at risk of sudden cardiac death for patients of HF. However, the effects on ventricular arrhythmias remain unknown in CRT. We evaluated the relationship

between the improvement of left ventricular function and ventricular arrhythmias in CRT.

Methods: Twenty-two consecutive patients (11 males, mean age 63 ± 10 years) had HF with NYHA class III–IV and QRS duration >130 ms on optimal treatments. We evaluated ventricular arrhythmias by Holter electrocardiogram and left ventricular function by echocardiogram before and 1 month after CRT.

Result: Ejection fraction was significantly improved 1 month after CRT ($24.7 \pm 6.1\%$ to $31.5 \pm 5.6\%$, $p = 0.05$). Premature ventricular contractions (PVCs) were not significantly decreased after CRT (2.9% to 2.7%, $p = \text{NS}$). Nonsustained ventricular tachycardia (VT) was not significantly decreased after CRT ($n = 7$ (32%) to $n = 4$ (18%), $p = \text{NS}$). And moreover 2 patients had new Nonsustained VT. Although no patient had sustained VT and syncope before and after CRT, one patient died suddenly after CRT during follow up period (20.2 ± 12.9 months).

Conclusion: In many cases, ventricular arrhythmias decreased according to the improvement of the ventricular function. Although CRT improved ventricular function, CRT did not decrease ventricular arrhythmias. It is necessary to care of ventricular arrhythmias for patients with HF after CRT and to prevent sudden cardiac death.

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Heart rate turbulence assessment in patients with chronic heart failure treated with cardiac resynchronisation therapy

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Heart rate turbulence (HRT) which reflects baroreflex sensitivity is regarded as a new factor in the patients' (pts) stratification for the risk of sudden cardiac death (SCD). HRT has not been investigated in pts treated with cardiac resynchronisation therapy (CRT) so far.

The purpose of the study was to assess HRT in pts with advanced chronic heart failure (CHF) treated with CRT in 6 months follow-up.

The study group consisted of 53 pts (17F, 36M; aged 55 ± 8 years) with CHF at NYHA class III–IV, EF below 35% (mean $23.6 \pm 6.8\%$) and significant systolic dyssynchrony of the left ventricle, confirmed by tissue Doppler imaging, in whom BIV pacemakers were implanted. Within study group in 6 months follow-up 37 pts were qualified as responders and remaining 16 as non-responders. HRT parameters: turbulence onset – TO [%] and turbulence slope – TS [mm/RR interval] were assessed based on 24 hours digital Holter monitoring using HRTView program. HRT parameters before BIV implantation and after 6 months of CRT were calculated and compared. Pts with atrial fibrillation were excluded from the study.

Results: In the whole group before CRT mean TO was: 0.004 ± 0.02 and after 6 months of CRT its value although has not changed significantly, but reached value below zero regarded as a normal: -0.008 ± 0.007 . TS in 6 months follow-up increased significantly and its baseline value was 2.04 ± 1.8 vs 3.7 ± 3.0 ($p = 0.0001$) after 6 months of CRT. In responders, contrary to non-responders, significant increase of TS after 6 months of CRT was observed, reaching then value above 2.5 considered as a low risk factor for SCD.

Conclusions: During 6 months of CRT therapy increase of HRT parameters is observed, especially expressed in pts who respond to the therapy. Therefore, CRT may improve baroreflex sensitivity.

	TO		p	TS		p
	Before CRT	6 mo follow-up		Before CRT	6 mo follow-up	
Responders	0.005±0.02	0.0003±0.02	NS	1.9±1.5	4.5±3.0	<0.001
Non-responders	0.002±0.01	-0.03±0.1	NS	2.2±2.4	1.5±1.4	NS

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Predictive value of transmural dispersion of repolarization parameters for appropriate therapy in biventricular implantable cardioverter-defibrillator

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Background: Transmural dispersion of repolarization (TDR) is associated with an increase risk of ventricular arrhythmias. We sought to explore the value of TDR electrocardiogram parameters to predict appropriate implantable cardioverter-defibrillator (ICD) therapy in patients who have undergone a cardiac resynchronization(CRT) ICD implant.

Methods: We retrospectively analyzed 99 patients who underwent CRT-ICD. All patients had stable heart failure, New York Heart Association functional class III or IV HF symptoms, left ventricular ejection fraction $\leq 35\%$, and QRS duration >130 ms or QRS ≤ 130 ms with left intraventricular dyssynchrony. For each patient, we assessed electrocardiogram indices of TDR before and after CRT implantation (QTc, T peak-T end (Tp-e) and their dispersions).

Results: After a mean follow up of 10.5 ± 7.5 months, 24 patients experienced an appropriate ICD therapy. ICD therapy and no ICD therapy groups had similar baseline characteristics, including prevalence of ischemic cardiomyopathy and secondary prevention implantation. At baseline, TDR parameters were higher in the ICD therapy group. After CRT implantation, the ICD therapy group exhibited a higher increase in TDR compared no ICD therapy group. Baseline QT dispersion, baseline Tp-e dispersion and post-implantation Tp-e were independent predictors of ICD therapy. Post-implantation Tp-e was the best parameter in predicting ICD therapy ($p=0.006$), for a value ≥ 110 ms, with a specificity of 75% and a sensitivity of 71%.

Conclusions: Both baseline and post-CRT implantation TDR parameters were independent predictors of appropriate ICD therapy.

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Pacing site-dependent changes in ECG markers of ventricular repolarization in heart failure

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Our previous data suggest that biventricular pacing may reduce QT dispersion (QTd) and transmural dispersion of ventricular repolarization as indicated by T-peak-T-end interval (TpTe). Hitherto, we have little data about the pacing-site dependent differences in ECG markers of heterogeneity of ventricular repolarization.

The purpose of the study was to assess the pacing-site dependent changes in QTd and TpTe interval in patients with congestive heart failure after resynchronization therapy.

Methods used: thirty-one patients (age 62 ± 08 years, 6 female) with congestive heart failure (NYHA class III-IV, ejection fraction $28 \pm 06\%$) and left bundle branch block (QRS duration 156 ± 8.96 ms) underwent biventricular pacemaker or implantable cardioverter defibrillator (ICD) implantation. The 12-lead ECG at a paper speed of 50 mm/s was recorded before the implantation and compared to that obtained 24 hour after during LV epicardial (LVepi), RV endocardial (RVendo) and biventricular stimulation. QTd was determined as the difference between the maximal and the minimal QT interval in any lead. TpTe interval was measured from the peak of the T wave to the end of the T wave.

Summary of results

	QTd (ms)	TpTe (ms)
Before implantation	84.6 ± 10.65	98.2 ± 12.56
Biventricular pacing	54.4 ± 10.08	77.4 ± 11.13
LVepi pacing	104 ± 11.42	112.4 ± 10.54
RVendo pacing	90.6 ± 10.05	101.3 ± 14.04

Conclusions: both right ventricular endocardial and left ventricular epicardial pacing increased QTd and transmural dispersion compared to

baseline sinus rhythm ($p < 0.05$). On the contrary biventricular pacing decreased QTd and TpTe ($p < 0.05$). These data suggest a possible advantage of biventricular stimulation compared to LVepi and RVendo pacing as far as potential arrhythmia is concerned.

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Increase in LVEF with resynchronization therapy is associated with improved cardiac sympathetic activity assessed by 123 I-MIBG scintigraphy

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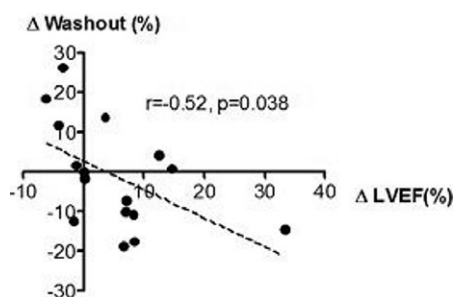
Background: Patients with severe heart failure may have an increase in sympathetic tone. Cardiac resynchronization therapy (CRT) has been shown to improve outcome and left ventricular ejection fraction (LVEF) in these patients. Whether CRT also improves cardiac sympathetic activity has not been well studied. 123 I-MIBG is a noradrenalin analog, and may be used to assess cardiac adrenergic activity.

Aim: To assess changes in cardiac adrenergic activity with CRT, and to assess whether these changes are related to an improvement in LVEF.

Methods: Sixteen patients (13 males, age 66 ± 7 years) were studied at baseline and after >6 months of CRT (mean follow-up 9.2 ± 3.2 months). LVEF was assessed by nuclear angiography, and cardiac adrenergic activity by 123 I-MIBG scintigraphy. Heart to mediastinal (H/M) ratios were evaluated at 20 and 240 minutes, and 123 I-MIBG washout (indicating competition with plasma noradrenalin) was calculated.

Results: LVEF was significantly improved at follow-up (30.1 ± 14.7 vs 24.7 ± 8.2 , $p = 0.04$). There was a significant correlation between improvement in LVEF and change in 123 I-MIBG washout (see figure).

Conclusion: In patients treated by CRT, improvement in LVEF is associated with an improvement in cardiac sympathetic activity. This may contribute to the improvement in outcome and reduction of cardiac arrhythmias observed with CRT.



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Clinical deterioration after cardiac resynchronization therapy

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Background: Although cardiac resynchronization therapy (CRT) is effective treatment for refractory congestive heart failure, in some patients clinical status deteriorates following this therapy. We sought to investigate the incidence, prognosis and predictors of poor response to CRT.

Methods: One hundred and twenty five consecutive patients implanted with a CRT device were included in the present study. We recorded clinical parameters (age, NYHA class, quality of life questionnaire, 6-minute walk and BNP levels) electrocardiographic parameters (QRS duration) and echocardiographic parameters (left ventricular (LV) ejection fraction (EF) and dimensions, MR grade and intra- and inter LV asynchrony by tissue doppler imaging), at baseline and up to 6 months post implantation. Deterioration was defined in patients who had an increase in NYHA class by at least 1 point or a 6-minute walk reduction of $>10\%$.

Results: Deterioration was found in 19 patients (15%). There were no significant differences in baseline clinical characteristics between the groups, except that patients who deteriorated after CRT had a higher baseline LVEF compared to other patients (25±4 vs. 21±6 respectively; $p=0.04$). Over long term (up to 18 months of follow up) 3 patients had further deterioration, 3 had an improvement and in all other patients there was no clinical change.

Conclusions: Clinical deterioration after implantation of CRT occurred in 15% of our patients. Long term CRT did not change the clinical status of most of these patients. There are no reliable baseline predictors for deterioration following implantation.

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Atrial fibrillation at implant is a major predictor of death in patients receiving CRT devices

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Cardiac resynchronization therapy (CRT) has proved to improve quality of life, morbidity (heart failure hospitalizations, functional class) and mortality in sinus rhythm (SR) patients. Atrial fibrillation (AFib) is highly prevalent among heart failure patients. Patients with atrial fibrillation have been excluded from most of the CRT trials, and the best strategy for these patients has yet to be defined. This single center study is a retrospective comparison of the outcomes in patients in sinus rhythm versus patients with AFib in whom a CRT device was implanted.

Population: Between 2000 and 2005, CRT devices were implanted in 132 patients at our unit. Of these, 78 were in SR at implant, and 54 were in Afib (12 had paroxysmal Afib and 42 persistent/permanent Afib). An adequate delivery of biventricular pacing was assured, in patients in Afib, either with AV blocking agents to assure low heart rate, or with AV nodal ablation (50%). There was no difference among patients in SR or patients in Afib, concerning the age (68.3±8.8 vs 65.9±9.7 years old), the ejection fraction (26.2±8.1 vs 25.6±9.5), the etiology of the heart failure (54% of ischemic patients in both groups), or the number of CRT defibrillators (83% SR vs. 75% AFib, NS).

Results: The mean follow-up was comparable in both groups (20 months). The rate of biventricular pacing was the same in both groups (93.4±14.3% vs. 95.4%±12.8%). Patients in AFib at the time of implant had a higher rate of death – 19% vs 1.3% ($p<0.001$), and more hospitalizations for heart failure (50% vs 33%, $p=0.04$). In a multivariate analysis, persistent/permanent AFib at implant and NYHA class after implant were strong predictors of death in the follow-up (OR for Afib – 51.88, 2.135 to 1142.73, 95% CI)

Conclusions: Persistent or permanent atrial fibrillation at implant are markers of poor prognosis in patients submitted to CRT implant, even with adequate delivery of biventricular pacing. It remains to be proved if adequate strategies for rhythm control, such as AFib ablation, will improve this outcome.

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Effect of baseline renal insufficiency on outcomes after cardiac resynchronization therapy

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Background: Renal insufficiency (RI) is common in patients (Pts) with heart failure (HF) and predicts worse outcome. Cardiac resynchronization therapy (CRT) is associated with survival benefit in selected Pts with HF yet the impact of RI on outcome in this Pt population, is unknown.

Methods: To determine this, we reviewed all Pts undergoing CRT at Mayo Clinic between 1999–2005 and compared outcome based on the presence of RI and changes in renal function following CRT. All data were prospectively entered into a registry and retrospectively reviewed. Renal function was assessed prior to and following CRT (creatinine clearance (CrCl) by Modification of Diet in Renal Disease equation), and RI was classified as moderate (CrCl < 60 ml/min/1.73 m²), severe (CrCl < 30 ml/min/1.73 m²), or normal (CrCl > 60 ml/min/1.73 m²).

Results: A total of 511 Pts (80% male) aged 68±12 years (62% ischemic cardiomyopathy, EF 22±8%) were included and followed for 20.5±15.7 months. RI was present in 374 Pts (moderate in 325, CrCl = 46.4±8.9 ml/min/1.73 m² and severe in 49, CrCl = 24.0±5.1 ml/min/1.73 m², $p<0.01$). Renal function was normal in only 137 Pts (CrCl = 73.3±14.3 ml/min/1.73 m²). Overall, CrCl declined in Pts with normal renal function but improved somewhat in Pts with severe RI ($p<0.01$). Severity of RI was directly related to prognosis ($p<0.01$).

Conclusions: Even in Pts with normal renal function at baseline, renal function declines despite CRT. RI at the time of CRT predicts worse outcome and should be considered when selecting Pts.

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Poster Area

Non invasive cardiac arrhythmic assessment

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Is it really time to abandon quinidine completely?

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Background: Quinidine is the oldest known antiarrhythmic drug, used since 1918. When Coplen reported increased mortality associated with quinidine, its use began to decline. However, as appeared recently, quinidine could be important for selected patients with serious arrhythmogenic heart diseases (i.e. Arrhythmogenic right ventricular dysplasia, Brugada syndrome, Short QT syndrome etc.). The aim of this paper is to contribute to creation of more positive image of quinidine.

Materials and Methods: A group of 342 pts with long-lasting persistent atrial fibrillation (AFib) received oral loading dose of quinidine sulphate (200 mg in 2 hour-intervals during 24 hours, up to 2.4 g), while continuously monitored by telemetry and 12-lead ECG recorded every 2 hours during 48 hours. Drug was discontinued when sinus rhythm was restored or if complications (QTc > 500 ms, frequent premature ventricular complexes (PVCs), nonsustained ventricular tachycardia (VTns), QRS widening >40 ms and/or complains of gastrointestinal or neurological disturbances) were recorded.

Patient data and recorded complications

Males	237 (69.3%)
Age (years)	17–78 (56±11)
Males	237 (69.3%)
Lone AF	137 (40.0%)
Hypertension	130 (38.0%)
CHD	23 (6.7%)
Cardiomyopathies	36 (10.5%)
Mild valv. disease	20 (5.8%)
Prosth. valves	15 (4.4%)
Dilated LV	78 (22.8%)
LVEF<55%	63 (18.4%)
LVH	21 (6.1%)
Dilated RA/RV	17 (5.0%)
Polymorphic VT/VF	3 (0.88%)
VTns/freq. PVCs	16 (4.6%)
QT prolongat	27 (7.9%)
QRS widening	5 (1.5%)
1:1 AFI	12 (3.5%)
GIT or neurological disturbances	20 (5.8%)

CHD: Coronary Heart Disease, LVEF: left ventricular ejection fraction, LVH: left ventricular hypertrophy, AFI: atrial flutter.

Results: Patients data and recorded complications are shown in Table 1. The most frequently administered dose of quinidine was 1400 mg (range 200–2400). Sinus rhythm was restored in 265 pts (77.5%). Drug was discontinued in 50 pts (14.6%) due to complications. Serious rhythm disorders (polymorphic VT/VF) developed in three patients with significantly reduced EF (<30%) after 200–600 mg of quinidine. There were no fatal events.

Conclusion: As appeared, quinidine could be a safe drug for selected patients with preserved left ventricular function. If results of 48 hour close monitoring during and after drug administration are to be extrapolated to out-of-hospital settings and lower doses of quinidine, it seems that outpatient administration of this drug certainly deserves more investigation before it is finally discarded.

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Predictive factors of a positive response to flecainide test in patients with non diagnostic electrocardiogram for Brugada syndrome

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Coved type ST segment elevation ³ 2 mm in leads V1-V3 is considered a confirmatory ECG pattern of Brugada Syndrome (BS). Sodium channel blockers are used to exacerbate ST segment elevation in a case of non diagnostic ECG's. There haven't been described any basal ECG predictors of a positive response to flecainide test, but prolongation of PR interval. Moreover, the safety of this approach remains unclear. The aim of this work was to analyze the predictive factors of a positive response to the flecainide test in patients with suspected but not confirmed BS.

Methods: A group of 175 consecutive patients with suspected and non-diagnostic ECG's for BS were included and classified in three groups: Normal or right bundle branch block (RBBB), type 2 BS ECG (saddleback appearance), and type 3 BS ECG (saddleback or coved appearance with ST-segment elevation of <1 mm). Clinical data was taken for all patients, including family history of BS, sudden death or symptoms. Flecainide test was performed with 2 mg/kg in 10 minutes and continuous ECG recording until the presence of coved-type, or the end of the infusion.

Results: A 59% of the patients were males with a mean age of 36±15 years. The test was confirmatory of BS in 27.4% of the patients. There were no complications nor adverse effects in any patient. Univariable analysis showed that older patients (...) patients and those with basal type 2 or 3 BS ECGs had a significant higher rate of positive response. Multivariable analysis showed that the type 2 SB ECG was the only independent predictor of a positive response (OR 7.3; 95% CI from 3.0 to 17.6; P < 0.001).

Conclusions: Flecainide infusion is a safe test to unmask the coved type ECG in patients with doubtful BS diagnosis. Only the saddleback type ECG proved to be an independent predictive factor of a positive response.

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Does the antihypertensive therapy is beneficial in all patients with primary hypertension?

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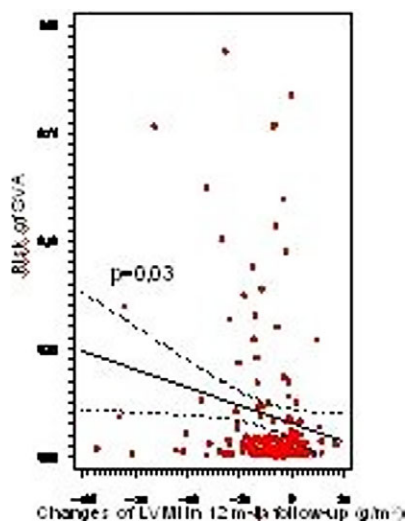
Hypertension has been linked to the development of AF and other supraventricular arrhythmias (SVA). However, it is not fully elucidated, that antihypertensive pharmacotherapy is safety and always beneficial for patient with SVA.

Aim: The aim of the study was to investigate the risk of important SVA during 1 year follow-up antihypertensive therapy in patients with primary hypertension.

Methods: 145 uncomplicated patients with mild to moderate never treated hypertension were enrolled in the study. Patients underwent a clinical examination, BP measurement, ABPM, ECG, 24-hour Holter monitoring ECG, echocardiographic tracings with estimation of LVMI, and atrial SAECG including innovatory parameters (40–250 Hz Butterworth filter) two times: at the beginning and at the end of the 1 year follow-up. Important SVA was defined as an occurrence of PAF, an episode of SV tachycardia or SV premature beats >100/24 hour.

Results: Maximum heart rate (HRmax_1), duration of P-wave in Butterworth filtered atrial SAECG (hfP_S1), envelope of the last 10 ms P-wave vector magnitude (obw10_S1) and left atrial internal area (LAar_1) were identified as the model of important SVA predictors. It was found that occurrence of high degree regression of LVMI was associated with an increase of risk of SVA (fig.), especially in patients with concentric LVH at the beginning of the study.

Conclusion: High, rapid regression of the LVH can lead to supraventricular electrical instability of the heart, especially in patients with concentric LVH.



Risk of SVA and LVMI regression

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Abnormal values of heart rate turbulence in ARVD pts estimated higher risk for sudden cardiac death if coupled with TAPSE

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Purpose: Heart rate turbulence (HRT) encompasses initial acceleration and a subsequent deceleration of sinus rhythm following ventricular ectopic beat with a compensatory pause. The changes in sinus rhythm are thought to be mediated by a baroreflex response to the lower stroke volume of the ectopic beat.

Methods: Among group of 80 patients with ARVD 32 were having arrhythmia of different kind at their presentation before institution of any therapy. 16 female and 16 male patients as compared to the control group (45 pts) with no arrhythmia and confirmed diagnosis by ISFC criteria. In all of them Holter monitoring was assessed and heart rate turbulence, heart rate variability and late potentials analysed. Progression of the disease were measured by 2D echo: RVOTfs% and TAPSE.

Results: All arrhythmia prone patients showed abnormal HRT whereas all ARVD patients showed irregular pattern for heart rate variability. Also of importance the lower EF of right chamber the higher the risk for SCD as confirmed with.

Conclusion: TAPSE correlates well with progression of ARVD and also with heart rate turbulence by estimating higher risk for sudden cardiac death even better than heart rate variability.

HRT coupled with TAPSE on echo

Total number of participants	RVOTfs%	TAPSE	HRT (TO)%	HRV
32 ARVD pts. with arrhythmia	25±4.35	12±2.35	-5.4±3.86	100% positive
48 ARVD pts. with no arrhythmia	38±4.15	18±2.72	-4.17±4.35	negative

Prediction sensitivity of coupling TAPSE derived on echo examination with HRT

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Lack of sensitivity of current ARVC criteria for right ventricular arrhythmias in high-level endurance athletes

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Background: Hypertrophic cardiomyopathy, coronary disease and arrhythmogenic right ventricular cardiomyopathy (ARVC) are the most common causes of ventricular arrhythmias (VA) in athletes. When athletes present with ventricular arrhythmias and the former two entities are ruled out, ARVC is often suspected but not supported by current diagnostic criteria.

Methods: Twenty-two male high-level endurance athletes (median 38 y, 17 cyclists), performing $\geq 3 \times 2$ h endurance exercise/week for ≥ 5 years, underwent electrophysiological evaluation of symptomatic VA. Presenting symptoms were lightheadedness/fatigue/palpitations in 14 (64%), syncope in 6 (27%) and sudden death in 2 (9%). Diagnostic work-up included transthoracic echocardiography (n=22), cardiac MRI (n=19), signal-averaged ECG (n=19) and coronary angiography (all pts >30 yr, n=17). Furthermore, a right ventricular (RV) angiography was performed with quantitative analysis of RV volumes and ejection fraction (EF, n=22), compared to a reference group of 15 high-level endurance athletes without VA.

Results: There was no evidence for hypertrophic cardiomyopathy or coronary disease in any athlete. Based on current Task Force criteria (including qualitative RV imaging with echocardiography and cardiac MRI), the diagnosis of ARVC was established in 6/22 (27%), leaving sixteen patients (73%) without explanation for the observed arrhythmias. Electrophysiologic testing induced sustained VA in 14/22 (64%) athletes, being a monomorphic VT with left bundle branch morphology (RV origin) in 10/14 and due to a definite re-entrant mechanism in 8. Two more patients had repetitive nonsustained arrhythmias with left bundle branch morphology.

Quantitative angiographic analysis showed a significantly decreased RV EF in athletes with VA vs. athletes without VA ($49.1 \pm 10.4\%$ vs. $63.7 \pm 6.4\%$, $p < 0.001$). A RV EF $< 50\%$ did not occur in any athlete without VA, but was present in 14 athletes with VA (64%). When considering induction of sustained VA of RV origin during invasive EPS or a RV EF $< 50\%$ on quantitative RV angiography as additional major criteria, 12 of the 22 athletes (55%) would qualify for a diagnosis of ARVC.

Conclusions: Ventricular arrhythmias in high-level endurance athletes frequently originate in the RV, often in athletes not fulfilling current ARVC criteria. Athletic activity may induce VA in a phase where RV function is only moderately impaired and the overt characteristics of ARVC are absent. Expansion of diagnostic tests and defining specific criteria might be required in athletes.

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Malignant ventricular tachyarrhythmias in young adults with thalassemia major

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Thalassemia Major (TM) is not a rare disease in south east of Europe. Ventricular malignant tachyarrhythmias in young adults with TM are not often reported. We have followed 21 children and young adults with TM, including ekg, echocardiography and 24 h Holter monitoring biannually for more than 4 years. 3 pts, age 15 year old – 2 pts. (1M and 1F) and 16 year old – 1 pt.(1M) – with TM were diagnosed with ventricular life threatening ventricular arrhythmias – ventricular tachycardia (VT) and/or ventricular fibrillation (VF). All 3 pts had developed restrictive and/or dilated cardiomyopathy and developed VT. 2 pts had syncope and had to be resuscitated. VF was diagnosed in one pt. One pt. required an implantable cardioverter defibrillator (ICD) for VT and VF but died

6 month following his ICD implant for end stage heart failure. One pt had recurrent syncope and died with VF and the 3rd pt. is been followed for 3 years having recorded non sustained VT on Holter monitoring. She is on oral antiarrhythmic therapy.

We conclude that cardiomyopathy and ventricular malignant tachyarrhythmias should be search for and diagnosed earlier in these pts. Echocardiography and Holter monitoring should be used as screening methods for young adults with TM as they can develop cardiomyopathy and VT/VF as vital complications of TM.

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Correlation of echo progression parameters to radionuclide ventriculography findings in the follow-up of ARVD pts

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Purpose: ARVC/D is inherited condition characterized by ventricular arrhythmias typ LBBB and progressive lost of right ventricular function due to fibro-fatty apoptotic process in right ventricle. This condition is unrecognized in many patients due to its diverse clinical presentation. Currently there are clinical signs obtained from an ESC/WHF expert consensus including major and minor criteria.

Methods: We have performed radionuclide ventriculography in group of previously diagnosed 20 ARVD patients (9 male and 11 female, age 41 ± 12.54) in a follow up period of 24 ± 8.45 . Radionuclide ventriculography was done in all subjects in a standard way after in vivo labeling of red blood cells with 740 MBq of ^{99m}Tc-pertechnetate.

Results: We found significant global reduction of RVEF in all observed ARVC/D patients ($5 \pm 0.6\%$) compared to first examination (RVEF = $38 \pm 3.8\%$), $p < 0.05$, respectively. Mean difference between LVEF and RVEF was also higher between check ups ($20.2 \pm 7.7\%$ first test vs. $30 \pm 8.5\%$ last test), $p < 0.01$. Left ventricular function was normal in both cases (LV EF $62.3 \pm 5.4\%$), $p > 0.05$, respectively. Also TAPSE showed negative progression.

Conclusion: Our preliminary results indicate that radionuclide ventriculography may be a potent tool in detecting worsening of the disease as an adjunct method for echocardiography evaluation of right chamber. They both can better predict higher risk for fatal outcome of those pts.

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The value of Holter monitoring in the assessment of pediatric patients

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Purpose: Holter monitoring (HM) has been established over the past four decades as one of the most effective noninvasive clinical tools in the diagnosis, assessment and risk stratification of cardiac patients. However, studies in the pediatric age group are limited. The present work aims at determining the value of HM in the diagnosis and management of children.

Methods: Three channel Holter records of 1319 pediatric patients (54.1% males and 45.9% females) presenting to the Arrhythmology clinic, department of Pediatrics, Faculty of Medicine, Cairo University were reviewed. Their average age was 6.7 ± 4.1 years (5 days-16 years). Patients with less than 23 hours of artifact free data were not included in the work. Indications for which Holter monitoring was done were analysed as well as all the abnormalities diagnosed and factors that may increase Holter yield.

Results: The most common indications were palpitations (19.8%), syncope (17.8%), cardiomyopathy (12.6%), chest pain (10%), evaluation of antiarrhythmic therapy (6.8%), postoperative assessment (2.6%) and complete heart block (2.4%). Symptoms occurred in 9.6% of patients during the time of the recording, however symptoms had a poor correlation to abnormalities ($p = 0.2$) and a higher percentage of abnormal recordings were among asymptomatic patients. A sum of 156 Holter recordings were found abnormal with a total diagnostic yield of 11.8%. The highest contribution to diagnosis was in postoperative assessment (29.4%) and in cardiomyopathy (19.9%) where the most common abnormalities were

frequent supraventricular / ventricular premature beats, supraventricular tachycardia, ventricular tachycardia and heart block. Diagnostic yield was low in patients with palpitations (5.7%) and syncope (3.8%). An abnormal ECG was significantly associated with a higher diagnostic yield ($p=0.0001$). None of the children with chest pain had abnormal Holter recordings. The mean, maximum and minimum heart rates and incidence of benign arrhythmias in each group of children are described. This data can be taken as a basis for the analysis of 24 hour ambulatory ECG in children.

Conclusion: HM has an extremely valuable role in the assessment of high risk patients (postoperative and cardiomyopathy). However in children with palpitations, syncope and chest pain HM has a low yield. In this group of patients an abnormal ECG is more likely to be associated with abnormal Holter recordings.

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Labeled stem cells transplantation with ^{99m}Tc HMPAO to the myocardium of patients with dilated cardiomyopathy

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Introduction: Stem cells transplantation is a new therapy intended to produce cardiac regeneration by differentiation, increase cardiac myocytes or neovascular proliferation for patients with end-stage of congestive heart failure secondary dilated cardiomyopathy, but the results are unknown.

Patients and Methods: We studied five patients with known congestive heart failure who underwent stem cells transplantation. Four of them received peridural anesthesia and bone marrow cells were obtained by punctures from the crest of iliac bone, and 20 ml of mononuclear cells suspension was obtained using the technique described in the literature. Three milliliter of the suspension was labeled with ^{99m}Tc HMPAO. Stem cells suspension was slowly injected (1 ml/minute) in coronary arteries. Fifty percent of the suspension was injected in the Left Anterior Descending artery, 25% in the Left Circunflex artery and 25% in the Right Coronary artery. The ^{99m}Tc HMPAO labeled cells were injected only in the Left Anterior Descending artery. One patient received stem cells transplantation by mini thoracotomy technique. All patients were submitted to previous nuclear perfusion study with SESTAMIBI ^{99m}Tc .

Results: Scintigraphic images 2 and 6 hours after the intracoronary transplantation of labeled stem cells (four patients) revealed their accumulation and retention in previous non uptake SESTAMIBI areas and remaining activity was distributed mainly to the liver and spleen. Patient submitted to stem cells transplantation by minithoracotomy showed diffuse uptake tracer at local injection.

Conclusion: This study shows that significant amount of stem cells is preferentially attracted to non uptake areas and retained in these target areas (chronic ischemic or fibrotic myocardium) after intracoronary technique. A large amount of stem cells was attracted and retained at local injection with stem cells transplantation by mini thoracotomy technique.

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Micro-T-wave-alternans – agreement of results with atrial and ventricular stimulation

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Background: Micro-T-wave-alternans (TWA) has been established as an useful risk stratifier for ventricular arrhythmias in ischemic cardiomyopathy. A negative test result is helpful in the MADIT-II-population to select those patients who might not need an implantable cardioverter-defibrillator (ICD). However atrial fibrillation and other irregular supraventricular arrhythmias preclude TWA-analysis in many of these patients. Bundle-branch-block has been shown not to hamper the results significantly. If TWA during ventricular pacing would show agreement

with the results during atrial pacing, this test might also be useful in patients with atrial fibrillation.

Aim: To compare the results of TWA with atrial and ventricular pacing at two rates in patients with high and low risk of ventricular arrhythmias.

Methods: 30 patients in sinusrhythm (18 men, age 67 SD 13; 15 with DDD-pacemakers and low risk, 15 with dual-chamber ICDs because of high risk for ventricular arrhythmias) had 3 minutes of atrial and 3 minutes of ventricular stimulation (DOO with AV-time 50 ms to avoid capture- and fusionbeats) at a rate of 95/min and of 105/min with each stimulation. TWA was found positive when $>1.9\mu\text{V}$, >1 minute and alternans ratio >3 ; negative when these criteria were clearly not met and indeterminate otherwise. Analysis was done separately by 3 experienced cardiologists without knowledge of patient or form of stimulation, for different opinions a consensus was reached.

Results: Agreement between the results of TWA in atrial versus ventricular stimulation was low with a stimulation rate of 95/min. When stimulation rate was 105/min, agreement stayed low for positive results, but was acceptable for a negative TWA. The rate of indetermined results for ventricular pacing was low.

Conclusions: If these results can be confirmed in a larger cohort, a clearly negative TWA with ventricular pacing might be useful in risk-stratifying patients with atrial fibrillation.

Pacing 105/min	Positive	Negative	Indetermined
Atrial	(8/25) 32%	(17/25) 68%	(0/25) 0%
Ventricular	(4/25) 16%	(19/25) 76%	(2/25) 8%
Agreement	(4/8) 50%	(15/19) 79%	

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Post-myocardial infarction intraventricular conduction defects and brain natriuretic peptide levels

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Background: Levels of brain natriuretic peptide (BNP), a significant marker of left ventricular dysfunction may provide information on the severity of heart failure in patients with intraventricular conduction defects.

Aim: To measure serum BNP levels in post-myocardial infarction patients with intraventricular conduction defects and an old myocardial infarction.

Methods: In 173 patients admitted to the cardiac ward in 2004–2005 at 6–12 months after acute myocardial infarction BNP was measured using an immunoenzymatic method. Of them 126 had intraventricular conduction defects: 31 – left bundle branch block (LBBB), 36 – right bundle branch block (RBBB), 30 – left anterior hemiblock (LAH) and 29 – left posterior hemiblock (LPH). Thirty two patients with a previous myocardial infarction but without intraventricular conduction defects served as controls, whereas 15 healthy subjects entered the comparative group.

Results: In patients with post-myocardial infarction intraventricular conduction defects the level of BNP was 280.2 pg/ml being significantly higher than in their counterparts without conduction disorders (181.7 pg/ml; $p < 0.001$) and in healthy subjects (39.5 pg/ml; $p < 0.001$). The highest BNP level was found in patients with LBBB (422.9 pg/ml) and RBBB (246.1 pg/ml).

Conclusions:

1. Serum BNP levels are significantly higher in patients with previous acute myocardial infarction than in healthy subjects.
2. BNP levels in patients with previous myocardial infarction and intraventricular conduction defects are significantly higher than in their counterparts without intraventricular conduction defects.
3. The highest BNP levels were found in patients with LBBB and RBBB. In patients with LAH and LPH levels of BNP were insignificantly higher than in patients without intraventricular conduction defects.

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Predictors of rhythm disorders in children at early age after surgical correction of tetralogy of Fallot

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Aim: to reveal most frequently occurred rhythm disorders and their predictors in the early postoperative period after surgical correction of tetralogy of Fallot in children at early age.

Material and Methods: 60 patients with tetralogy of Fallot were enrolled in our study. They were divided into 2 groups according to the age: in group A mean age was 21.3±2.4 months, in group B – 12.6±1.3 months. All patients underwent radical surgical repair of main pathology. Inclusion criteria were: arrhythmias and conduction disorders in early postoperative period after surgical correction of tetralogy of Fallot. Exclusion criteria were: children at the age of over 3 years and arrhythmias before surgery. We analysed 2 groups: group 1 – 24 (40%) patients with arrhythmias early after surgery and group 2 – 36 (60%) patients without arrhythmias after surgery. Along with noninvasive methods of histological investigation of right ventricle was performed.

Results: Ventricular arrhythmias (VA) occurred in 83.3% of patients early after radical surgical correction of tetralogy of Fallot, supraventricular arrhythmias (mainly single ectopic beats in 66.7% of patients) and atrioventricular (AV) nodal tachycardia – in 62.5%. Ventricular arrhythmias occurred significantly more often than supraventricular arrhythmias. These rhythm and some conduction disorders (i.e., AV block 2 degree) were mostly transient. Preoperative predictors of these arrhythmias were age >18 months and the history of palliative surgery. Intraoperative predictors included cardiopulmonary bypass time >90 minutes and aortic cross clamping time >50 minutes. Predictors of VA were as follows: QRS duration >100 ms, QT dispersion >50 ms, calculated pressure in right ventricle (RV) >65 mm.Hg. and the RV end diastolic volume >50 ml. Predictors of supraventricular arrhythmias turned out to be P-wave duration >95 ms and P-wave dispersion >20 ms.

Conclusion: In children at early postoperative arrhythmias after surgical correction of tetralogy of Fallot occur due to initial hemodynamic changes, leading to hypoxemia, myocardial electrical disorders, dilatation of heart chambers and ventricular hypertrophy additionally to intraoperative risk factors (surgical trauma).

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Predictors and Frequency of Conduction Disturbances After Open-Heart Surgery

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Introduction: The risk of developing conduction disturbances after coronary bypass grafting (CABG) or valvular surgery has been well established in previous studies, leading to permanent pacemaker implantation in about 2% to 3% of patients, and in 10% of patients undergoing repeat cardiac surgery.

We sought to determine the incidence, features and predictors of conduction disorders in the immediate post-operation of patients subjected to open-heart surgery, and the need for permanent pacemaker implantation.

Material and Method: We prospectively studied 374 consecutive patients who underwent open-heart surgery in our institution: Coronary artery bypass (CABG) (n=128), Mitral valve replacement (MVR) (n=18), Aortic valve replacement (AVR) (n=21), MVR and AVR (n=56), repair of ventricular septal defect (VSD) (n=51), repair of tetralogy of fallot (TF) (n=57), CABG and valvular surgery (n=6), others (n=37).

Results: Among 374 patients included in our study (mean age 34.46±25.68; 146 males), 192 developed new conduction disorders: symptomatic sinus bradycardia in 8%, low response atrial fibrillation (AF) in 4.5%, first-degree atrioventricular block (AVB) in 6.4%, second-degree AVB in 0.3%, third-degree AVB in 7%, new RBBB in 33%, and new LBBB in 2.1%. In 21 (5.6%) patients, a permanent pacemaker was

implanted, 47.6% of them underwent valvular surgery. In 165 (44.1%) of patients the conduction defects occurred in the first 48 hr. after surgery. In CABG group, 38 patients developed new conduction disturbances; the most common of them was symptomatic sinus bradycardia. After valvular surgery forty-two patients developed conduction disturbances, of those the most common was low response AF. After VSD and TF repair, the most common disturbance was new RBBB. The occurrence was compared with patient age, sex, occurrence of perioperative myocardial infarction, ejection fraction (EF), postoperative β-adrenergic receptor blocking agents and use of digitalis, type of cardiac surgery. By regression analysis there was a correlation between type of surgery and new conduction defects, being significant for CABG and TF repair. Only the occurrence of perioperative MI was related to PPM implantation.

Conclusion: Irreversible AVB requiring a PPM is an uncommon complication after open-heart surgery. Peri-operative MI is a risk factor.

Key words: Post operative conduction disturbances; permanent pacemaker

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The tachyarrhythmic cardiomyopathy in children and young adults – antiarrhythmic therapy or radiofrequency ablation?

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Objective: The tachycardiomyopathy is rare form of cardiomyopathy asecondary to an incessant arrhythmia. This form of cardiomyopathy is one of the few reversible (fully or partially) if arrhythmia is stopped.

Material and Method: 8 pts diagnosed with incessant supraventricular tachycardia were hospitalized between 1st January 2001 – 1st January 2006, in our department of pediatric cardiology. Pts mean age was 9 years (3 – 17 years); there were 6 boys and 2 girls. They represent <1% of pts admitted during the analysed period in our department of pediatric cardiology. All patients were admitted initially as emergency. All pts were investigated clinical, rest 12 lead ECG, chest XRay, 2D and M mode echocardiography, pulsed, continuous and color Doppler and 24 hours Holter monitoring. In 4 cases an electrophysiological study was done. The patients were seen for a check up biannually. Pts with repetitive tachycardia despite treatment were readmitted earlier.

Results: Time of the 6 pts had signs of heart failure at the admission: 2 pts were in stage II NYHA, 2 pts were in stage III and 2 pts in stage IV. The first ECG taken at the time of admission have shown: paroxysmal supraventricular atrio-ventricular tachycardia at 300 bpm ventricular rate (in a 5 years old pt), four cases the ECG was typical for focal atrial tachycardia (3 pts had foci in the right atrium) and in one pt the ECG was typical for chaotic atrial tachycardia. In 2 pts surface ECG could not help to identify the mechanism. The electrophysiological study was performed in 4 pts and arrhythmia mechanisms were confirmed. A radiofrequency ablation procedure was successful in 2 pts. In all other cases the arrhythmia was kept under control by medical treatment. The initial decreased left ventricular ejection fraction (LVEF) mean 37% improved to almost 49% after six month follow up but the best recovery was seen in pts who underwent atrial foci successful ablation.

Conclusions: We conclude that tachyarrhythmic cardiomyopathy being secondary to incessant supraventricular tachycardias has as best treatment focus ablation but pharmacological antiarrhythmic treatment when ablation is not an option could be used with good results.

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Efficacy of low energy rectilinear biphasic cardioversion for regular atrial tachyarrhythmias

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Background: Biphasic, external cardioversion (Bi-DC) in comparison to monophasic cardioversion requires lower energy and has been documented to be more effective in restoration of sinus rhythm in atrial fibrillation (AF). There are, however limited information on efficacy, outcome and optimal protocol of low energy, rectilinear Bi-DC in atrial

flutter (AFL) and regular atrial tachyarrhythmias (AT) have not been evaluated.

Aim: To assess the efficacy of low energy rectilinear Bi-DC in patients with AFL or AT.

Methods: Prospective, single-center, randomized study was conducted. Consecutive patients admitted for cardioversion of persistent AFL or AT were randomized into two protocols of subsequent rectilinear Bi-DC (ZOLL M-Series) shocks: (1) 10 J – 20 J – 50 J – 100 J – 200 J or (2) 20 J – 50 J – 100 J – 200 J.

Results: 51 consecutive patients (mean age: 70.8±8.7; 24 males) were included into the study. Initial energy was efficient in 9/28 (32%) patients in protocol 1 and in 12/22 (52%) patients in protocol 2 (p=NS). Cumulative success rate of Bi-DC in both protocols was 98%. Efficacy of initial energy in patients with AT or AFL was 9/22 (41%) and 12/29 (41%) respectively. In 10 of 12 patients with pacemaker initial energy of 10 J or 20 J restored a sinus or atrial paced rhythm. Mean cumulative energy and mean number of shocks for restoration of sinus or atrial paced rhythm was 67 J vs 64 J (p=NS) and 1.56 vs 1.96 (p=0.05) for both protocols respectively. In both protocols, in approximately 25% of patients, after initial energy conversion of AFL/AT into AF was observed. Mean cumulative energy for conversion of AF was 102 J. No serious complications were observed in both protocols.

Conclusions: Rectilinear Bi-DC shocks 20 J, as initial energy, are effective in more than 50% of patients with AFL/AT. Initial energy of 20 J seems to be optimal (especially in patient with pacemakers) however is associated with 25% of conversion of AFL/AT into AF and requires comparison with 50 J.

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Transtelephonic ICD monitoring in patients with Brugada Syndrome. Gadget or real help?

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Introduction: Brugada syndrome (BS) diagnostic is made in a young otherwise healthy population. In case of high risk of sudden cardiac death (SCD), the only currently recommended tool is ICD. However follow-up is contraignant and complications in this population is more frequent than adequate ICD therapy. We sought to investigate whether transtelephonic ICD monitoring could prevent complications and simplify follow-up.

Methods: Twenty-three patients (19 males, 48±8 yo) implanted with an ICD for Brugada syndrome with telecardiology (group 1) were matched for age, sex and follow-up duration with 23 Brugada patients implanted with an ICD without this system (group 2).

Characteristics of the 2 groups

	Group 1: Telecardiology (n=23)	Group 2: Without Telecardiology (n=23)	p-value
Follow-up (months)	17±13	21±24	0.40
ICD indication			0.64
Syncope	10	7	
Positive EPS	11	13	
Familial history of SCD	2	3	
Appropriate shock	1	0	1
Inappropriate shock	1	5	0.19
Alert or consult leading to reprogramming	5	0	0.05
Number of ICD consultations	2.4±1.8	5.3±4.9	0.01

Results: See table. With a mean follow-up of 19±19 months, 7 patients in group 1 had 16 alerts. One had 4 alerts for non sustained VTs which were sinus tachycardias, 6 had 10 alerts for aborted shocks, 2 had alerts shock delivery (1 appropriate and 1 inappropriate). These alerts resulted in a rapid consult and reprogramming to avoid inappropriate shock in 5 patients; in group 2, one patient experienced SCD. Further investigations revealed that he got an inappropriate shock (lead failure), which induced VF. Transtelephonic ICD monitoring was not working in 3/23 of the patients assigned to it (1 patient with inappropriate shock) because of geographical issues. The number of ICD consultations was significantly lower in group 1 compared to group 2 (p=0.01).

Conclusion: Transtelephonic ICD monitoring in patients with BS decreases ICD consultations and may avoid some inappropriate shocks. This system seems worthy in patients with Brugada syndrome.

Monday, 25 June 2007

Oral Sessions

MONDAY, 25 JUNE 2007, 16:30–18:00

Guimaraes

Cardiac resynchronisation therapy in patients with atrial fibrillation

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AF in CRT patients: Baseline characteristics of the patients recruited in the MASCOT study

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Background: As heart failure (HF) promotes atrial fibrillation (AF) and atrial fibrillation worsens heart failure, AF is frequently diagnosed in HF patients and its presence or development is associated with worsened quality of life and prognosis. HF patients candidate for Cardiac Resynchronization Therapy (CRT) could benefit from the AF Suppression algorithm (St Jude Medical, Sylmar, USA). The European Management of Atrial fibrillation Suppression in AF-HF Comorbidity Therapy (MASCOT) study is a prospective, multicenter, randomized, single-blind parallel study evaluating the safety and efficacy of AF Suppression in CRT patients without permanent AF.

Methods: 406 patients have been enrolled. Their mean age is 68±10 years and they are mainly male (79%). 85% are in NYHA class III, and 49% have ischemic heart disease. Their baseline QRS is 164±29 ms, their Quality of Life (Minnesota Living with Heart Failure) is 45±21. Their LV ejection fraction is 25±7%. 89% were receiving an ACE inhibitor or ARB, 74% a beta-blocker and 95% a diuretics. 77 patients (19%) have history of AF. These patients were more often in NYHA class IV and had bigger left atria. 53 (68.5%) of these patients developed HF first and then AF within 66±80 months. The other 31.5% developed AF first and HF within 39±44 months. 396 of the enrolled patients were successfully implanted (95% implant procedure success rate) and received either a CRT-P (43%) or CRT-D device (57%). 389 patients were randomized at the time of the post-implant pre-hospital discharge to either AF Suppression ON (n=194) or OFF (n=195), and are being followed-up.

Conclusions: The patients enrolled in the MASCOT study are well representative of the CRT population, in which AF is frequently documented. The patients will be followed-up for 2 years to evaluate the efficacy of the AF Suppression feature at preventing the development of new-onset and permanent AF in the CRT population.

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Cardiac resynchronization therapy also beneficial in atrial fibrillation

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Background: Prevalence of atrial fibrillation (AF) in patients with heart failure is high. Data on the effects of resynchronisation therapy (CRT)

in chronic AF are scarce. We compared clinical and echocardiographic results of cardiac CRT in patients with chronic AF compared to sinus rhythm (SR).

Methods: In this prospective observational study of 263 consecutive patients, CRT was performed in 96 patients (37%) with chronic AF and 167 patients (63%) with SR. Echocardiographic and clinical parameters were evaluated at baseline, 3 months and 12 months. Reverse LV remodeling was defined as LV end systolic volume reduction ≥10%. Hospitalization rate for congestive heart failure in the year before and after the implant was compared.

Results: Baseline characteristics between patients with and without AF were comparable, but the AF group had smaller LV end systolic and diastolic volumes and larger left atrial dimensions. NYHA class, 6-minute walking distance, QOL, LV ejection fraction and mitral regurgitation improved significantly at 3 and 12 months in both groups and the changes were comparable. Reverse LV remodeling after 3 and 12 months was 74% and 82% (AF group) versus 77% respectively 83% (SR group, p=0.79). After 1 year, spontaneous cardioversion to SR had occurred in 28% of AF patients. In the year after the implantation a significant decrease in hospitalization for heart failure in both groups (84% and 90%) could be documented. Long-term mortality was almost equal in both groups.

Conclusion: This large scale study shows that benefit of CRT in patients with chronic AF and heart failure is comparable to patients with SR. Patients with chronic AF and heart failure should be considered as candidates for CRT.

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Cardiac resynchronization therapy in patients with atrial fibrillation – A meta-analysis

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Introduction: Cardiac resynchronization therapy (CRT) is an effective therapy in patients with heart failure (HF) associated to cardiac dyssynchrony. Virtually, all patients who participated in the clinical investigations of CRT were in sinus rhythm, and there is little experience of applying CRT in patients with HF and atrial fibrillation (AF). In this patient subgroup an adequate heart rate control, obtained by drugs or AV junction (AVJ) ablation, often provides a relief of symptoms and improves functional capacity. Whether CRT is an adjunctive benefit associated to heart rate control is still unknown. In this study, we performed a meta-analysis in order to clarify the impact of CRT on survival and clinical outcomes in patients with AF, using data from the published literature.

Methods: Randomized controlled trials (RCT), including patients with symptomatic HF and AF, were selected. Active CRT versus optimal medical therapy were compared. Six-minute walk test distance, peak oxygen consumption, quality of life, left ventricular function and mortality were the outcomes measured. We conducted a meta-analysis of summary statistics from the individual trials. Calculations included: relative risk (RR) for dichotomous variables; weighted mean difference (WMD) for continuous variables. All results were reported with 95% confidence intervals (95% CI).

Results: We identified 4 RCTs, including 360 patients. All patients required permanent ventricular pacing (mostly right apex pacing) due to slow ventricular rate, either spontaneously or induced by AVJ ablation. Follow-up ranged from 2 to 6 months. CRT did not improve six-minute walk distance (WMD 18.80 m, 95% CI – 4.20 m to 41.81 m), peak oxygen consumption (WMD 1.56 ml/kg/min, 95% CI – 0.13 to 3.26 ml/kg/min), and quality of life (WMD reduction of – 3.47 points, 95% CI – 9.77 to 2.82 points on the Minnesota Living with HF Questionnaire). Left ventricular ejection fraction was increased (WMD 4.02%, 95% CI 1.64

to 6.41%) and all-cause mortality was reduced by 49% (RR 0.51, 95% CI 0.28 to 0.92). Both these results were statistically significant.

Conclusions: In patients with HF and AF, CRT improves survival on top of a strategy combining drug treatment and ventricular rate control with permanent pacing. This effect could be related to improvement of left ventricular function. Finally, CRT seems to provide modest favourable effects on functional parameters compared with optimal medical therapy, including “ablate and pace” strategy.

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Cardiac remodelling in patients with atrial fibrillation and cardiac resynchronization therapy

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Introduction: Cardiac resynchronization therapy (CRT) has shown to reduce morbidity and mortality in patients (p) with heart failure and to promote left ventricular positive remodelling in patients in sinus rhythm. However, there is little information about the impact of CRT in presence of atrial fibrillation (AF).

Objective: To study left ventricular and atrial remodelling in patients with AF treated with CRT.

Methods: 26 p (15%) out of 170 p treated with a CRT at our centre, had a history of AF (24 males, 69±9 years, 10 p with ischemic heart disease, ejection fraction 31±10%, 21 p with ICDs and 5 p with PM). Of these, AF was paroxysmal in 10 p, persistent in 6 and permanent in 10 (5 of them with chronic right ventricular pacing). A complete echocardiogram was also performed, and left ventricular and atrial volumes (Simpson's method and Area-length method: area 4C × area 2C × 0.85/L) and function were measured. All p were under optimal medical therapy and anticoagulated.

Results: See table. The mean time follow up was 17.14±12.6 months. LV function improvement was observed in all three types of AF. The reduction of the left atrial size was also seen in all groups although the change was more significant in p with persistent and permanent AF.

Conclusion: Patients in atrial fibrillation treated with CRT show a positive LV remodelling with improvement of the ejection fraction and reduction of left ventricular and atrial volumes.

Basal and follow-up echo parameters

n=26	LVEDD (mm)	LVEDV (mL)	LVESV (mL)	EF (%)	LA Vol Simpson (mL)	LA Vol AxL (mL)	MR
Basal	68.31	214.14	149.67	31.37	106.9	107.67	1.48
Post	62.87	155.70	90.32	41.7	98.91	101.59	0.96
p	0.008	0.007	0.006	0.002	0.064	0.033	0.007

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Atrial fibrillation, an independent predictor of cardiovascular mortality in patients submitted to CRT

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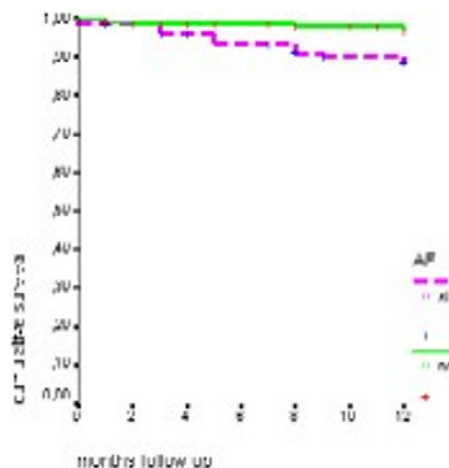
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The role of resynchronization therapy (CRT) in patients with permanent atrial fibrillation (AF) is still under debate. The aim of our study was to analyze whether AF remain a predictor of cardiovascular mortality in patients treated with CRT.

Methods and Results: A cohort 470 consecutive patients, who underwent CRT were included in a retrospective multicenter study. There were 126 patients in AF (All of them were paced >85% of time). At 12 months, 46 patients had died (overall mortality 9%); Death was of cardiovascular cause in 36 (7.7%) of them 26 (72%) died due to refractory heart

failure, 8 (22%) suffered sudden death and 2 (6%) died of refractory ventricular arrhythmias. There were no basal differences in age, gender, % defibrillators or medical therapy in survivors as compared to patients who died due to refractory heart failure. The percentage of patients in AF (see figure 1), NYHA functional class IV and serum creatinine level >1.5 mg/dl were significantly higher (p < 0.005), whereas Ejection fraction (EF) was lower in patients who died due to refractory heart failure (22±6% vs. 27±9% p=0.025); furthermore, left ventricular end diastolic and end systolic diameters were larger in those who died: 76±10 mm vs. 70±11 mm and 64±11 mm vs. 57±11 mm respectively (p < 0.05). At logistic regression analysis, AF and creatinine levels were identified as independent predictors of mortality due to refractory heart failure: AF OR 4.1 [1.39–12.1]; Creatinine levels >1.5 mg/dl OR 5.5 [1.1–16.3].

In conclusion: AF remain and independent predictor of mortality due to refractory heart failure at 12 months in patients treated with CRT.



Mortality in patients with AF vs. SR

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Effect of response to cardiac resynchronization therapy on the persistence of atrial fibrillation

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Background: The benefit of cardiac resynchronization therapy (CRT) on atrial remodeling has been demonstrated. Left atrial size reduction has been correlated to a decrease of persistent AF incidence. However, biventricular pacing did not reduce the global incidence of all types of AF.

Objective: We evaluated (1) the clinical impact of the reversal atrial remodeling induced by CRT on the evolution of persistent AF and (2) the effect of CRT response on the persistence of AF.

Methods: We retrospectively analyzed data from 96 patients (59±15 years; 78% male) who underwent CRT. All patients had class III-IV NYHA symptoms despite maximal medical therapy, left ventricular ejection fraction (LVEF) ≤35%, QRS >130 ms and sinus rhythm before implantation. CRT response in patients who survived at 6 months of follow-up was defined as: (i) no hospitalization for heart failure and (ii) improvement of one or more grades in the NYHA classification.

Results: CRT responders (n=54) and non-responders (n=42) had similar baseline characteristics, including the incidence of persistent AF within 6 months before implantation. Six months after implantation, compared to baseline, CRT responders exhibited a significant decrease in left atrial size (47.5±7.1 mm vs. 44.6±7.7 mm, p < 0.01) and in the incidence of persistent AF (17% vs. 2%, p=0.02). At 6 months, CRT responders demonstrated shorter mean AF duration (7.5±43.3 hours vs. 48.8±129.0 hours, p=0.03) and less persistent AF incidence (2% vs. 19%, p=0.004) compared to non-responders.

Conclusion: Cardiac resynchronization therapy response is associated with a reversal atrial remodeling and a decrease in persistent AF.

MONDAY, 25 JUNE 2007, 16:30–18:00

Evora

Antiarrhythmic treatment in atrial fibrillation

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Pretreatment with statins protects against atrial fibrillation after coronary artery bypass graft surgery

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Purpose: Atrial fibrillation (AF) is a common complication after coronary artery bypass grafting (CABG). Patients with postoperative AF have an extended hospital stay with accompanying increased costs as well as a increased risk of stroke. Recently, the role of inflammation in pathogenesis of AF has been evaluated and inflammatory biomarker C-reactive protein (CRP) was elevated in patients with AF. Statins, aside from lowering lipids, have an anti-inflammatory effect, as suggested by a reduction in serum CRP level. We hypothesized that pretreatment with statin would be associated with a decreased incidence of AF after CABG.

Methods: We randomly assigned 101 patients who were scheduled for CABG to statin (n=55) and control (n=46) group. Statin was started 48 hours before CABG. High-sensitivity C-reactive protein (hsCRP) and N-terminus pro-brain natriuretic peptide (NT-pro-BNP) levels were measured before and after surgery. Continuous electrocardiographic monitoring in intensive care unit and telemetry on ward were used during hospital stay to detect AF. AF was defined by an irregular atrial rhythm without clear P waves that was confirmed by a 12-lead ECG. The primary end point was the development of AF during hospital stay after CABG.

Results: AF occurred in 9.1% of the patients in the statin group and 23.9% of the patients in the control group (relative risk in the statin group as compared in the control group, 0.32; 95 percent confidence interval, 0.10 to 0.99; p=0.04). Preoperative plasma NT-pro-BNP and hsCRP levels were higher in the postoperative AF patients (1705 versus 442 pg/mL, p<0.001; 1.07 versus 0.46 mg/dL, p=0.03). Patients in the control group had a nonsignificantly longer length of hospital stay as compared with the statin group (8.9±5.3 days vs 8.5±4.7 days; p=0.61).

Conclusion: The preoperative use of statin may be protective against AF after CABG. The preoperative hsCRP and NT-pro-BNP levels may predict post-CABG occurrence of AF.

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Incidence of postoperative atrial fibrillation (AF) following off-pump coronary artery bypass grafting (CABG) surgery

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Purpose of the study is to identify risk factors for developing atrial fibrillation in short-term period after off-pump CABG.

Methods: 80 patients (M73, 57±6.5 years) with coronary artery disease were undergone off-pump CABG and were enrolled in our study. 65 patients had I-II Heart Failure NYHA class (mean value of left ventricle ejection fraction [LVEF] was 56%±16). Mean number of vessels grafted was 3.1±0.8. Before operation all patients were examined with ECG, Echocardiography, angiography. ECG monitoring was performed for patients during short-term period after operation. All patients were treated with β-blockers.

Results: Patients were divided into 2 groups. Group 1 included 14 patients with paroxysmal AF. Group 2 included 66 patients without onset of

AF. Rate of AF episode during first 7 days after CABG was 17.5%. AF episodes width was 30sec and more and were registered with ECG and ECG monitoring. There was a significant increase in AF episode on 2–4 day postoperatively (86% AF episodes). Baseline patient characteristics are in the table. Statistically significant risk factors for developing atrial fibrillation after off-pump CABG were old age, duration of the coronary artery disease, preoperative AF, left atrial size. We determined that myocardial infarction, LVEF, number of vessels grafting and potassium concentration didn't have effect on rate of AF episode.

Conclusions: (1) Patients after off-pump CABG have the high rate of AF episodes during short-term post operation period, despite on treating with β-blockers. (2) Risk factors for developing atrial fibrillation depend on structural, morphological and electrophysiological changes of atria, which happened due to old age, coronary artery disease, recurrent AF.

Baseline patient characteristics

Parameters	Group 1 (n=14), AF	Group 2 (n=66), Non-AF
Age, years	59±5.4*	49±7.7*
Duration of the coronary artery disease, years	11±4.5*	5.0±4.0*
Myocardial infarction, %	35**	33**
Preoperative AF, %	42*	11*
LVEF, %	56±18**	55±15**
Left atrial size, mm	45±8.1*	40±3.5*
Number of vessels grafting	3.0±0.9**	3.1±0.8**
Potassium concentration, mmol/l	4.4±0.3**	4.5±0.3**

*P<0.001; **P>0.05.

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Ibutilide versus direct current cardioversion for paroxysmal atrial fibrillation termination during supraventricular tachycardia radiofrequency ablation

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Aim: To compare the efficacy and safety of ibutilide and direct-current electrical cardioversion (DC-ECV) for termination of paroxysmal atrial fibrillation (PAF) complicating radiofrequency ablation (RFA) of supraventricular tachycardias (SVT).

Methods: PAF occurred in 66 out of 386 patients (17%) undergoing SVT-RFA. PAF was self-terminated in 32 patients. The remaining 34 patients in whom PAF persisted for more than 15 minutes, were randomized to two groups. Group A consisted of 17 patients (8 males, including 6 patients with a trial flutter, 7 with atrioventricular-nodal re-entry tachycardia, 2 with atrioventricular re-entry tachycardia, and 2 with atrial tachycardia) who received ibutilide (1–2 mg intravenously). Group B consisted of 17 patients (10 males, including 6 patients with a trial flutter, 6 with atrioventricular-nodal re-entry tachycardia, 3 with atrioventricular re-entry tachycardia, and 2 with atrial tachycardia) who randomized to DC-ECV (biphasic shock 200–360 J). No patient had structural heart disease.

Results: Ibutilide infusion (mean 1.35±0.49 mg) cardioverted successfully 16 out of 17 patients (94%) within 11.5±6.5 minutes (time needed for iv preparation and infusion until sinus rhythm restoration plus 10 min waiting period and reinfusion for three patients that received additional dose). DC-ECV (200 J, two patients received second shock of 360 J) was successful in all patients (100%) within 11.1±2.6 minutes (time needed for calling the anesthetist team, patient preparation, sedation, DC shock, and recovery plus additional shocks). Efficacy and total time to cardioversion between the study groups was not statistically significant (p>0.05). One patient from ibutilide group received DC-ECV and restored sinus rhythm. No adverse events were observed. After sinus rhythm restoration PAF did not relapse in ibutilide patients, whereas a second shock of 360 J was applied in one of the DC-ECV treated patients. Tachycardia inducibility was not affected, apart from one patient with history of atrial tachycardia, that was not inducible after ibutilide infusion. Inducibility of atrial flutter was not examined, as the procedure was carried out using anatomic criteria during coronary sinus pacing. RFA was accomplished successfully in all patients.

Conclusions: In PAF complicating SVT-RFA, ibutilide offers an option for restoring sinus rhythm, eliminating the need for electrical cardioversion and reducing unwanted time delays. Tachycardia inducibility is not affected in such cohort of patients, thus RFA may be completed without further delays.

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Pre-treatment with amiodarone before electrical cardioversion of persistent atrial fibrillation. Result from the BIFAC study phase 1

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Background: The use of antiarrhythmic drugs as pre-treatment of electrical cardioversion (ECV) of persistent atrial fibrillation (AF) is still debated. Aim of the phase-1 of the BIFAC study was to evaluate the efficacy of AMIODARONE in preventing early (ERAF, 1-week) and subacute (SRAF, 3-month) recurrences of AF after successful ECV.

Methods: The study group consists of 188 patients (pts) with persistent AF (1 month to 1 year). We excluded pts with left atrium dimension >55 mm, acute heart failure, myocardial infarction <3 months, heart surgery <3 months, contraindication to amiodarone.

Results: The mean age was 70±7 years, left atrium dimension 43±5 mm, left ventricular ejection fraction 54±8%. The target AF episode was the first one in 26% pts and lone AF was present in 6% pts. The pts were randomized to received in a 2:1 fashion, oral loading of amiodarone (GrA) or other antiarrhythmics (class 1C or sotalol) (GrD), one month prior to ECV and during the follow-up. All pts were properly anticoagulated for at least 4 weeks before and after the procedure. ECV was performed using a biphasic rectilinear waveform (Zoll M-series) Resumption of sinus rhythm (SR) before ECV was observed in 16/125 (13%) pts in GrA vs 16/63 (25%) in GrD; p=0.05. ECV was successful in 105/107 (98%) pts GrA vs 45/46 (98%) pts in GrD. The effective energy was 103±45 joules. ERAF was observed in 6/105 (6%) in GrA vs 11/45 (24%) pts GrD; p=0.002. SR was present (with or without further CV) after 3 months in 104/120 (87) pts GrA vs 44/62 (73) pts GrD, p=0.018. Treatment was stopped due to side-effects in 8/125 (6%) pts in GrA vs 1/63 (2%) pts GrD, p=NS.

Conclusion: Oral loading of Amiodarone is superior to other antiarrhythmic drugs in preventing early and subacute arrhythmia recurrences after successful electrical cardioversion of persistent atrial fibrillation.

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Treatment of recent onset atrial fibrillation with acute oral administration of 1C antiarrhythmic drugs on-top of chronic antiarrhythmic therapy

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Background: Data about the use of oral loading of 1C antiarrhythmic drugs (1C-AAD) on-top of chronic antiarrhythmic therapy to convert atrial fibrillation (AF) to sinus rhythm (SR), are lacking.

Methods: The study group consists of 241 patients (pts) with history of paroxysmal AF without heart failure, ischemic heart disease and conduction disturbances, prophylactically treated with chronic 1C-AAD. In case of relapse of recent onset (<48 hours) AF pts randomly received 1C-AAD (Gr.1C) (propafenone 600 mg or flecainide 300 mg) in a single loading oral dose at the time scheduled for next chronic drug administration or adding placebo (PLA) (Gr.PL) to the usually administered chronic drug. Conversion to SR after 2, 4, 6 hours, was considered as criterion of efficacy.

Results: The 2 groups were comparable in terms of gender, age, etiology, duration of AF, mean ventricular rate at baseline and left atrial dimension. Mean time to treatment was 3.2±2.0 hs in Gr.1C vs 3.5±1.7 hs in Gr.PL

(P=NS). Twenty pts (8.3%) (11 in Gr.1C, 9 in Gr.PL) spontaneously reverted to SR before drug administration. Conversion rate to SR was higher in Gr.1C compared to Gr.PL, at each considered time-frame: 50/109 (46%) vs 24/112 (21%) after 2 hs, 80/109 (73%) vs 40/112 (36%) after 4 hs, 87/109 (80%) vs 58/112 (52%) after 6 hs (all P < 0.0001). No serious adverse events were detected in each group, 1 case of regular tachycardia (RT) with 1:1 AV conduction were noted in Gr.PL. Minor side effects ensued in 18 (17%) pts Gr.1C (12 RT, 6 bradycardia), and in 11 (10%) (RT only) in Gr.PL, p=NS. Mean time to conversion was lower in Gr.1C (135±100') compared to Gr.PL (198±105'), p < 0.001.

Conclusions: Single loading oral dose with 1C drugs is safe and efficacious in converting recent onset atrial fibrillation to sinus rhythm in patients chronically treated with the same drug for prophylaxis.

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Combination therapy of angiotensin receptor blockers and bepridil is useful for maintaining sinus rhythm in the patients with atrial fibrillation

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Background: The present study has evaluated the effect of treatment with angiotensin receptor blockers (ARB) on maintaining SR after conversion from persistent atrial fibrillation (AF). However the efficacy of ARB for AF is not clear. The aim of our study was to clarify the maintenance of SR by combination therapy of ARB and bepridil for AF.

Methods and Results: We prospectively administered bepridil in consecutive 105 patients. Three groups of patients were compared: Bepridil-group was treated with bepridil alone (n=35), and ARB-group was treated with bepridil plus candesartan (n=35) and Beta-group was treated with bepridil plus carvedilol (n=35). The primary end point was length of time to a first recurrence of AF. In this study, paroxysmal AF was defined as self-terminating AF within 48 hours and persistent AF as non-self-terminating AF lasting more than 48 hours and requiring pharmacological or electrical conversion to restore sinus rhythm. In paroxysmal and persistent AF, 18 (52%) patients were maintained of SR in Bepridil-group and 27 (77%) patients were maintained of SR in ARB-group and 23 (66%) patients were maintained of SR in Beta-group. There was a significant difference between ARB-group and Bepridil-group (P < 0.05). In persistent AF, 8 (38%) patients were maintained of SR in Bepridil-group and 15 (75%) patients were maintained of SR in ARB-group and 16 (76%) patients were maintained of SR in Beta-group. There was a significant difference between ARB-group and Bepridil-group. And there was a significant difference between Beta-group and Bepridil-group too. In paroxysmal AF, there was no significant difference between three groups. There were no major complications, but QT prolongation was observed 5 patients.

Conclusions: Combination therapy of ARB and bepridil may be useful for maintenance of SR with persistent AF. And Combination therapy of carvedilol and bepridil may be useful for maintenance of SR with persistent AF too.

MONDAY, 25 JUNE 2007, 16:30–18:00

Guarda

Electrocardiogram based risk stratification

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Positive versus not negative microvolt T-wave alternans after acute MI

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Acute MI patients' outcomes has been changed in the era of early primary coronary intervention (PCI). Assessment of microvolt T-wave alternans (MTWA) has been found to be important prognostic factor, however some discrepancies exist in interpretation of the indeterminate results of MTWA

In prospective mode 115 consecutive patients with acute MI undergoing PCI <12 hours from the onset of symptoms, with successful LAD opening, treated according to current guidelines were enrolled. Demographics, established and recently proposed risk factors, as well as index event data were assessed. Major adverse cardiac events (MACE) – death, recurrent MI, malignant ventricular arrhythmias and rehospitalization due to heart failure – were recorded during 18 month follow-up. At 30 days MTWA test was performed.

Results: 27 MACE's occurred at 18 months (9 cardiac deaths including 5 sudden, 3 reinfarctions, 1 sustained VT and 14 rehospitalizations for HF). Kaplan–Meier MACE-free cumulative survival curves did not differ between TWA(+) [50%] and TWA not (–) [55%] patients (versus 87% TWA (–) pts at 18months, both log rank $p < 0.001$)

Conclusions: Positive and nonnegative MTWA results carry similar predictive power of MACE occurrence during long-term follow-up.

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HRV and repolarization disturbances in children with hypertrophic cardiomyopathy

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The aim of study was evaluation of the HRV parameters and duration of QRS complexes, QT and transmural QT as sudden death predictors in children with hypertrophic cardiomyopathy (HCM).

Study population consisted of 10 children: 6 boys and 4 girls aged from 1.5 to 18 years (mean 12.3 years) with hypertrophic cardiomyopathy and increased risk of SCD. Control group consist of 18 children sex and age matched to the studied group. Based on 12-lead ECG recorded in all pts, the following parameters were evaluated: (a) duration of QRS complex, maximal duration of QTc interval and dispersion of QTc intervals (dQT); (b) transmural QT dispersion (t-QTd); (c) mean duration of T wave, measured from peak to end (in leads V5 and V6). The following HRV parameters were evaluated based on 24-hour ECG: standard deviation of RR intervals (SDNN), root mean square of successive differences (rmsSD) power spectrum of low (LF) and high (HF) frequencies as well as HF/LF balance.

Results: Children with HCM revealed significantly prolonged QTc intervals (542.5 vs. 408.3 ms, $p < 0.001$) as well as dispersion of QTc (134.8 vs 42.5 ms, $p < 0.001$), transmural dispersion of repolarization – tQTd (91.4 vs 59.8 ms, $p < 0.02$) and LF/HF HRV balance (3.48 vs 1.19, $p < 0.001$). Parasympathetic-related HRV parameters were significantly depressed in pts with HCM (rmsSD – 22.3 vs 46.1 ms; $P < 0.02$; HF power spectrum (0.08 vs 0.301 s² $p < 0.001$) whereas SDNN (147.3 vs 125.5) and sympathetic-related LF power spectrum did not differ significantly. Mild prolongation of QRS was observed in pts with HCM (98.5 vs 77.6 ms, $p < 0.06$)

Conclusions:

1. Children with hypertrophic cardiomyopathy presents significant disturbance of repolarisation.
2. Changes of HRV observed in children with hypertrophic cardiomyopathy are mainly related to lack of parasympathetic drive.
3. Both HRV and ventricular depolarization parameters seems to be useful in risk stratification in children with hypertrophic cardiomyopathy.

439 Withdrawn

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Relationship between qrs duration and prognosis in non st-segment elevation acute coronary syndrome

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Background: Previous studies have shown that prolonged QRS duration increases the risk of death in patients with heart failure and after Q-wave

myocardial infarction (AMI). Very little data exist about the prognostic implications of QRS duration in the non ST-segment elevation acute coronary syndrome (NST-ACS): unstable angina and non Q-wave AMI. The aim of this prospective and observational study was to assess the relation between QRS duration on admission (QRSd) and risk of cardiovascular death (CvD) in the long-term in 502 patients (age 71 ± 10 years, 68% males, 29% diabetes, 30% unstable angina) consecutively admitted for NST-ACS. QRSd was manually measured from the 12-lead electrocardiogram.

Results: Mean QRSd was: 93 ± 19 ms (dQRS equal or greater than 120: 12%). After a median follow-up of 450 days, the cumulative incidence of CvD was: 17.8%. QRSd correlated with the incidence of CvD during the follow-up period: $c = 0.72$ ($p < 0.001$). The best cut-off point was 90 ms (sensitivity, specificity and negative predictive value of QRSd equal or greater than 90 ms for CvD: 82, 68 and 93%). According to the Kaplan–Meier analysis, QRSd equal or greater than 90 ms was associated with an increase in the risk of CvD: 26.6% versus 7.2% (log rank: 28.6; $p < 0.001$). Cumulative incidence of CvD was higher in QRSd equal or greater than 90 ms in patients with unstable angina: 15.5% versus 4% ($p = 0.02$), and in those with non Q-wave myocardial infarction: 30.5% versus 8.9% ($p < 0.001$). After adjusting for age, gender, risk factors, clinical variables, left ventricular function, coronary revascularization and medical treatment on discharge (Cox-regression analysis), QRSd equal or greater than 90 ms persisted as an independent predictor for overall CvD (95% Confidence Interval: 1.44–4.74; $p < 0.001$). To determine the prognostic significance of different degrees of QRS duration, we further subdivided our population into five groups according to the QRS: 0–79 ms (A), 80–89 ms (B), 90–100 ms (C), 101–119 ms (D), and equal or greater than 120 (E). The incidence of CvD increased with the duration of QRS: A: 5.8%; B: 8%; C: 22.8%; D: 23.3; E: 39.4%. A-B vs C-D: $p = 0.002$; C-D vs E: $p = 0.03$.

Conclusion: In NST-ACS, QRSd (even in normal ranges) is independently associated with an increased risk of CvD in the long-term.

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The value of heart rate variability for determining prognosis in patients with heart failure in beta-blocking era

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Aims: To assess whether analysis of 24 hour heart rate variability (HRV) provides information about mode of death (pump vs sudden death) in chronic heart failure (CHF).

Methods and Results: We prospectively enrolled 135 pts with symptomatic CHF and systolic dysfunction in sinus rhythm, mean age 52.4 ± 11.9 years, 56 (42%) in NYHA class II, 55 (40%) in class III, and 24 (18%) in class IV, mean left ventricle ejection fraction (LVEF) $30.1 \pm 6.7\%$, 91 (68%) with ischemic and 43 (32%) with nonischemic cardiomyopathy. Time and frequency domain measures of HRV were obtained from 24h Holter ECG monitoring. During follow-up (28.8 ± 21 months), 63 pts died, 21 of them suddenly. Stepwise regression analysis was applied. In multivariate model, independent predictors for pump failure death were: NYHA class III-IV and standard deviation of all mean of all RR intervals ≤ 705 ms (heart rate ≥ 85 bpm) (RR = 1.5, 95% CI 1.1–3.8; $p = 0.02$). Independent predictors of sudden death were: NYHA class II, LVEF $\leq 26\%$, and ratio of low frequency to high frequency (LF/HF) ≤ 1.5 (RR = 1.5, 95% CI 1.2–2.9 $p = 0.001$). Neither runs of nonsustained ventricular tachycardia (NSVT) nor frequent ventricular ectopic activity independently predict risk of sudden death.

Conclusion: Increased heart rate during 24 h recording > 85 bpm (mean RR ≤ 705 ms) independently predicts risk of pump failure death in pts with symptomatic CHF and LV systolic dysfunction. Measures of spectral analysis (depressed LF/HF ≤ 1.5) identifies pts at increased risk for sudden death. HRV measures identify pts with CHF at increased risk for sudden death better than traditional markers of bad prognosis.