EMJ INTERVENTIONAL CARDIOLOGY

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EuroPCR 2022

EDITOR'S PICK

A Single-Centre Retrospective Study on the Impact of Reducing Surgical Prophylaxis from 48 Hours to 24 Hours in Cardiothoracic Surgery

INTERVIEWS

Salvatore Brugaletta, Clifford Kavinsky, and Lloyd Klein

Contents

"We are proud to present interviews by key experts who share insights into their clinical research and their take on the latest developments in the field."

Editorial Board

VIEW IN FULL ←

Aims and Scope

EMJ is an online only, peer-reviewed, open access general journal, targeted towards readers in the medical sciences. We aim to make all our articles accessible to readers from any medical discipline.

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Front cover and contents photograph: Paris, France, home of EuroPCR 2022. © NicoElNino / 123rf.com

EMJ Welcome letter

Dear Readers,

I would like to welcome you to the 2022 issue of *EMJ Interventional Cardiology*, bringing you content from this year's European Association of Percutaneous Cardiovascular Interventions (EAPCI) congress in Paris. It was an absolute pleasure for our team to attend the congress in person and get a first-hand taste of the highly engaging presentations of experts in the field.

A session of interest in this year's congress is artificial intelligence and its applications in interventional cardiology, and we are proud to be featuring a summary of this in our journal. Of interest are also late-breaking trials and solutions to unmet needs, such as that of a minimally invasive device for aortic regurgitation. Of course, like in previous years, it was particularly exciting to watch the live cases of interventional procedures from across the world, which present great learning opportunities for experts and a chance to discuss the challenges along with solutions.

As always, in addition to our congress coverage, we are proud to present interviews by key experts who share insights into their clinical research and their take on the latest developments in the field. The journal also features a review article on the 'leave nothing behind' strategy in sirolimus coated balloons and a case report of a challenging and rare procedural complication, in which stent delivery shaft fracture required emergency snare extraction.

I would like to extend a big thank you to the EMJ team and Editorial Board for their hard work in putting this issue together. As always, our authors and peer reviewers have helped contributed with great content and insights to the journal. I hope you enjoy reading through all this great content.

Koutsouki

Evgenia Koutsouki, PhD.

Editor

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Foreword

Dear Readers,

It is my pleasure to present the latest issue of *EMJ Interventional Cardiology*, containing peer-reviewed literature reviews, research articles, and case reports on hot topics. The journal covers matters from coronary and peripheral artery disease to single-centre retrospective studies on reducing surgical prophylaxis in cardiothoracic surgery. Additionally, this issue highlights the key take-home messages and sessions from this year's EuroPCR congress.

This year, EMJ received numerous high-quality papers and we are pleased to share them with you in this journal. Brandon et al. discuss the case of a challenging and rare complication of stent delivery shaft fracture, emphasising challenges, and reminding healthcare professionals that it is important to keep learning and remain upskilled in managing these rare complications. Other articles in this issue share insights into sirolimus-coated balloons, transcatheter aortic valve replacement, and much more.

The congress review of EuroPCR shares abstract summaries, highlights, and in-house features based on the most fascinating and informative sessions from the congress, aimed at healthcare professionals. It is an informative read for those who were unable to attend the congress, or would like to re-live the success of the 2022 EuroPCR.

Moreover, *EMJ Interventional Cardiology* includes exclusive interviews with experts at the top of their field, namely Clifford J. Kavinsky, Associate Director of the Cardiovascular Disease Fellowship Programme, Chicago, Illinois, USA, and Lloyd W. Klein, Clinical Professor of Medicine, University of California, San Francisco, USA. Both physicians share their personal motivations, insights into their clinical research, and innovations that are on the horizon for interventional cardiology.

I hope you enjoy reading the 2022 edition of the *EMJ Interventional Cardiology* journal and that the insightful content will help to enhance your knowledge in your field. I would like to thank all the authors, interviewees, and peer-reviewers for devoting time to this journal.

Enjoy reading!

Pablo Sepúlveda Varela

Interventional Cardiologist, Cardiology Department; Head, PAH Outpatient Clinic, Hospital San Juan de Dios; Associate Professor of Medicine, University of Chile, Santiago, Chile

Congress Review

Review of EuroPCR 2022

Location: Paris, France

Date: 17th–20th May 2022

Citation: EMJ Int Cardiol. 2022;10[1]:9-14. Congress Review. DOI/10.33590/emjintcardiol/22E0628. https://doi.org/10.33590/emjintcardiol/22E0628

FOR THE FIRST time since 2020, EuroPCR welcomed over 700 colleagues to an in-person congress in Paris, France. Paris, often referred to as La Ville Lumière (the City of Light), has been home to several scientists and innovators since the 17th century.

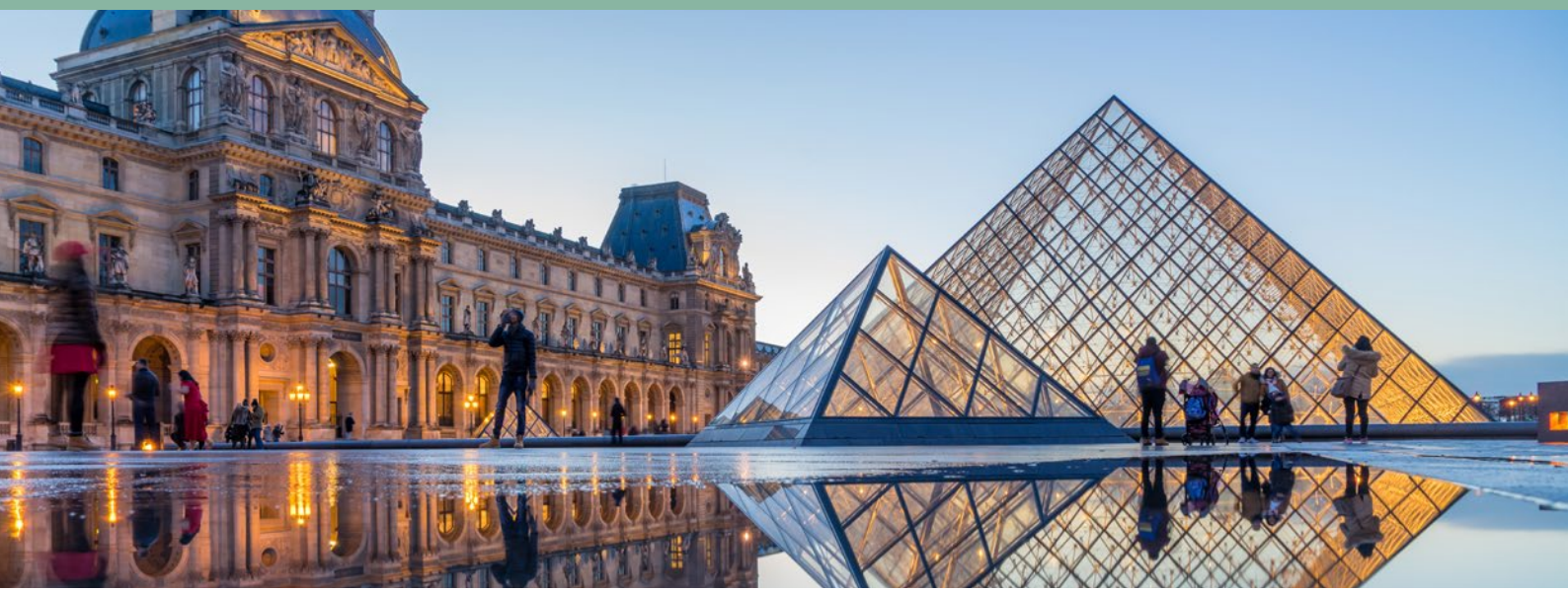
In an emotional opening, the congress committee shared how special it was to be reunited after 3 difficult years, and how this new hybrid format would enable healthcare professionals around the world to be illuminated by innovative ideas in interventional cardiology. The committee referred to the congress as a "spark" of driving new ideas, knowledge, and change, which tied in nicely with this year's theme of innovation.

This year's congress received an impressive 578 abstract submissions from participants across 53 countries, ranging from Mexico to Hong Kong. There were several pioneering posters, symposiums, and abstract sessions to attend, detailing the management of patients, results from clinical trials, and advances in surgical procedures.

Fortunately, for those who missed this year's EuroPCR conference, sessions are on-demand for members until 20th August 2022. Additionally, key highlights, abstract summaries, and congress interviews are featured in this year's EMJ interventional cardiology eJournal, alongside peer-reviewed articles from renowned scientists around the globe.

Topics from the congress covered the economic and societal burdens of the pandemic, as well as local and national strategies implemented to mitigate the impact of COVID-19. Highlights discuss cardiovascular care in a post-pandemic world, management of hypertension, emerging data on renal denervation, and much more.

EuroPCR wanted to celebrate those who ignite change, which drives the field of interventional cardiology forward.



The president of EuroPCR announced with pride: "This year is a year of anniversaries and celebrations."

During the pandemic, the importance of nurses and allied healthcare professionals (NAP) came to light. At the start of the pandemic, Lynne Hinterbuchner, a cardiology nurse, revealed that she experienced anger from patients due to cancelled appointments; however, this soon shifted, and "one positive [from the pandemic] is that everyone has begun to see how important nurses are."

Therefore, in recognition of NAPs' outstanding contributions to interventional cardiology, the Andreas Grüntzig Ethica Award was awarded to NAPs, and Hinterbuchner received this award on behalf of other NAPs around the world.

The welcoming ceremony also celebrated leading innovators in interventional cardiology, namely Alain Cribier, Professor of Medicine and Director of Cardiology, University of Rouen's Charles Nicolle Hospital, France, and Ferdinand Kiemeneij, an interventional cardiologist in Bussum, the Netherlands.

Cribier celebrates 20 years since performing the first transcatheter aortic valve implantation. He now focuses on travelling the world to teach people the procedure and improve patient lives. Cribier enlightened the audience by sharing three valuable pieces of advice for young cardiologists: put your patients first, think analytically about a challenging case, and finally, learn from complications.

Kiemeneij is often referred to as the father of transradial intervention, a procedure which is now celebrating its 30th anniversary.

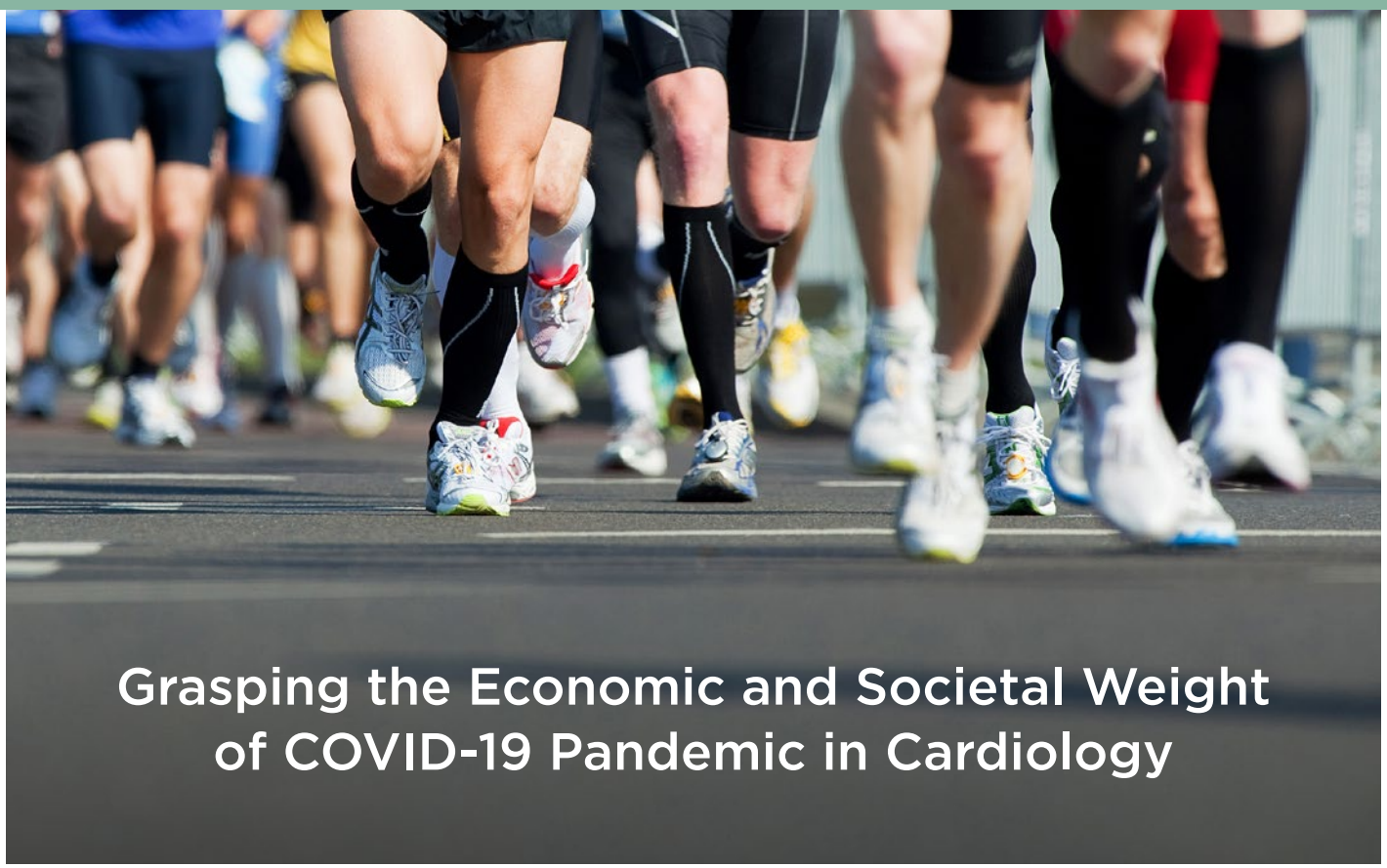
Celebrating the past leads to considerations about the future, the congress committee invited three futurists in interventional cardiology to the stage to discuss their visions for the field going forward. The speakers noted that although we have digital platforms that are open access to many people, there is still a lot to be done since access to these training platforms is limited, and developing countries continue to fall behind.

Technology is an important driver of innovation because it allows effective, quick, and concise communication. The speakers discussed how patients require healthcare professionals to innovate, and interventional cardiology is the therapy area leading the way with regard to innovation. The future of teaching could include simulation-based learning and labs, spreading technological resources, and increasing the breadth of knowledge to help drive change.

To end this long-awaited reunion of colleagues, the committee asked the audience to turn on their phone torches to shine a light on the future of interventional cardiology.

We look forward to attending next year's EuroPCR congress in Paris; however, for now, please enjoy our highlights and review of this year's congress. ■

EUROPCR 2022 REVIEWED →



Grasping the Economic and Societal Weight of COVID-19 Pandemic in Cardiology

"an average loss of 1.86 years of survival for a patient having a STEMI during the first month of lockdown, compared with pre-lockdown"

We CARE, a joint initiative of PCR and Stent-Save a Life, that was launched at the European Association of Percutaneous Cardiovascular Interventions (EuroPCR) in 2021 presented their first study at the EuroPCR Congress, which took place on 17th–20th May 2022, covering a UK investigation on the health economy in the long-term consequences and cost for ST-elevation myocardial infarction (STEMI) during the COVID-19 pandemic.

Several national studies were carried out by We CARE, including various countries such as Spain, Sweden, the UK, and USA. The UK study was the first to be presented in the EuroPCR 2022 and discussed the effects of the March–April 2020 lockdown on the STEMI population and compared with the pre-lockdown population.

According to the UK study, the findings showed that reduced care in affected patients leads to a significant societal burden. Mattia Lunardi, Department of Cardiology, Galway University Hospital, Ireland, one of the study authors stated that a lot of the patients were scared of going to the hospitals during the lockdown period, despite the severity of their conditions. The government urged people to stay at home and this increased hesitation of going to hospitals, which meant fewer interventions took place during this period and resulted in increased mortality rates and a substantial increase in heart failure cases. In terms of financial burden in the UK, the study found that the healthcare cost has risen due to the medical complications that further worsened due to the lockdown. The quality of life was considerably lower and furthermore, Lunardi said: "An average loss of 1.86 years of survival for a patient having a STEMI during the first month of lockdown, compared with pre-lockdown".

We CARE confirmed that they are working to prevent and reduce the impact of the pandemic and any other future risks. The next Phase II of the project is to create a progressive network, with evidence-based approaches, that will allow the healthcare system to rebuild trust with patients suffering from cardiac conditions. Phase III of the We CARE initiative is to build relationships between local and international foundations with other stakeholders to improve cardiovascular specialty on a comprehensive level. ■

EuroPCR 2022: An Innovative Blended Event

A PIONEERING hybrid format was adopted for this year's EuroPCR, allowing delegates to meet onsite in Paris, France, and online. The conference was notable for its global outreach, with over 750 presenters from 78 different countries. Furthermore, as of 27th April, 107 countries were represented by course participants.

A key element of the 2022 congress was the opportunity for simulation-based learning, covering antegrade chronic total occlusion strategies, image-guided bifurcation stenting, and transseptal puncture for mitral interventions. Leading experts also provided demonstrations of techniques such as robotic percutaneous coronary intervention and transcatheter mitral edge interventions directly from the cardiac catheterisation laboratory. The focus on advances in clinical practice and cardiovascular interventions ensured that patient care was at the centre of EuroPCR 2022.

The 2022 meeting offered a fully blended experience. Participants were encouraged to share comments and ask questions during live-streamed sessions. This was complemented by a new digital channel (EuroPCR+), which broadcast live news, discussions, and interviews, with repeat broadcasts 24 hours a day. This not only meant participants received scientific insights into important topics, but was also key to promoting discussion and the exchange of knowledge.

The theme of EuroPCR 2022 was 'Let's celebrate'. Of course, EuroPCR was celebrating being back in Paris, in-person, for the first time in 3 years. However, there were also a number of noteworthy anniversaries to commemorate. These included 20 years since the first transcatheter aortic valve implantation was performed by Alain Cribier at the Charles Nicolle University Hospital in Rouen, France, and 30 years since Ferdinand Kiemeneij performed the first successful transradial coronary angioplasty procedure at Onze Lieve Vrouw Gasthuis in Amsterdam, the Netherlands. ■

New Study Data on Renal Denervation to Treat Hypotension

PRESENTATIONS at EuroPCR 2022 shared data and results from three ongoing clinical trials that contribute to ongoing efforts to develop effective device-based treatments using renal denervation (RDN). Despite a plethora of safe and effective drugs available, treatment adherence remains a significant concern for hypotension management in 2022. Reporting on data from three ongoing trials, SPYRAL-HTM On MED, RADIANCE-HTN SOLO, and TIOA aimed to help refine approaches to RDN and widen its adoption.

The global registry study, Global SYMPLICITY Registry, reported 3-year results on the safety and efficacy of RDN in real world patients with uncontrolled hypotension. By using a time in target range (TTR) analysis, researchers were able to estimate the proportion of time that patients achieve an ideal blood pressure and the relationship this has with death, myocardial infarction, and stroke, which as major adverse cardiovascular events (MACE). A 10% increase in TTR for 12 months was associated with decreased risk of a MACE in the next 24 months. The global registry found that patients with radiofrequency RDN spent a greater amount of time in TTR reducing MACE risk.

Secondly, an update from the SPYRAL-HTN ON MED trial was shared. Though patients who underwent RDN were shown to have lower blood pressure compared with a control group, the effect on blood pressure burden overtime was not well understood. Comparing TTR analysis over years of control and patients who had been treated with RDN demonstrated that RDN groups had significantly increased TTR, affirming the sustained efficacy of RDN long-term.

Data shared from the RADIANCE-HTN SOLO and RADIANCE-HTN TRIO trials. Explored responses to ultrasound RDN in drug resistant populations and in populations with mild to moderate hypertension. The pooled analysis suggested that response to ultrasound RDN in the presence or absence of medications is similar and consistent across the spectrum of severity of hypertension.

The emerging long-term data shared was positive and the promise of an effective treatment using RDN offers one way to tackle the challenge of adherence to hypotension management. ■

"By using a time in target range (TTR) analysis, researchers were able to estimate the proportion of time that patients achieve an ideal blood pressure"

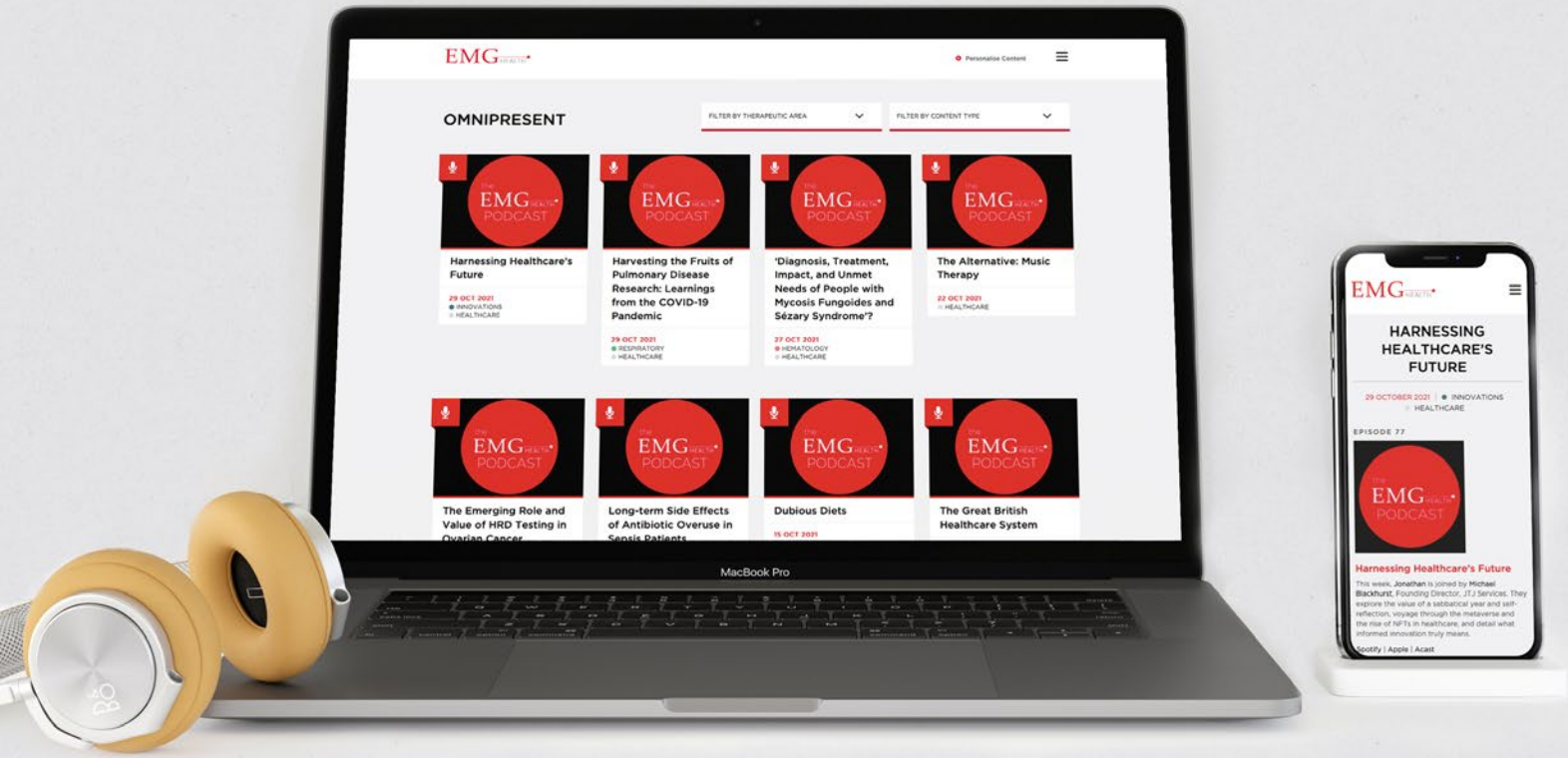
The Andreas Grüntzig Ethica Award 2022: The Nursing and Allied Professionals Community

THE ANDREAS Grüntzig Ethica Award represents the highest honour in the field of interventional cardiology. This year's award was presented to the nursing and allied professionals (NAP) community at the EuroPCR 2022 congress, which took place from 16th–19th May in Paris, France.

Taking place in the renowned Studio Havane of the Palais des Congrès Porte Maillot, Paris, France, the award ceremony was centred around the core values of EuroPCR. The continued proficiency and presence that NAPs provide to patients has been an essential cog in the advancement of modern interventional cardiology. Only emphasised by the COVID-19 pandemic, NAPs epitomise the fundamental EuroPCR principles of 'together we do more', displaying the importance of patient interaction and support to the multidisciplinary team.

Traditionally awarded to one or two individuals, the presentation of Andreas Grüntzig Ethica Award to the entire NAP community aims to not only commend and recognise their dedication, but also to draw attention to the need for further investment in their training and quality of life. Lynne Hinterbuchner, chair of the EAPCI NAPs Committee and Association of Cardiovascular Nursing and Allied Professions (ACNAP) Education Committee noted: "I think there is an unspoken acknowledgement of how much NAPs do and how they step up to meet each and every challenge, but this award is the first time that someone has said: 'We're really proud of you and want to recognise that you've done something very well.'" The breadth of NAP work that has supported the global and holistic vision of healthcare, emphasising the key role of patient advocacy and patient care management from diagnosis to discharge. ■

"The continued proficiency and presence that NAPs provide to patients has been an essential cog in the advancement of modern interventional cardiology"



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Artificial Intelligence in Interventional Cardiology

Theo Wolf
Senior Editorial Assistant

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ARTIFICIAL intelligence (AI) has begun to permeate and revolutionise interventional cardiology. Multimodality images, ECGs, electronic health records, and other routine medical media store underutilised patient data. AI has the capacity to learn from these data sources and apply knowledge from them to distinct medical circumstances. At this year's EuroPCR, a panel of experts explored a number of ways in which AI can be applied to the field in order to improve existing gaps in cardiovascular medical practice.

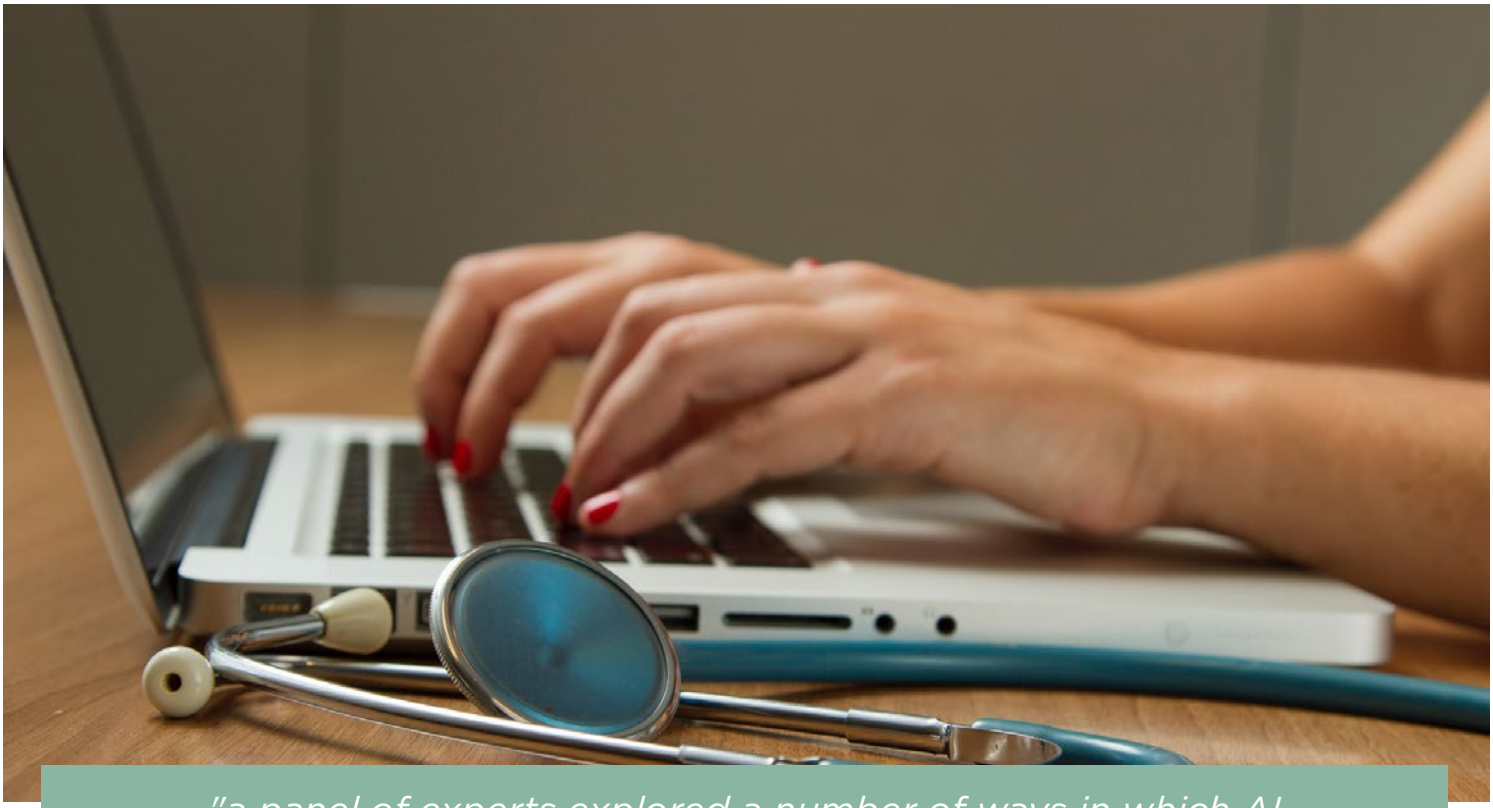
ARTIFICIAL INTELLIGENCE AND CORONARY ARTERY DISEASE

Coronary angiography is the gold standard for diagnosis and management of coronary artery disease. "As interventionalists, we use visual assessment as the de facto method for determining the severity of coronary artery disease," said Robert Avram, Montreal Heart Institute, Canada. However, Avram emphasised that this measurement suffers from significant intra- and interobserver variability. Consequently, Avram and colleagues considered whether it was possible to "develop an AI algorithm that will be able to fully interpret the coronary angiogram and reduce or minimise the variability."

Data from approximately 11,000 patients at the University of California, San Francisco, California, USA, were used for development and internal validation of the algorithm. In addition, "we also took 464 patients at the Ottawa Heart Institute [Canada], and we paired the images of the angiograms with the coronary angiography report," explained Avram. "We do angiograms of many vessels, not only the coronaries. We can do an angiogram of the renal artery or the femoral artery. So, it was very important for us to restrict this algorithm to the left and right coronary artery," noted Avram.

The algorithm was built to perform four different tasks: projection angle detection (Algorithm 1); anatomic structure identification (Algorithm 2); anatomy and stenosis localisation (Algorithm 3); and prediction of coronary stenosis severity (Algorithm 4). Avram revealed that "Algorithm 2 was able to identify left and right coronary arteries in 97 and 93% of cases in San Francisco, and 100% of the cases in Ottawa." Furthermore, "Algorithm 3 was able to localise 94% of the stenosis in San Francisco and 85% of the stenosis in Ottawa when compared to the angiogram report," highlighted Avram.

Regarding stenosis severity (discriminating between severe [≥70%] and non-severe stenosis), areas under the receiver operating characteristic curves (AUROC) of 0.862 and 0.869 were calculated for the University of California, San Francisco and Ottawa datasets, respectively. "This was a first proof that we can develop an AI algorithm that can take an angiogram, localise the stenosis, and predict the severity with a pretty good performance," summarised Avram.



"a panel of experts explored a number of ways in which AI can be applied to the field in order to improve existing gaps in cardiovascular medical practice."

The researchers also explored quantitative coronary angiograms (QCA) because visual assessment is an imperfect label, according to Avram. In total, data from 419 patients were extracted, and 1,098 lesions were isolated on the coronary angiogram with core-lab adjudicated QCA readings. The group applied the previous algorithm, called CathAI, to predict severe stenosis from non-severe stenosis on QCA-labelled datasets, and used a 50% cut-off on QCA. An AUROC of 0.73 was obtained for CathAI to detect a severe stenosis against QCA. "CathAI was replicating the visual bias, or the human bias, which is to overestimate severe stenosis, leading to over-stenting down the line," concluded Avram. Going forward, Avram and collaborators are "re-training this algorithm with QCA labels to have a less biased predictive value."

Even though most of the work previously done on coronary angiograms uses images of the vessels, videos can also be used, and these offer much richer datasets. The movement of the right coronary artery with each heartbeat and also the breathing of a patient makes it difficult for an AI algorithm to focus on one particular area. For this reason, the researchers built an algorithm to stabilise the vessel, meaning it adjusts for breathing and heart rate variability. Using this type of data, it is possible to determine the instantaneous wave-free ratio and fractional flow reserve. Work is also underway to "derive automated SYNTAX score to describe the plaque assessment such as calcification, the bifurcation type, and disease severity using stabilised videos of coronary vessels."

Avram finished by presenting a roadmap for AI implementation in medicine. This comprised five distinct stages: data generation; AI algorithm training; AI algorithm internal and external validation; randomised controlled trial demonstrating a positive impact on outcomes; and, finally, deployment of AI in clinical practice.

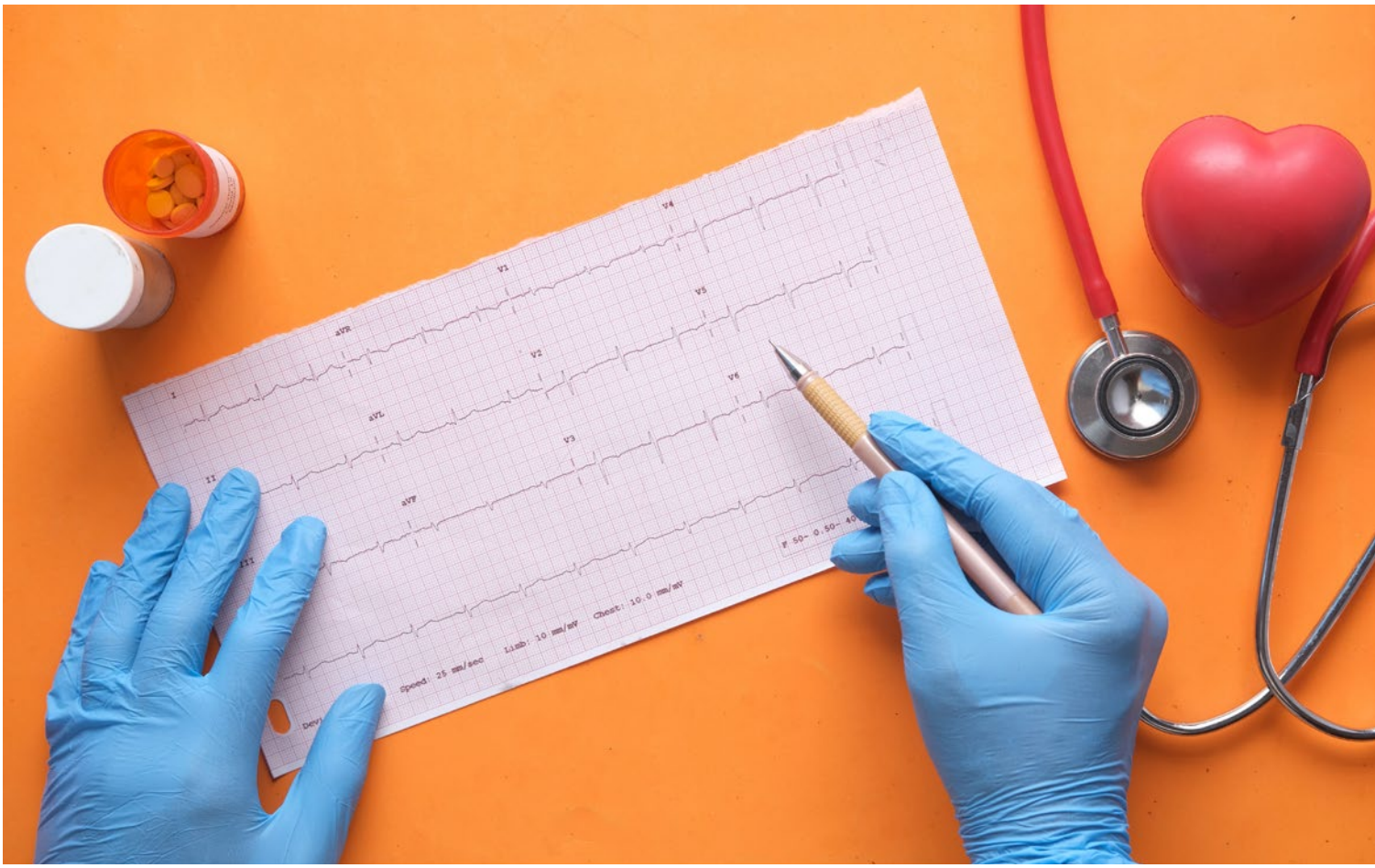
ARTIFICIAL INTELLIGENCE AND STRUCTURAL HEART DISEASE

Timothy Poterucha, Columbia University, New York City, New York, USA, expressed his belief that "AI is going to fundamentally change our approach to structural heart disease in the next decade across the patient journey." Poterucha began by considering initial suspicion of structural heart disease. "Over the last 15 years, we have seen TAVI [transcatheter aortic valve

implantation] quickly progress, initially from inoperable to high-risk patients, pushing into intermediate and low-risk patients. At each step, we've seen improved outcomes along the way," said Poterucha.

Now, studies are investigating transcatheter aortic valve implantation in asymptomatic individuals and those with moderate aortic stenosis that is complicated by heart failure. Clearly, there is a trend toward treating patients earlier and earlier when they have asymptomatic valvular heart disease. Therefore, in the next decade, wide-scale screening programmes will be necessary in order to detect asymptomatic, severe valvular heart disease. Currently, less than half of those patients with severe aortic stenosis have been clinically detected. "Most of those patients are enrolled in care, they are seeing doctors regularly, but that murmur isn't heard [...] and if we can't detect these patients, we can't change the natural history of the disease." The ideal way to screen all these patients would be to perform wide-scale echocardiography; however, this is expensive and requires expertise to obtain the images and interpret them. Therefore, Poterucha and his group asked the following research question: can AI analysis of 12-lead ECG detect moderate or severe valvular heart disease? To answer this, data were collected from 77,163 patients who had an ECG done within a year prior to an echo. "We split this data up into train, validation, and test sets," revealed Poterucha.

The group inserted the ECG raw waveform and ran these inputs through calculation layers. After the input was run through these calculation layers, an output was generated. In this case, the group investigated whether the patient's echocardiogram came from someone with moderate or severe aortic stenosis, aortic regurgitation, or mitral regurgitation. The model, developed by Poterucha and colleagues, was shown to accurately predict aortic stenosis with an AUROC of 0.88. In addition, the model predicted aortic regurgitation and mitral regurgitation with AUROCs of 0.77 and 0.83, respectively. "It can do very similarly in a composite model that's looking for any of these three diseases," continued Poterucha. In summary, deep learning can be used to analyse an ECG to detect a combination of several valvular heart lesions. As highlighted by Poterucha, the aim is to deploy this in patients. Currently, a 200-patient clinical



trial is being conducted at Columbia. Whenever an ECG is performed, it is put into the research servers and then run, in real-time, through deep learning models. If a patient with a high probability of valvular heart disease has not had an echo recently, they are recruited as part of the prospective clinical trial. "Our goal is to take these algorithms, develop them in retrospective datasets, and then prove that they work through prospective clinical trials," said Poterucha.

Poterucha next considered diagnosis and emphasised that ECGs are highly standardised and amenable to rule-based interpretation. However, the average echocardiogram is composed of around 100 clips, each of which is around 3 seconds long, and there are around 30 frames per second. This yields a total of 10,000 frames per echocardiogram, which is much more complex than an ECG that has 12 leads for 10 seconds at 250 Hz. The issue of complexity is compounded by the high variability between patients. Although rule-based interpretation models cannot process complex forms of data, AI can. The current state of the art is accurate view identification and structure segmentation, as well as left ventricular quantification similar to that achieved by cardiologists. In the near future, research will focus on preliminary report drafting and phenotype detection. Phenotype detection is a particularly exciting prospect, which involves training a series of deep learning models to look for the signals indicating that a patient might have a specific diagnosis, such as cardiac amyloidosis or low-flow, low-gradient aortic stenosis. This will allow cardiologists to target particular interventions at these patients.

According to Poterucha, the first advancement in terms of treatment will be improved prognostication. A recent study employed a variety of machine learning and traditional statistic methods to identify the minimum number of factors associated with prognosis. Overall, six variables (blood urea nitrogen, creatinine, haemoglobin, BMI, mean arterial pressure, and N-terminal pro B-type natriuretic peptide) yielded an AUROC of 0.772 in predicting mortality using the XGBoost machine learning technique. Poterucha highlighted two caveats of this research, namely that these clinical factors were already known to impact prognosis and that logistic regression was almost as good as the machine learning techniques. The second advance is going to be in treatment planning. Poterucha predicts that automated analysis of CT for annulus sizing will become mainstream in the next 5 years. However, although this software will shorten analytic time and match, Poterucha does not anticipate that it will outperform experienced readers.

CONCLUSION

Advances in AI and machine learning will positively impact the management of both coronary artery disease and structural heart disease across the patient journey, from improved patient identification to enhanced prognostication and faster treatment planning. Importantly, AI advances should be optimised to automate many of the computer tasks that currently take up much of medical practice, enabling interventionalists to spend more time in direct patient care.

"Advances in AI and machine learning will positively impact the management of both coronary artery disease and structural heart disease across the patient journey"

Abstract Highlights

The following highlights focus on several insightful and innovative abstracts at EuroPCR 2022, covering topics such as transcatheter aortic valves, catheter-directed therapy, and a novel renal denervation procedure.

Alternative to Systemic Thrombolysis Proves Successful

CATHETER-directed therapy (CDT) has a high success rate in patients with high-risk pulmonary embolism (HR-PE). Presenting the findings of the TROMPA Registry investigators at the 2022 EuroPCR, Pablo Salinas, Hospital Clínico San Carlos, Madrid, Spain, discussed the different approaches to treating patients with HR-PE and the results from the TROMPA Registry.

CDT is commonly used in patients with HR-PE when systemic thrombolysis (TL) has failed or is contraindicated. It is also indicated in patients with intermediate HR-PE (IHR-PE) as an alternative to systemic TL when a patient has haemodynamic deterioration.

The Registry studied patients presenting with HR-PE and IHR-PE (N=75) from eight centres across Spain from 2017 to 2021. The median age range of patients was 61, and 45% of patients were diagnosed with HR-PE on admission (mean BOVA score: 5.6; mean venous lactate: >3.3).

The main indication of CDT was a high bleeding risk (64.6%) and contradiction (54.7%) for systemic TL. Failure of systemic TL was represented in just 6.7% of cases. Patients with IHR-PE typically underwent CDT due to evolution into HR-PE. The patients were treated with three approaches to CDT: local TL (23%), mechanical thrombectomy (27%), and combined therapy (40%), with Salinas stressing that treatment should be decided collaboratively at PE response team meetings.

While the procedural success rate with 97.3%, there was still a high ratio of major bleeding (22.7%) and all cause in-hospital deaths (21.3%). However, Salinas stated that HR-PE has a mortality rate of 40–50%; therefore, intervention with CDT showed some improvements. Refractory shock was responsible for five out of 16 deaths, while two patients died as a result of CDT-related adverse events. However, CDT procedures lead to an increase of systemic systolic pressure (9.6±16 mmHg) and a decrease of pulmonary systolic pressure (12.5 mmHg)

Summing up these findings, Salinas stated that earlier CDT consideration, therapy awareness, and use of dedicated devices are warranted to improve results. ■

"While the procedural success rate with 97.3%, there was still a high ratio of major bleeding (22.7%) and all cause in-hospital deaths (21.3%)."

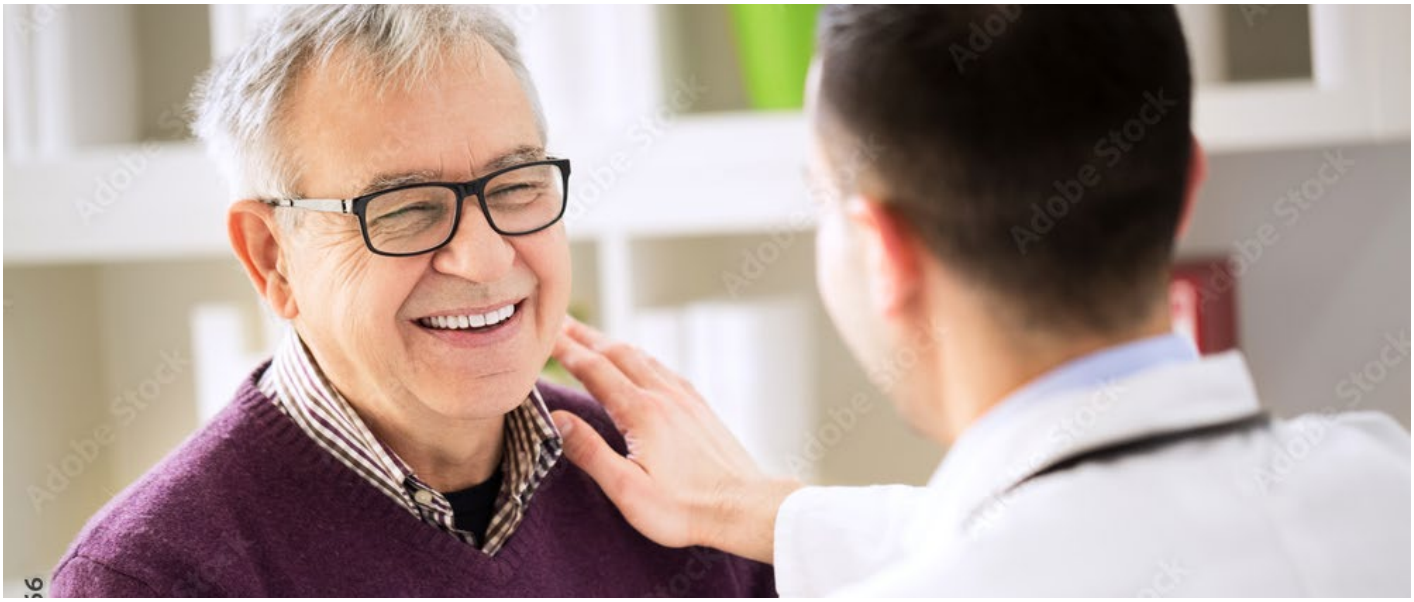
A Novel Approach For Performing Renal Denervation

ROBOTICS has been used in interventional cardiology for over a decade and has demonstrated some benefits in coronary interventions such as precision. A study presented at the European Association for Percutaneous Cardiovascular Interventions (EuroPCR) 2022, discussed a novel approach for performing renal denervation.

"precision of the robotic system can provide additional benefits to the patient"

Konstantinos Bermpeis, Cardiovascular Centre Aalst, Belgium, discussed the use of the Symplicity Spyral catheter (Medtronic, Dublin, Ireland) with the CorPath GRX system (Corindus, Siemens Healthineers, Erlangen, Germany) on a patient. The researchers confirmed that the catheter was successfully tested *in vitro* in the catheterisation laboratory before using it on the patient. The procedure setting for renal denervation surgery included a 6 Fr guiding catheter connected to the CorPath system, the Symplicity Spyral catheter, and an operator performing the procedure using the CorPath GRX console remotely. Bermpeis confirmed that all the operators were outside the surgery room and therefore protected from radiation.

The renal denervation procedure began with advancing the guidewire using standard navigation to the right renal artery, followed by advancing the implicity spiral catheter to the kidney, and ablation. The procedure was performed without any malfunction, the contrast colour used was 49, and radiation was 77 Gycm. The patient was discharged the same day and followed up 2 months later. In 2 months the systolic blood pressure was reduced by about 20 mmHg. This is the first case study to show that the CorPath GRX system is compatible with the Symplicity Spyral Catherter; however, Bermpeis stated that following this first case their team has performed four more successful renal denervation procedures using the robotic system. One of the noteworthy benefits of robotic-assisted renal denervation is that it can reduce occupation hazards, such as exposure to radiation, for the operators as the procedure can be performed remotely. The precision of the robotic system can provide additional benefits to the patient as well. Bermpeis confirmed that their team is working on a new study to demonstrate the safety and feasibility of robotics in renal denervation. ■



EURO PCR 2022 REVIEWED →

Insights from the OBSERVANT II Study: Comparing Transcatheter Aortic Valves

TRANSCATHETER aortic valve comparisons have previously been limited to two-arm design studies. During this year's EuroPCR Congress, in line with the theme of innovation, Giuliano Costa, Interventional Cardiologist, Division of Cardiology, University of Catania, Italy, and his colleagues shared their novel study comparing multiple transcatheter aortic valves in a multicentre study named OBSERVANT II.

Costa explained the importance of the study expressing the growing need to assess comparative outcomes of different transcatheter aortic valve replacement (TAVI) platforms in real-world practice; several manufacturers have their TAVI devices approved and available in several countries, but how do interventional cardiologists know which one is the best?

This clinical trial compared outcomes of patients using the most common second and third generation devices for TAVI in Italy. The primary outcome was death, stroke, or re-hospitalisation at 1 year. Researchers recruited n=2,989 patients with consecutive aortic stenosis undergoing TAVI from 28 medical centres across Italy from December 2016 and September 2018. Patients at the mean age of 83 years old were divided into 5 groups to receive different devices, these included: Evolut R (n=1125), Evolut PRO (n=337), SAPIEN 3 (n=768), ACURATE neo (n=290), and Portico (n=208).

Results showed the computed tomography angiography (CTA) varied across all devices as expected, with the Evolut R having the lowest CTA, and the ACURATE neo having the highest CTA. Importantly, there was no difference in the primary outcome between these five devices. Patients receiving SAPIEN 3 valve had lower rates of pulmonary vascular resistance and proton pump inhibitors; however, they had higher trans-prosthetic gradients after TAVI. Additionally, Evolut PRO had better outcomes than Evolut R, the latter being a previous generation device.

Overall, the study shows that the constant development of TAVI devices results in improved outcomes for patients undergoing TAVI, and over time the differences between these devices will be minimal, as they will continue to improve. ■

"the study shows that the constant development of TAVI devices results in improved outcomes for patients undergoing TAVI, and over time the differences between these devices will be minimal, as they will continue to improve."

Assessing the Lotus Valve in Transcatheter Aortic Valve Implantation

THE LOTUS valve (Boston Scientific Corporation, Marlborough, Massachusetts, USA) has recently been withdrawn from the market. However, the valve has a number of technical features that make it interesting for patients with a challenging aortic valve anatomy. For example, the valve has comparatively higher transprosthetic mean pressure gradient.

Long-term follow-up data of the first-generation Lotus valve are lacking. Therefore, a recent study analysed all patients treated with a Lotus valve for transcatheter aortic valve replacement at the Leipzig Heart Center and Heart Center Bad Segeberg, Germany, between November 2013 and February 2017. A clinical and echocardiographic follow-up was then performed at least 3 years after valve implantation. The results were shared at EuroPCR 2022.

The primary endpoints were all-cause mortality and late onset bioprosthetic valve failure (BVF) >30 days according to the standardised European Association of Percutaneous Cardiovascular Interventions (EAPCI)/European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) definition. The secondary endpoints were bioprosthetic valve dysfunction and their components (structural and non-structural valve deterioration, clinical valve thrombosis, and endocarditis).

Overall, 229 patients were included across the two heart centres. The cumulative incidence of all-cause BVF at 5 years was shown to be high relative to other valves. In this study, the adjusted cumulative incidence of BVF (adjusted for all-cause mortality) after 5 years was 6.7% (95% confidence interval: 3.6–11.1%). By comparison, in the CHOICE trial, the BVF after 5 years for the SapienXT (Edwards Lifesciences, Irvine, California, USA) and CoreValve (Medtronic, Minneapolis, Minnesota, USA) were 4.1% and 3.4%, respectively. Interestingly, BVF after Lotus valve implantation was mainly driven by endocarditis, not paravalvular leaks or structural valve deterioration. Furthermore, the specific valve characteristic might have caused the elevated thrombogenic potential and endocarditis rate.

Based on the research results, the authors recommended that specific attention is paid to these events during long-term follow-up of individuals treated with the Lotus valve. ■

"a recent study analysed all patients treated with a Lotus valve for transcatheter aortic valve replacement at the Leipzig Heart Center and Heart Center Bad Segeberg, Germany, between November 2013 and February 2017."

Study Shows No Adverse Outcomes for TAVI in Diabetic Patients

OUTCOMES from a recent trial focusing on transfemoral transcatheter aortic valve implantation (TAVI) in patients with diabetes were presented at the EuroPCR congress. Taking place from 17th–20th May 2022, this year's interventional cardiology meeting welcomed attendees to Paris, France, breaking the virtual format for the first time since 2019.

Within the TAVI population, diabetes presents with a 30% prevalence, yet its effects on procedure outcomes are still unknown. Collaborators from the Heart Center, Amsterdam UMC, The Netherlands, assessed the procedural risk and clinical outcomes in patients with diabetes undergoing transfemoral TAVI. This multicenter study included over 12,000 transfemoral TAVI patients aged 80±7 years, with a matched population of 3,281 patient pairs, dependent on diabetes status.

Presented by Astrid van Nieuwkerk, Heart Center, Amsterdam UMC, on behalf of the study collaborators, results showed that the clinical outcomes measured did not fluctuate between patients with diabetes, and those without diabetes. The outcomes measured included stroke, major bleeding, myocardial infarction, permanent pacemaker implantation, and the length of hospital stay following TAVI. Mortality rates of patients with diabetes compared with those without diabetes were also negligible, with a statistically insignificant hazard ratio of 1.1.

The experts noted some disparities between populations with insulin-treated diabetes versus non-insulin-treated diabetes. Patients treated with insulin were younger, and had a higher prevalence of renal failure, presenting in 17% of patients, compared with 11% in the non-insulin group. Although the threshold for statistical significance was not met, a clear trend was noted between patients with insulin-treated diabetes and mortality following the TAVI procedure.

Van Nieuwkerk went on to note the limitations of the study, which included the observational design of the study, and the lack of data available on the severity of diabetes. The endpoints also did not undergo central adjudication in this trial. This study concluded that the incidence of diabetes alongside TAVI was not associated with detrimental outcomes following the procedure, underpinning the safety of this interventional treatment in diabetic patients. ■

"the incidence of diabetes alongside TAVI was not associated with detrimental outcomes following the procedure"

Congress Interview

Salvatore Brugaletta

Senior Consultant Interventional Cardiologist, University Hospital Clinic, Barcelona, Spain; Associate Professor, University of Barcelona, Spain

Q1 What led you to want to specialise in cardiology, and specifically interventional cardiology?

When I was a medical student, I remained astonished by Attilio Maseri, the Professor of Cardiology at my university at that time. His charisma made me start cardiology with so much enthusiasm that I did not have any doubt about becoming a cardiologist. Later on, when I started my training in cardiology, I had the chance at the very beginning to join a senior interventional cardiologist during a primary percutanous coronary intervention, and it was love at first sight. I still remember the feeling during that night that we did something very positive for that patient with ST segment elevation myocardial infarction, whose pain was relieved so quickly by reopening the artery. Following that night, I am still here treating patients and improving their quality of life.

Q2 What are your particular research interests, and have these shifted since you began to practice?

My research interest has always been atherosclerosis and all its different aspects, from pathology to treatment. When I was a medical student, I was involved in basic research, specifically looking at lymphocyte populations in patients with unstable angina by using flow cytometry. I have worked on how endothelial dysfunction may contribute to coronary plaque worsening, and on comparing coronary stents for treating patients. In particular, under the supervision of Patrick Serruys in Rotterdam, the Netherlands, I was one of the first studying bioresorbable vascular devices in patients through various intra- and extracoronary imaging techniques. Then I worked with Manel Sabate, and am still working with him today, on testing the best device for treating patients with ST segment elevation myocardial infarction.

Q3 You have served as invited faculty, or given lectures, at around 100 international meetings, for the likes of the European Society of Cardiology (ESC), the European Association of Percutaneous Cardiovascular Interventions (EAPCI), and Transcatheter Cardiovascular Therapeutics (TCT). What do you feel are the benefits for yourself, as a clinician, to be so involved in the wider field? Which ideas do you hope to promote?

To join and participate in a conference always has a benefit, regardless of whether you are faculty,

"Congresses and courses are here for teaching others, and it is the responsibility of the faculties to do this in the best possible way."

a speaker, or an attendee. You are exposed to new science, technology, and drugs; you share opinions with your peers; and when you come back to your daily clinical life, you feel enriched from such an experience, and you may improve the treatment for your patients. On the top of this, when you are faculty, you have a big responsibility towards the attendees, as you are there not for increasing your visibility, but for helping others, and for teaching them. Jean Marco, the founder of PCR, whom I had the honour to meet several times, always says we are here for others. I totally agree with him; congresses and courses are here for teaching others, and it is the responsibility of the faculties to do this in the best possible way.

Q4 You are an Associate Professor at the University of Barcelona, Spain. How have you found your teaching has adapted since the COVID-19 pandemic? What have been the drawbacks, and have there been any unforeseen advantages in the shift to online learning?

The COVID-19 pandemic has unfortunately disrupted teaching at the universities overall. Medical students need the contact with their teachers, and even more so with patients. The latter was totally missing during the worst part of the pandemic, when hospitals were full of patients with COVID-19. Moving from face-to-face teaching to online learning has reorganised our lessons, because in an online class you need to catch more of the attention of the students. In this way, we have discovered many resources to make our teaching more attractive. Moreover, we have started many online resources useful for students and for fellows, such as webinars, case sharing, etc.

Q5 You have authored more than 400 manuscripts over your career to date. Can you pick out one or two which led you to discover something particularly important, or groundbreaking, within the field of interventional cardiology?

I am thinking about two papers. One describes how bioresorbable scaffolds may create a sort of cap on the top of an atherosclerotic plaque, potentially leading to stabilisation of a thin-cap fibroatheroma by transforming it into a thick-cap fibroatheroma. The other also belongs to the field of bioresorbable devices, and shows how vasomotion of the coronary segment treated by bioresorbable scaffold depends either on the grade of disappearance of the device from the artery, or on the composition of the plaque

underneath the devices. These two concepts of plaque sealing and vessel vasomotion were two benefits of bioresorbable scaffolds, and they should be the starting point for a new generation of these devices, whose need in clinical practice has not disappeared.

Q6 In January 2022, you co-authored a paper entitled 'Mid-term effects of SARS-CoV-2 infection on cardiovascular outcomes'. Please summarise what you discovered during this study, and what you believe the consequences of the pandemic will be on cardiovascular outcomes in the long-term.

The rationale behind this study was to understand if severe acute respiratory syndrome coronavirus 2 infection may have cardiovascular consequences beyond the acute phase. We analysed data from patients who underwent a PCR test, dividing them into two groups according to the result of the test. We found that the cardiovascular outcome was worse in patients infected versus control, but it was mainly driven by in-hospital events, without any consequences in the mid-term. We have now expanded this population by adding data from other centres, and we are currently working on 1-year outcome. We will then see if this trend will be confirmed in a larger population with a longer follow-up.

Q7 You have not one, but two PhDs, from Erasmus University, Rotterdam, and Sacred Heart University, Rome, Italy. Please tell us more about what you researched during your PhDs, and what led you to read for a second doctorate?

I was already in the middle of my first PhD in Rome, conducting basic research on vascular function after chronic total occlusion recanalisation, and I had the opportunity to go abroad to the Erasmus University, working with Serruys. He offered me the possibility to read for a second PhD about bioresorbable scaffolds. I did not have any doubts in starting, in parallel, a second PhD with him about this topic. I worked very hard during those 2.5 years, publishing more than 30 papers in 1 year, and being able to read both PhDs 1 month apart. Although in the end it is something that does not matter from an academic point of view, I feel proud of myself, because hard work always has a reward, and I like to have two PhDs on different topics, one from my own country, Italy, and the other one from the Netherlands, which I see as a recognition for all my time spent abroad. We live in a global world where students should be encouraged to move abroad for studying, and to see how the same problem may have different, and equally right, solutions.

Q8 How has the landscape of interventional cardiology shifted since you began to practice, and how has the technology developed?

The landscape has totally changed since I began. When I started, we were only focused on coronary interventions, and now not only are we better at treating the coronaries of our patients, but we are also treating structural heart disease, such as aortic stenosis. During the last 20 years, technology has had a strong evolution in terms of materials and devices, helping us to make difficult things easier. When I began, for example, nobody was thinking about percutaneous treatment of valvular disease. And it is incredible to see today how easy a transcatheter aortic valve implantation procedure may be. On the top of this, it is not only a matter of technology, but also a matter that today every procedure is more standardised, and there is much more consensus on how a specific coronary or structural procedure should be approached. All of these factors altogether have improved our profession as caregivers for our patients.

Q9 Which recent, noteworthy technological advances are you most excited by in the field of interventional cardiology, and why?

I am very much looking forward to percutaneous mitral valve implantation. Some devices are already on the market, and others will come soon. They may currently be implanted through a surgical transapical approach, but a plan to make them easily implantable by a trans-septal approach is under development. When this approach is feasible, safe, and effective, it will represent a major step forward in this kind of procedure, giving us the possibility to treat those patients who cannot be treated today. ■

Interviews

Clifford Kavinsky and Lloyd Klein spoke to EMJ about the experiences that inspired them to specialise in interventional cardiology, shared valuable insights into their clinical research, and discussed what innovations are set to stand out in the landscape of this rapidly evolving clinical field.

Featuring: Clifford Kavinsky and Lloyd Klein

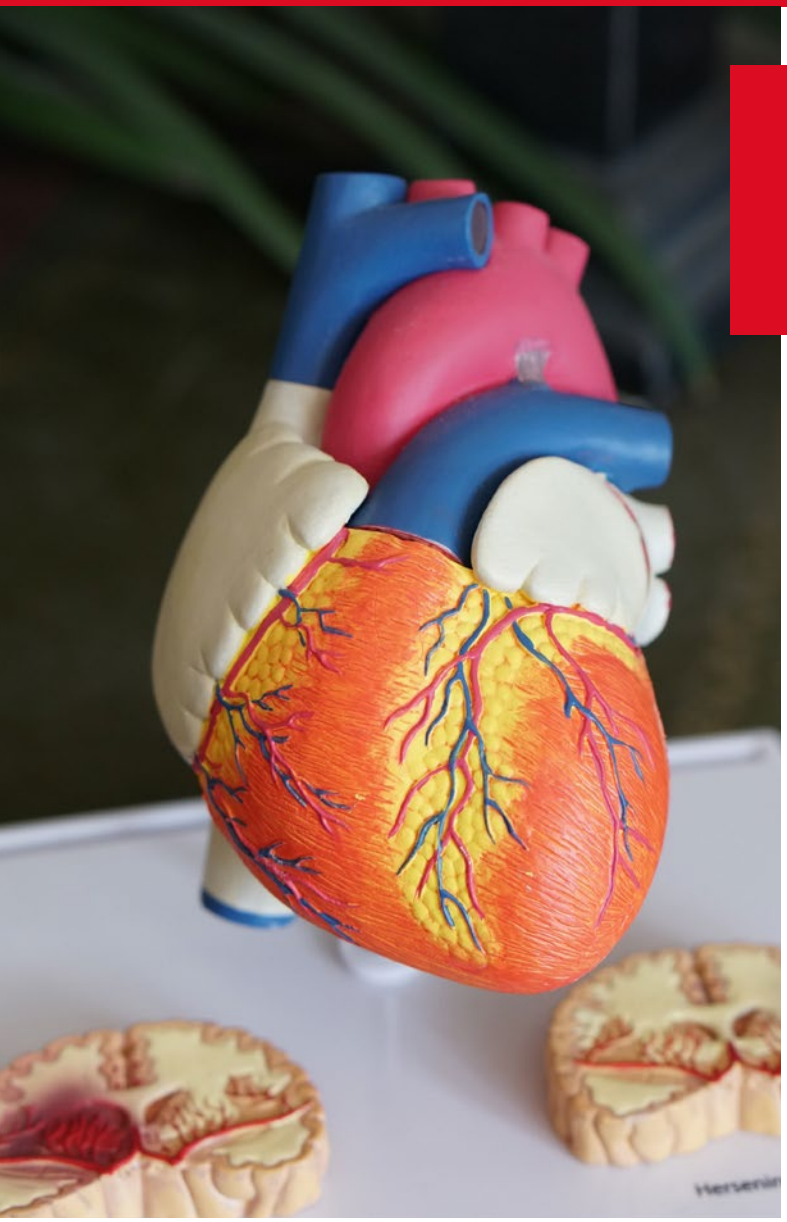
Clifford Kavinsky

Associate Director of the Cardiovascular Disease Fellowship Program; Program Director for the Interventional and Structural Heart Disease Fellowship Program; Professor of the Department of Internal Medicine and Pediatrics; Chief of the Section of Structural and Interventional Cardiology; and Director of the Rush Center for Adult Structural Heart Disease at Rush University Medical College, Chicago, Illinois, USA.

Q1

Following your initial medical training, what led you to specialise in cardiology and interventional cardiology?

Initially, I felt that cardiovascular medicine afforded the greatest opportunity to take advantage of a broad array of diagnostics and therapeutic interventions that had a direct effect on patient outcomes. I thought that physical bedside assessments and cardiovascular physiology made a lot of sense, and when I treated patients, I could often see immediate and compelling results. I felt that I could have a positive effect on patients' lives in term of longevity and quality of life and that interventional medicine represented the culmination of cardiology, allowing me to see a critically ill, unstable patient; treat their underlying problems; and watch them improve and, ultimately, go home. Whether it be performing percutaneous coronary intervention (PCI) in the setting of a ST-elevation myocardial infarction or providing mechanical circulatory



support to a patient in shock, interventional medicine is extremely rewarding. We cannot save everyone, but the rewards are greater than for any other field in cardiology.

Q2

As the Associate Director of the Cardiovascular Disease Fellowship Program at Rush University Medical College, Chicago, Illinois, USA, what were your key aims when developing the structure of the programme to provide optimal training for participants?

My goal is to train cardiologists that will go out and become leaders in their field. We try to instil into our fellows the three pillars of academic medicine: excellence in patient care, the education of those following behind you, and research into new innovative treatments that will move the field of cardiovascular medicine forward. We want to expose our fellows to the entire spectrum of acute and chronic cardiovascular disease. That is why we have developed rotations at three different hospitals: a tertiary care centre, a public service hospital, and a community hospital. Each provides the trainee with different patient demographics, disease spectrums, and ways of practicing medicine. Additionally, significant time is spent fostering and mentoring fellow research involvement.

"As physicians must be efficient in delivering the highest quality care to their patients, fellows are taught to work as part of a team to understand systems of care.

Q3

Are there any areas of the Cardiovascular Disease Fellowship Program that you have put an emphasis on or that you think are particularly important?

Health care is changing rapidly, and the training of physicians must change with it. Our focus is on shortening lengths of stay in hospitals, improving transitions in care, and providing longitudinal care. Fellow physicians do not work in isolation, but as part of a bigger multi-disciplinary care team. There are many great advances in cardiovascular medicine; however, many of these innovative therapies are expensive and the number of health care dollars entering the system is not increasing, so many hospital organisations are seeing narrowing profit margins. As physicians must be efficient in delivering the highest quality care to their patients, fellows are taught to work as part of a team to understand systems of care.

Q1

How did the COVID-19 pandemic affect the field of interventional cardiology, and are there any aspects of this shift that have now become standard practice?

For a short period of time in early 2020, interventional services for elective procedures were shut down. This policy was particularly harmful to our structural programme, where many of the procedures are elective, because we found that patients began dying at home waiting for their transcatheter aortic valve replacement (TAVR) procedures. There was also fear from the public in terms of coming to the hospital as they thought they would get COVID-19, which was fuelled by the media, so patients would not

come to the hospital even when they needed to. ST-elevation myocardial infarction interventions went down, and over time, these fears have slowly been assuaged. Yet, during the recent COVID-19 surge early this year, we once again saw a drop in our interventional volumes. To date, our interventional procedural volumes have yet to achieve the pre-pandemic levels seen in 2019. In terms of precautions, all patients must have a rapid COVID-19 test within 72 hours prior to their procedures and all staff caring for patients who are COVID-19-positive and are undergoing urgent or emergent procedures must use personal protection equipment.

Q5

You recently co-authored a paper entitled 'Percutaneous Right Ventricular Assist Device Using the TandemHeart ProtekDuo: Real-World Experience', which was published shortly before the Joint European Association of Percutaneous Cardiovascular Interventions (EAPCI) and Association for Acute Cardiovascular Care (ACVC) consensus on percutaneous ventricular assist devices. Did you agree with the information published, and would you amend or include any additional perspectives?

I think that the ProtekDuo® catheter is the most effective percutaneous catheter-based system for providing temporary right ventricular support. It is relatively easy to place and connects to a bypass circuit. The other commercially available device on the market is the Impella RP®, which can also provide temporary support for the failing right ventricle. However, this device is more challenging to place properly due to its large size and the need for the device to track through the right atrium, right ventricle, and across the pulmonic valve.

Q6

Where does the focus of your research currently lie?

Since 2002, when Alain Cribier implanted the first percutaneous aortic valve in a human being, the major advances in interventional medicine have resided in the structural heart disease space,

which is my area of focus and specialisation. The emergence of catheter-based therapies for cardiac disorders that were traditionally treated with large open cardiac surgical procedures represents a sea change in the management of patients with congenital and acquired structural heart disease. In congenital heart disease, our paediatric colleagues have done a superb job: a child now born with congenital heart disease has a >90% chance of living through to adulthood due to advances in interventional medicine. The randomised trials in TAVR have provided robust clinical data to support a paradigm shift in how we treat patients with severe aortic stenosis. The trials on patent foramen ovale (PFO) closure have finally established PFO closure as superior to medical therapy alone in preventing recurrent PFO-associated stroke. As we look forward, we will see this trend continuing. The next few years will be dedicated to developing and refining percutaneous therapies for the mitral and tricuspid valves. Transferring the success of the TAVR space to the mitral and tricuspid valves will not be easy; the mitral valve has many complexities that are not found with the aortic valve, such as its location internal to the heart, its large size, its non-planar conformation, and the associated challenges of anchoring a percutaneous valve. The tricuspid valve shares many of the same complexities. Despite these challenges, through partnership with industry, viable percutaneous technologies are emerging, and evaluating these new platforms will be my focus for the next several years. In addition, again through partnering with industry, we are trying to develop 'no footprint' techniques for closing a PFO without leaving a large device in the heart of patients who are young and have many years of life left to live.

Q7 Over the years you have spent practising as an interventional cardiologist, how have you seen the technology and treatment landscape develop?

It was in 1929 that Werner Forssmann cannulated his own basilic vein and advanced a urinary catheter to his right atrium, which opened up the field of invasive cardiology. I am in awe of the advances that have been made in interventional medicine since then: the emergence of coronary angioplasty, the development of the coronary stent, and, finally, the drug-eluting stent have revolutionised how we treat patients with coronary artery disease. And, as we have discussed, the emergence of catheter-based therapies for treating congenital and acquired structural heart disease has resulted in huge benefits to our patients. TAVR is now the default treatment for patients with symptomatic aortic stenosis. In 2016, there were more TAVRs performed than surgical aortic valve replacements in the USA, and these curves still continue to separate. While this trend will continue with sustained emphasis on percutaneous, non-surgical, less invasive techniques for treating our patients, this is not to say that surgery is less important. However, surgeons are increasingly asked to operate on more complex patients than they were previously, which will be a challenge for the cardiac surgery field.

Q8 Have you found that the public are generally receptive to new technologies in interventional cardiology, or do you occasionally experience resistance?

Most new technologies are usually evaluated in the context of a clinical trial. Clinical trials, particularly randomised clinical trials, require careful discussions with the patient and their family. Almost all patients will opt for the less invasive treatment strategy when offered. The early TAVR trials evaluating high, intermediate, and low risk patient subsets are randomised against surgery. It was very easy to enrol patients before the U.S. Food and Drug Administration (FDA) approval of the first TAVR valves. After FDA approval, enrolment in a randomised trial became difficult when there was a commercially available FDA-approved TAVR valve available. This is particularly true for the latest left atrial appendage closure devices, where there are now randomised trials comparing one device to another as well as against newer non-warfarin oral anti-coagulants. If a patient wants a left atrial appendage closure procedure to avoid oral anti-coagulants, why would they agree to participate in a clinical trial where they might be randomised to a treatment arm where they will just continue the medicine that they are already taking and don't want? Instead, they will go to where a proceduralist will just implant a device commercially to be taken off of the anti-coagulants.

"Refinements in PCI techniques and equipment will provide the coronary interventionalist with a toolkit that will allow them to address the coronary lesions for which treatment was not possible in the past, including chronic total occlusions."

Q8 Are there any innovations on the horizon that you think are noteworthy, and how do you think these will impact patient quality of life?

I believe that, in another 10 years, the routine cardiac valve replacement will be largely percutaneous, with surgery reserved for more complex patients. I think that bypass surgery for coronary artery disease will be relegated to patients who cannot technically be treated with PCI, including left main disease and disease of the proximal left anterior descending coronary artery. Refinements in PCI techniques and equipment will provide the coronary interventionalist with a toolkit that will allow them to address the coronary lesions for which treatment was not possible in the past, including chronic total occlusions. The structural heart disease space will continue to expand for the next 10 years. There are several viable percutaneous mitral and tricuspid valve technologies that I think will prove effective and are poised to begin important clinical trials. We will continue to ride the wave of innovation begun by Werner Forssmann, Alain Cribier, Philipp Bonhoeffer, and Andreas Gruentzig. ■

Lloyd W. Klein

Clinical Professor of Medicine, University of California, San Francisco, USA

Q1 With 40 years of experience as an interventional cardiologist, what initially led you to pursue a career in this field?

I was very fortunate to be drawn to interventional cardiology during its early stages. The potential to be a pioneer in a highly promising field attracted me and sustains my interest. And the prospects for innovation haven't stopped: the rapidly evolving advances in device technologies for the treatment of valvular and structural cardiac abnormalities and expanding indications for the use of these technologies as alternatives to cardiac surgery continue to motivate me.

My personal goal has been to provide outstanding clinical care to my patients while also making significant investigational contributions. It has been most rewarding to positively impact patients' lives while making a tangible difference in how intervention is practiced. Additionally, intervention is not just a procedural speciality; one builds gratifying long-term clinical relationships with patients.

Q2 You have been an advocate for spreading awareness about occupational health hazards related to chronic, low-level exposure to fluoroscopy in catheterisation labs. What originated this interest?

Several of my friends, colleagues, and staff lost time from work, curtailed their careers, and even developed life-ending illness due to a work environment that did not consider occupational safety be a priority. Frequent turnover led the most experienced, technically savvy individuals to pursue other opportunities, leaving gaps in knowledge among those remaining.

There is ample clinical data documenting the prevalence of serious occupational health risks engendered by the fluoroscopic laboratory environment. Despite the attention to these occupational health issues in clinical studies, advances to improve worker safety remain inadequate. My response to seeing the important stakeholders ignore this issue stimulated me to take the lead. The solution is to bring together catheterisation lab staff and physicians, hospital

and practice administration, professional societies, and private industry to acknowledge that this is a serious problem and then to work together to find cost-effective solutions.

Q3 What is in your opinion on the future of catheterisation labs and interventional procedures, particularly relating to health and safety?

The interventional laboratory of the future will combine the results of diverse imaging modalities, so that information obtained by one method is incorporated into the information acquired by other technologies. This will limit operator and patient exposure to radiation and improve the selection of treatment strategies. In the coronaries, the composition of the plaque, the presence of vulnerable plaque, its 3D geometric character, its physiologic consequence, and the simulated effect of the planned therapy will be unified. CT scanning will take the place of diagnostic coronary angiography, decreasing the number of normal results. In valvular cases, computational modelling and other artificial intelligence techniques are promising in regard to guiding case selection and implantation strategy.

"The interventional laboratory of the future will combine the results of diverse imaging modalities, so that information obtained by one method is incorporated into the information acquired by other technologies.

As simulation technology advances, increased utilisation of virtual interfaces, i.e., 'robotic' techniques, can be anticipated. Increasingly, the operator will be separated from the procedural bedside in order to protect the operator from the radiation environment.

Q1 One of your research focuses is acute coronary syndromes. How have you seen the treatment of these pathologies change in terms of advancements to the technology used?

I became involved in acute ST-elevation myocardial infarction interventions from its inception in the USA in 1980. It always seemed that opening the vessel in acute coronary syndromes ought to be the best solution, and it has been greatly rewarding to participate in its progress through the paradigm of scientific study, improved application, and established standard of care. The use of point-of-care clotting testing and adjunctive pharmacologic approaches to prevent thrombotic complications while minimising the risk of bleeding has been one of our areas of interest and will continue to evolve as better drugs are developed. The promise of systemic anti-inflammatory treatments remains but practical development seems to have stalled; yet I have no doubt a solution will eventually be devised.

Q5 As both a clinician and an educator, how do you believe new interventional cardiologists should be trained?

The volume of coronary arterial interventions will continue to exceed other interventional areas. Acute or critical care cardiology should increasingly be under the purview of interventional-trained personnel who thoroughly understand the risks and benefits of ventricular assist devices and other life-saving techniques.

Maintaining proficiency in a broad variety of procedures will become impossible. The development of super-subspecialties will require interventional cardiology societies and training programmes to seriously consider how best to alter their training practices to produce the right number of young operators with the right specialisations. These manpower implications have never been adequately addressed, leading to the problem of very low volume operators with a lack of experience. The team must be comfortable interacting with the sickest patients and their families, particularly those likely to not survive; and the team must also be familiar with advanced imaging and haemodynamic support technologies, a combination of skills that necessitates years of experience.

Q6 Since you were appointed as a clinical professor at University of California, San Francisco, USA, what has been your proudest achievement?

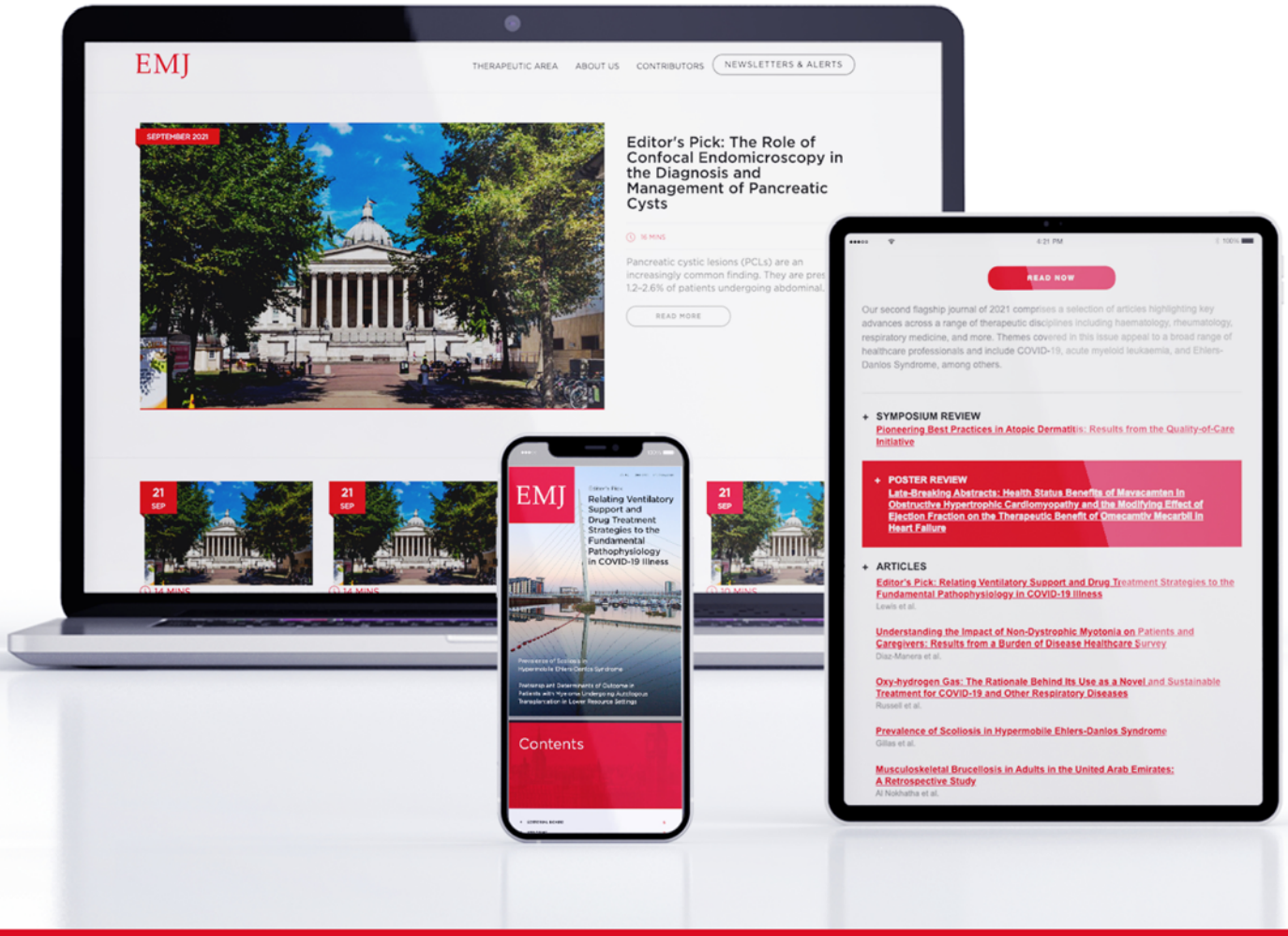
Placing emphasis on how interventional cardiologists can improve treatment decisions has been our recent focus. In particular, how best to incorporate the evidence-base and modify guideline and Appropriate Use Criteria to integrate shared-decision making into clinical practice. Engaging in a dialogue between the clinician and patient to jointly make decisions is most likely to ensure the best decision is made for that patient.

We have led efforts to define quality practice as more than just high volume or guideline adherence. Making the right decision requires understanding what patients really care about. They routinely tell us that quality of life is more important to them than its length, which is rarely the focus of clinical trials. With the reality of physician report cards, third-party assessments of hospital and physician quality, ties between outcomes and reimbursement, and the public reporting of outcomes, can we better define what is quality practice?

Q7 What are some points of emphasis you believe clinicians should incorporate into practice to be the best interventional cardiologists they can be?

The most significant challenge for an interventional cardiologist in contemporary practice is to do what is best for the patient. Diminishing reimbursement despite rising costs has resulted in greater dependence on interventional volume to maintain the revenue stream of cardiology practices. In this context, the results of the ISCHEMIA trial challenge our conceptions of what comprises excellence in practice. Revascularisation in stable ischaemic heart disease of patients with moderate-to-severe ischaemia had no benefit beyond medical therapy in preventing major cardiovascular events at 4 years. How the consequences of this finding are resolved, with its myriad resource allocation, cost, and value considerations, will be a defining moment for the field.

Increasing utilisation of intravascular imaging to guide performance and appraise results is another neglected area. Although success has been traditionally defined by an angiogram showing improvement, this standard should be modified to include imaging that provides information about stent apposition, expansion, and the absence of dissection. ■



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A Single-Centre Retrospective Study on the Impact of Reducing Surgical Prophylaxis from 48 Hours to 24 Hours in Cardiothoracic Surgery

EDITOR'S PICK

The duration of surgical antibiotic prophylaxis (SAP) and choice of antibiotics in cardiothoracic surgeries are key for the prevention of sternal wound infections. Hence, the Editor's Pick for this year's issue of *EMJ Interventional Cardiology* is the research article by Chung et al., which reviewed the impact of the updated SAP guidelines pre- and post-implementation. The authors evaluated the effects of reducing SAP from 48 hours to 24 hours in a retrospective single-centre study, comparing how choice of antibiotics, duration of prophylaxis, and timing of antibiotic administration affects the incidence of surgical site infections.

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Abstract

Introduction: In November 2016, surgical antibiotic prophylaxis (SAP) guidelines for cardiothoracic surgeries at the authors' centre were updated. SAP was reduced from 48 to 24 hours, and dual cover with vancomycin and cefazolin instead of vancomycin monotherapy was recommended for patients colonised with methicillin-resistant *Staphylococcus aureus*. This study was conducted to review compliance to the updated guidelines, and compare the incidence of surgical site infections (SSI).

Methods: A list of patients undergoing sternotomy in National Heart Centre, Singapore, from March 2016 to February 2019 was extracted from the hospital's electronic database; every fourth patient was included in the analysis. The patients were divided into three groups: Group 1 (before guideline revision, March–October 2016), Group 2 (post-guideline implementation, July 2017–May 2018), and Group 3 (July 2018–February 2019). Compliance to guidelines, incidence, and epidemiology of SSIs within 90 days of surgery were evaluated.

Results: 509 patients (Group 1: 149; Group 2: 184; Group 3: 176) were included. There was appropriate selection and timely administration of SAP across all three groups. Post-guideline implementation, the proportion of patients on SAP for >24 hours decreased from 149 (100%) in Group 1 to 55 (29.9%), and 67 (38.1%) in Group 2 and 3, respectively (p <0.001). Despite the reduction in SAP duration, SSI rates remained stable: 4.7%, 3.3%, and 5.1% in Group 1, 2, and 3, respectively (p=0.662).

Conclusion: Guideline implementation significantly reduced SAP duration in the authors' cardiothoracic surgeries, with no increase in SSIs. Continual feedback to ensure sustained compliance may be necessary.

INTRODUCTION

Sternal wound infections post-cardiothoracic surgeries are associated with increased morbidity and mortality.[1,2] More than half are due to *Staphylococcus aureus* or coagulase-negative *Staphylococcus epidermidis*. Yet, there is limited evidence for optimal choice (monotherapy versus combination therapy) and duration of surgical antibiotic prophylaxis (SAP) in cardiothoracic surgeries for the prevention of sternal wound infections.

Most guidelines support the use of a first-generation cephalosporin (e.g., cefazolin) for perioperative prophylaxis of sternotomy, and in patients with β-lactam allergy, vancomycin.[1-3] In institutions with high incidence of methicillin-resistant *S. aureus* (MRSA), vancomycin monotherapy is often used as first-line prophylaxis. However, β-lactams may have superior activity against methicillin-susceptible *S. aureus* (MSSA) compared to vancomycin.[4] For example, Finkelstein et al.[5] showed that MSSA surgical site infections were more common in patients receiving vancomycin monotherapy for cardiothoracic surgery. Therefore, combination antibiotic therapy with vancomycin and cefazolin have been used for perioperative prophylaxis in patients who are at risk of MRSA infections (e.g., patients colonised with MRSA undergoing sternotomies), with vancomycin limited to one or two doses[2,6-8] to mitigate the risk of acute kidney injury associated with the concurrent use of β-lactams and vancomycin.[6,9]

Another area of controversy pertains to the duration of cardiothoracic surgical prophylaxis. Surgical prophylaxis durations are often extended in clinical practice, despite recommendations from the Society of Thoracic Surgeons, American College of Cardiology/American Heart Association, as well as the American Society of Health-System pharmacists to limit the duration from 24 to 48 hours.[3] Administering antibiotic prophylaxis beyond 48 hours may have no additional benefit, but it may result in the development of infections with drug-resistant organisms.[10,11] In contrast, the comparative data to show whether perioperative prophylaxis for 24 hours is as effective and safe as 48 hours is scarce.[1-3,10] The recommended duration of prophylaxis for 24–48 hours is based on expert opinion.

In November 2016, the Antimicrobial Stewardship Unit in Singapore General Hospital (SGH), Singapore, collaborated with the Department of Cardiothoracic Surgery in National Heart Centre Singapore (NHCS), Singapore, in updating the antibiotic prophylaxis guidelines for cardiothoracic surgeries (Table 1). The most significant change in the guideline was the reduction in the duration of surgical antibiotic prophylaxis from 48 to 24 hours. In addition, for patients who were colonised with MRSA, there was an added recommendation for both vancomycin and cefazolin to be administered,[6-8] as there was an increasing trend of MSSA sternal wound infections in patients on vancomycin-only prophylaxis from routine surveillance (based on the authors' local unpublished data).

Table 1: Cardiothoracic surgery antibiotic prophylaxis guidelines in Singapore General Hospital and National Heart Centre Singapore.

	First-line antibiotic prophylaxis	Alternative prophylaxis for patients with severe β-lactam allergy	Prophylaxis for patients colonised with MRSA colonised	Duration of prophylaxis
Previous Guidelines	IV cefazolin 2 g as single dose, followed by 1 g q8h post-surgery	IV vancomycin 15 mg/kg followed by 15 mg/kg q12h post-surgery	No recommendation	48 hours
Updated guidelines in November 2016	IV cefazolin 2 g as single dose, followed by 1 g q8h post-surgery	IV vancomycin 20 mg/kg, followed by 15 mg/kg q12h post-surgery	IV xefazolin 2 g +IV vancomycin 20 mg/kg single dose, followed by both antibiotics post-surgery	24 hours

*MRSA decolonisation was performed for all patients who are MRSA-positive prior to surgery pre and post-guideline implementation.

Note: No local antibiotic prophylaxis was administered, as this is not a routine practice in this institution.

IV: intravenous; MRSA: methicillin-resistant *Staphylococcus aureus*; q8h: every 8 hours; q12h: ever 12 hours.

The authors reviewed the impact of the updated SAP guidelines pre- and post-implementation, as described below.

METHODS

Study Design

This was a retrospective single-centre study, conducted as a quality improvement project to primarily evaluate the surgeons' compliance to SAP for cardiothoracic surgeries involving sternotomies, and compare the incidence and epidemiology of surgical site infections (SSI) after shortening perioperative prophylaxis from 48 to 24 hours as part of the secondary objective. A waiver of informed consent was obtained from SingHealth Centralised Institutional Review Board (CIRB).

Pre-guideline Implementation

The SGH antimicrobial stewardship unit reviewed international recommendations on SAP in cardiothoracic surgery, as well as the authors' hospital data on the incidence and epidemiology of post-surgical sternal wound infections. These findings, and the authors' proposed SAP guideline updates (Table 1) were shared with the cardiothoracic surgeons, who then accepted the changes. To improve compliance to the updated guidelines, education roadshows with the cardiothoracic surgery department were conducted and the anaesthesiology department was also informed of the changes. Order sets in the electronic prescribing system were also created concurrently for ease of physician prescription. The guidelines were finally implemented in November 2016.

Post-guideline Evaluation and Data Collection

A list of all patients (above 18 years old) undergoing cardiothoracic surgery with sternotomy in SGH/NHCS from March 2016 to February 2019 was extracted from the hospital's electronic database. As this study was done to quickly assess the outcome of the interventions and to provide timely feedback to surgeons, the authors opted to systematically sample every fourth patient in the list, and include only these patients in the analysis. The patients were then divided into three groups: Group 1 (patients admitted between March–October 2016, prior to guideline updates), Group 2 (patients

admitted between July 2017–May 2018, after the implementation of the revised guidelines), and Group 3 (patients admitted between June 2018–February 2019, to assess persistence of guideline compliance). Even though the updated guidelines were implemented in November 2016, compliance to guidelines was only evaluated from July 2017, to factor time for guideline adoption.

Patient demographics, MRSA colonisation status, drug allergy, antibiotic administration records pre- and post-surgery, and clinical documentation of SSIs, as well as microbiological data from surgical site specimens collected within 90 days of surgery were retrospectively extracted from electronic health records, and recorded in a standardised data collection form.

Primary Objective

Compliance to guidelines in regard to choice of antibiotics, duration of prophylaxis, and timing of antibiotic administration were assessed for all three groups. Choice of antibiotic prophylaxis and duration of prophylaxis was deemed appropriate if they were in line with guideline recommendations as outlined in Table 1. Timing of antibiotic administration before surgery was deemed appropriate if cefazolin was given within 30 minutes before incision, and vancomycin at least 1 hour before incision.[3]

Secondary Objective

SSI was defined as infection of the skin, subcutaneous tissue, and deep soft tissues (e.g., fascia or muscle) of the incision. It includes one of the following: purulent drainage; organisms isolated from superficial incision cultures; at least one sign of inflammation, for example pain, tenderness, induration, erythema, local warmth of wound; or if a surgeon declared the wound infected.[12]

The incidence of SSIs within 90 days of surgery and the causative pathogens (isolated from sternal wound/tissue cultures) were compared between groups to evaluate the efficacy of perioperative prophylaxis (comparing 48 hours with 24 hours). All-cause mortality within 30 days post-surgery and post-surgical length of hospital stay were also compared as additional safety indicators.

Statistical Analysis

All statistical analyses performed were two-tailed tests at 5% significance level, using IBM® SPSS® Statistics for Windows Version 25.0 (Armonk, New York, USA). Chi-square or Fisher's exact tests were used for categorical data. For continuous data, one-way Analysis of Variance was used for normally distributed data, while the Kruskal–Wallis test was used for non-normally distributed data. For post-hoc comparisons, significance level was adjusted via Bonferroni correction. All post-hoc comparisons involved three pairs of comparisons. Hence, significance level was adjusted to 0.0167.

RESULTS

A total of 2,036 patients undergoing cardiothoracic surgery with sternotomy were extracted from the patient database. These procedures were mainly coronary artery bypass surgeries with or without valve surgery. After selecting for every fourth patient, 509 patients were included in the study (Group 1: 149 patients; Group 2: 184 patients; Group 3: 176 patients). Patient demographics were similar across all three groups, and are as presented in Table 2. Most patients were males (87.2%), with a mean age of 62.8±8.6 years.

In general, the surgeons consistently selected the right antibiotics for surgical prophylaxis (>90% across all three groups [Table 2]). A small group of patients received inappropriate choice of antibiotic prophylaxis (e.g., vancomycin in the absence of β-lactam allergy [n=14]), single antibiotic therapy instead of dual vancomycin and cefazolin in MRSA colonised patients post-guideline implementation (n=5), dual antibiotics for prophylaxis in non-MRSA colonised patients out of guideline recommendations (n=10), or receipt of antibiotic prophylaxis other than cefazolin and/or vancomycin (n=2). None of the MRSA-colonised patients in Group 1 received dual antibiotic prophylaxis with vancomycin and cefazolin. Following implementation of revised SAP guidelines, one out of three (33.3%) and two out of seven (28.6%) received dual cover for prophylaxis in Groups 2 and 3, respectively.

Antibiotic prophylaxis was administered in a timely fashion for >85% of the patients in all three groups (Table 2). After reaching out to

Table 2: Patient demographics, compliance to antibiotic prophylaxis guidelines, and incidence of surgical site infections.

	Group 1 (March 2016–October 2016), N=149	Group 2 (July 2017–May 2018), N=184	Group 3 (June 2018–February 2019), N=176	p
Patient demographics				
Age (years)	62.8±8.9	62.1±8.4	63.7±8.5	0.205
Male	130 (87.2%)	159 (86.4%)	155 (88.1%)	0.895
Race				0.067
Chinese	103 (69.1%)	117 (63.6%)	132 (75.0%)	N/A
Malay	20 (13.4%)	32 (17.4%)	25 (14.2%)	N/A
Indian	23 (15.4%)	27 (14.7%)	11 (6.3%)	N/A
Others	3 (2.0%)	8 (4.3%)	8 (4.5%)	N/A
MRSA colonised	1 (0.7%)	3 (1.6%)	7 (4.0%)	0.103
β-lactam allergy	8 (5.4%)	6 (3.3%)	12 (6.8%)	0.305
Surgical antibiotic prophylaxis				
Choice of antibiotic Appropriate selection of antibiotic prophylaxis	141 (94.6%)	178 (96.7%)	168 (95.5%)	0.632
Antibiotic prophylaxis received				
Cefazolin monotherapy	133 (89.3%)	174 (94.6%)	156 (88.6%)	0.101
Vancomycin monotherapy	11 (7.4%)	8 (4.3%)	13 (7.4%)	0.399
Cefazolin+vancomycin	5 (3.4%)	2 (1.1%)	7 (4.0%)	0.212
Antibiotic administration				
Timely administration of antibiotic prophylaxis*	135 (90.6%)	178 (96.7%)	154 (87.5%)	0.005
Outcomes				
Patients with surgical site infection within 90 days of surgery	7 (4.7%)	6 (3.3%)	9 (5.1%)	0.662
30-day all-cause mortality post-surgery	3 (2.0%)	2 (1.1%)	1 (0.6%)	0.480
Length of hospital stay (days)	7 (6–9)	7 (5–9)	7 (5–9)	0.300

*Cefazolin to be given within 30 minutes of incision; vancomycin to be given at least 1 hour before incision.

Duration of 48 hours was considered compliant based on the previous antibiotic prophylaxis guideline.

The data is presented as mean±standard deviation, or median (interquartile range), or number (percentage), where appropriate.

MRSA: methicillin-resistant *Staphylococcus aureus.*

the cardiothoracic and anaesthesiology teams to communicate the changes in SAP, and to reinforce good practice, the authors observed a trend showing improvement in the proportion of patients who had timely administration of SAP, from 90.6% (Group 1) to 96.7% (Group 2) (p=0.019, not statistically significant after Bonferroni correction). However, this effect had worn off a year later. The proportion of patients who received SAP on time decreased significantly from 96.7% in Group 2 to 87.5% in Group 3 (p<0.001).

After the revised SAP guidelines were implemented, the proportion of patients on prolonged antibiotic prophylaxis (>24 hours) decreased significantly from 149/149 (100.0%) in Group 1 to 55/184 (29.9%) patients in Group 2 (p<0.001). With time, there was a trend towards reverting to old habits of prolonging SAP; the proportion of patients with SAP >24 hours increased from 55/184 (29.9%) in Group 2 to 67/176 (38.0%) in Group 3 (p=0.08) (Figure 1A).

Despite the reduction in duration of antibiotic prophylaxis from 48 hours to 24 hours since November 2016, the incidence of SSIs remained stable across the three groups (4.7% versus 3.3% versus 5.1%; p=0.662). Similarly, in a separate subgroup analysis of all patients post-guideline implementation (i.e., Groups 2 and 3 combined), there was no difference in the SSI rates among those receiving SAP ≤24 hours versus >24 hours. SSI incidence were 9 (3.8%) versus 6 (4.9%), respectively (p=0.627). After guideline implementation, the authors also did not observe any adverse impact on post-surgical mortality and length of stay (Table 2).

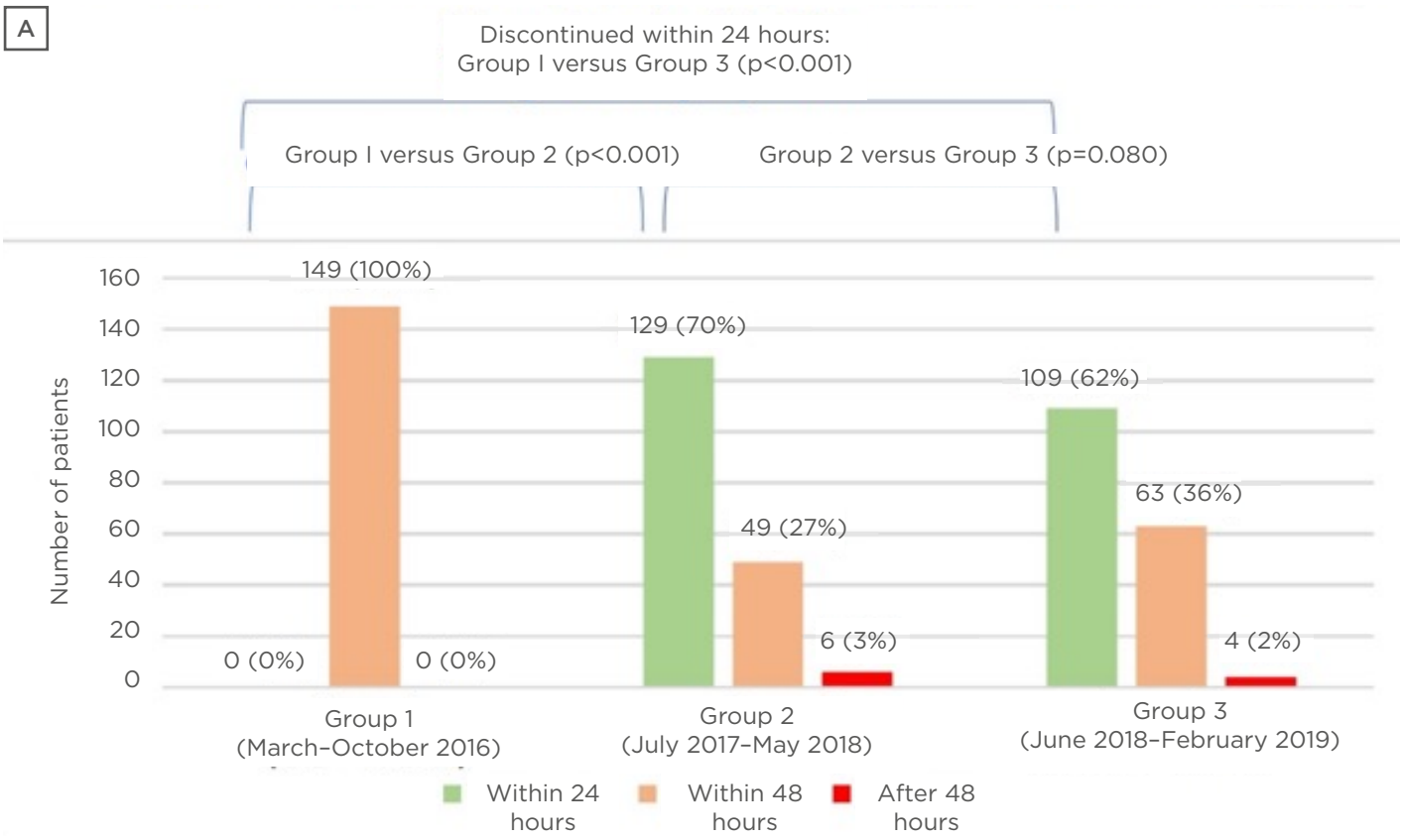
Almost all patients with SSIs received appropriate antibiotics based on guideline recommendations, except for one patient who received dual antibiotic prophylaxis for an individual who is not colonised with MRSA. Of those who developed SSIs, three out of 22 patients (13.6%) did not receive SAP within the correct period; two out of these three cases occurred in patients from Group 1, before the revision and implementation of the SAP in November 2016. These two patients developed coagulase-negative *Staphylococcus* and MRSA SSIs; vancomycin was not served on time for both cases.

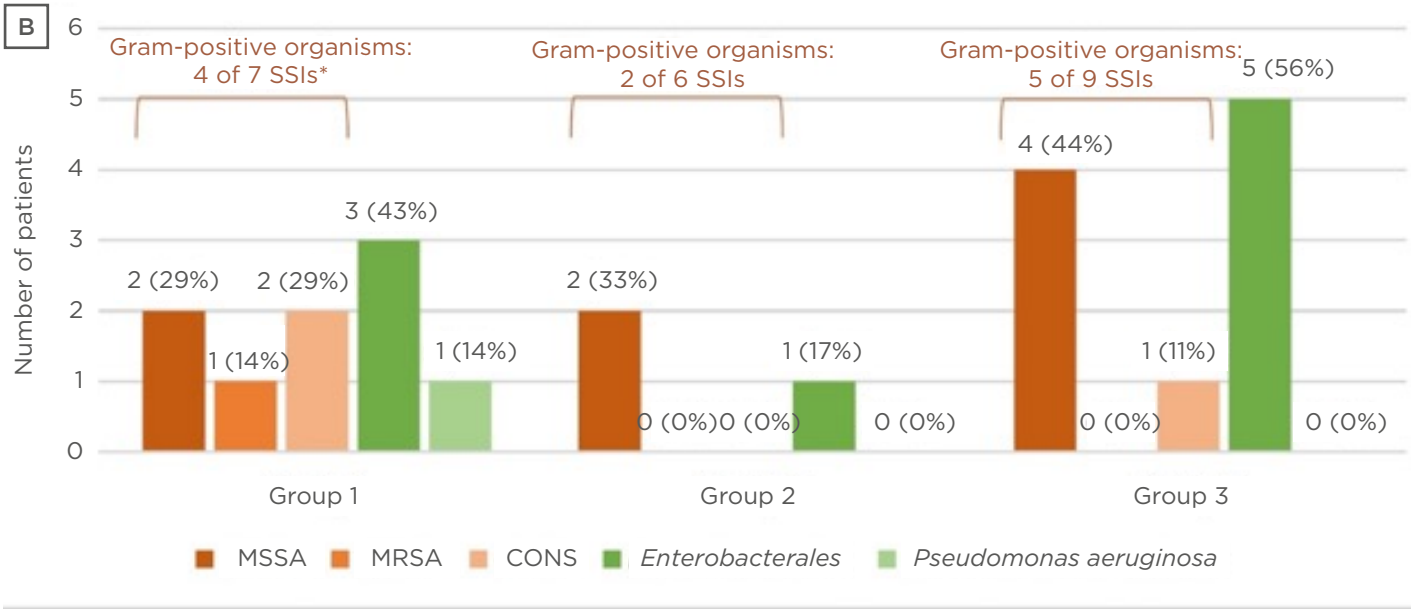
For patients with culture proven SSIs, a significant proportion are caused by Gram-positive organisms such as *S. aureus* and coagulase-negative *Staphylococci* as illustrated by Figure 1B. MSSA remains a common causative pathogen for sternal wound infections. Interestingly, MRSA was only isolated before the implementation of the revised SAP guidelines (Group 1), but not in Groups 2 and 3. The authors also did not observe a major shift in susceptibility of pathogens after the implementation of revised SAP guidelines.

DISCUSSION

Whilst it is established that SAP is important for the prevention of SSIs,[3] antibiotic misuse for the purpose of perioperative prophylaxis is not uncommon. Although local and international guidelines are available, compliance to SAP guidelines is often variable and suboptimal.[13] In clinical practice, SAP is also frequently extended beyond 24 hours, especially in cardiothoracic surgeries.[14,15] In this small retrospective before–after single centre study, the authors' team evaluated the impact of reducing SAP from 48 hours to 24 hours in cardiothoracic surgery. Two things stood out. Firstly, and unexpectedly, they observed a relatively high compliance to a revised SAP guidelines co-developed together with the cardiothoracic surgeons, especially when it was first implemented. Secondly, reduction of SAP from 48 hours to 24 hours did not result in an increase in SSIs.

To ensure that the revised SAP guidelines will be adopted, the antimicrobial stewardship team implemented a multi-prong approach to increase awareness of the updated guidelines, and to optimise the prescription of antibiotic prophylaxis for cardiothoracic surgeries. This involved the direct engagement of cardiothoracic surgeons during review of the SAP, and education roadshows to the departments of cardiothoracic surgery and anaesthesiology to communicate the rationale for changes in guidelines, and inform the team of the changes implemented, including the creation of antibiotic prophylaxis order sets in the electronic prescribing system. In addition, the authors had the head of the cardiothoracic unit working alongside their team, championing this initiative. With this bundled approach, they observed high compliance rates to the updated guidelines in terms of antibiotic choice and





Note: Some patients had more than one micro-organism isolated.

Figure 1: Trends in the duration of surgical prophylaxis duration and surgical site infections before and after guideline implementation.

A) shows the distribution of patients who received 24 hours, 48 hours and >48 hours of surgical prophylaxis across the three groups. After guideline implementation, most patients received surgical prophylaxis for 24 hours instead of 48 hours. B) shows the pathogens from the SSI across the three groups.

*One patient had both CONS and MRSA isolated from their surgical wound site.

CONS: coagulase-negative *Staphylococcus*; MSSA: methicillin-susceptible *Staphylococcus aureus*; MRSA: methicillin-resistant *Staphylococcus aureus*; SSI: surgical site infection.

duration, immediately after the implementation of our new guidelines. This illustrates the point that evidence alone is unlikely to change practice.[16,17] For practice change, it is also necessary to adopt a more collaborative and inclusive approach, engaging stakeholders in the decision making process;[16,18,19] address the surgeon's prescribing bias;[16,20] and incorporate electronic tools such as clinical decision support systems to improve prescribing.[21] For the cardiothoracic team, apart from evidence-based practice and local guidelines, a surgeon champion was instrumental to ensure that the unit's concerns were addressed, and goals were aligned.[20]

Having said this, compliance rates to SAP decreased 18 months after guideline implementation. The initial high SAP compliance rate is probably due to a visible stewardship presence during the initial launch of the revised guidelines. After the revised SAP was implemented, audits were not conducted for antibiotic prophylaxis, and education on appropriate use of antibiotics for prophylaxis was not reinforced thereafter. This phenomenon is not unexpected, and when stewardship presence is withdrawn, antibiotic use or misuse of antibiotics may increase.[22,23] Although time-consuming, continued stewardship engagement and regular educational sessions with the surgical teams are crucial.[24] In addition, targeted reviews of prescriptions for SAP and feedback may be important for sustained improvements.[25]

The optimal duration of SAP in cardiothoracic surgeries is not so well established. In a randomised controlled trial, Gupta et al.[26] showed that 48 hours of SAP is as effective as 72 hours. In subsequent meta-analyses, Mertz et al.[10] and Lador et al.[27] reported that SAP for >24 hours reduced the risk of sternal SSIs; however, the studies included for those reviews were heterogeneous and confounded by biases. There is emerging evidence to support a shorter course of prophylaxis (e.g., <48 hours).[28,29] Similar to the findings by Surat et al.,[29] this study showed that SAP for 24 hours is safe and did not affect the incidence of SSIs. The authors' SSI rates (3.3–5.1%) were also comparable to these studies (Hamouda et al.[28] reported 5.4%, while Surat et al.[29] reported 3.6%). There are also other reports supporting shorter courses of SAP to reduce antimicrobial usage and *Clostridioides difficile* infection.[30]

By and large, SSIs post-sternotomies are caused by Gram-positive organisms, *S. aureus*, and coagulase negative *Staphylococcus* being more common. Based on in-house data, the authors also observed breakthrough infections with MSSA in patients on vancomycin monotherapy for SAP, likely due to poorer activity of vancomycin monotherapy (relative to β-lactam antibiotics) against MSSA.[5,9,31,32] This is also reported in the literature. In a USA-based quasi-experimental pragmatic prospective study evaluating SSIs in patients undergoing cardiac, hip, or knee surgery, the rate of complex *S. aureus* SSIs was in MRSA-colonised patients receiving vancomycin and cefazolin or cefuroxime for perioperative prophylaxis.[8] This prompted the guideline revision at the authors' centre to recommend dual cover, with both vancomycin and cefazolin for patients colonised with MRSA undergoing sternotomies. After this change in practice, they did not have breakthrough MSSA infections in patients colonised with MRSA. The authors acknowledge that this is a small study, and larger studies would be warranted to corroborate observations.

MSSA remained the predominant pathogen in this study, even after the revision of guidelines. In Groups 2 and 3, five out of six MSSA SSIs occurred after prophylaxis with cefazolin monotherapy, while one MSSA SSI occurred after prophylaxis with vancomycin monotherapy. This suggests that appropriate antibiotic prophylaxis is not the only solution in preventing SSI, as the aetiology of SSI can be multi-factorial.[33] Additional interventions beyond the scope of antibiotic prophylaxis, may need to be evaluated and considered to further reduce SSI rates.[33]

Appropriate timing of administration for perioperative prophylaxis also plays a role in reducing incidence of SSIs. In this study, three out of 22 patients with SSIs (13.6%) did not receive perioperative antibiotics within the correct timeframe. With incorrect timing, there may be ineffective plasma and tissue antibiotic concentrations, increasing risk of SSIs as proven by Zelenitsky et al.[34] While compliance to this aspect of the guidelines improved significantly immediately after guideline implementation, there was a significant decline in compliance in Group 3. This highlights the need for regular reminders and continued engagement with the surgical teams for continued compliance.

LIMITATIONS

While the authors had positive findings demonstrating high surgical compliance to SAP and stable SSI rates with 24 hours of SAP, they acknowledge that this is a small retrospective study with potential for recorder bias. Given the small sample size and low incidence of SSIs, they cannot comment on shifts in the epidemiology of SSIs during the study period. Also, the complexity of the cardiothoracic surgeries was not graded in this study, and this could be one of the confounders affecting SSI rates.

CONCLUSION

A bundled approach to SAP in cardiothoracic surgery (guideline update, provider engagement or education, and creation of electronic order sets) was effective at this centre in improving compliance to SAP. While there was a significant reduction of SAP from 48 hours to 24 hours, there was a creep in proportion of patients with extended SAP (>24 hours) with time, highlighting the importance of continued engagement with cardiothoracic surgeons by the stewardship team. The authors' data has shown that reduction of surgical prophylaxis to 24 hours is effective and safe, without any increase in incidence of SSIs.

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Stent Delivery Shaft Fracture Case Report: A Fractured Relationship

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Abstract

Percutaneous coronary intervention has been a major interventional medical development of our times, being a life-saving procedure in the setting of acute coronary syndrome, and providing significant improvements in quality of life for patients with chronic coronary syndromes.

Complications of coronary intervention have continued to downtrend, facilitated by improvements in stent and wire technology, the aggressive use of antiplatelets, and the regular use of invasive anatomical and physiological assessments.

The authors present the case of a challenging and rare procedural complication, that of stent delivery shaft fracture requiring emergency snare extraction.

INTRODUCTION

A 65-year-old female was transferred for an emergency coronary angiogram from a peripheral centre with a diagnosis of acute coronary syndrome (ACS).

The patient reported three episodes of severe central chest pain radiating to their left arm, associated with sweats and occurring at rest, with ongoing mild chest pain in the emergency department of the peripheral hospital. Their ECG showed sinus rhythm with a Wellens pattern in V1–V4.

The patient was given aspirin 300 mg and ticagrelor 180 mg, and transferred for invasive coronary angiography. The patient had reported exertional chest pain prior to this hospital presentation and was awaiting an outpatient coronary angiogram.

They had a background history of hypertension and high cholesterol, and a strong family history of premature atherosclerosis, with their sister requiring percutaneous coronary intervention (PCI) at 60 years of age and their father having a coronary artery bypass graft at 52 years of age. The patient was a non-smoker.

Their pre-hospital medications included atorvastatin 40 mg, pantoprazole 40 mg, lercanidipine 10 mg, bisoprolol 2.5 mg, and aspirin 75 mg.

The differentials that were considered at this point included: ACS; Takotsubo cardiomyopathy; myocarditis; pulmonary embolism; and aortic dissection.

INVESTIGATION AND MANAGEMENT

The patient underwent coronary angiography via a 6 Fr right radial approach. This revealed a normal left main stem, a 90% ostial lesion of the left anterior descending coronary artery (LAD), a co-dominant left circumflex artery with moderate atheroma of an obtuse marginal artery branch, and a proximal right coronary artery lesion of approximately 70% (Figure 1).

The authors proceeded to PCI of the LAD. The LAD was wired with a sion wire and a second sion wire was placed in a large diagonal branch.

The authors attempted to direct stent the proximal LAD lesion with a 3.5x24.0 mm Promus stent (Boston Scientific, Galway, Ireland). The stent travelled into position easily and was connected to the inflation system; however, when the authors went to deploy the stent, the balloon of the stent did not inflate. At this point, they attempted to withdraw the entire stent apparatus from the vessel, but the balloon and stent remained *in situ*. They discovered on further withdrawal and removal from the patient that there was a fracture in the delivery shaft, leaving behind residual shaft, balloon, and undeployed stent in the left main (LM) or LAD (Figure 2).

At this point the patient became unstable, likely due to occlusive flow in the LAD from the residual balloon and stent, developing ST elevation with VT and loss of cardiac output. They required emergency cardioversion, were given intracoronary adrenaline, and anaesthetics were called.

The authors attempted to snare the residual shaft in the aortic root from the right radial with an Nsnare™ Stent Retriever (Cook Medical, Bloomington, Indiana, USA); however, they could not capture it despite guide manipulation and wire retraction. Of note, the authors could not visualise the residual shaft, it being radiolucent. The patient developed severe right subclavian spasm following these manipulations, and the Nsnare could no longer advance nor retract.

The authors established right femoral arterial access with an 8 Fr sheath. They again attempted to snare the residual shaft with an Nsnare, followed by an Amplatz Goose Neck™ snare (Medtronic, Watford, Hertfordshire, UK), and an IR snare, using a JL3.5 guide, then switching to a Q3.5 guide to change possible snare angles in the aortic root (Figures 3 and 4).

Thereafter, the authors tried another approach, where they advanced a coronary wire past the undeployed stent in the LM artery, that travelled into a diagonal branch. They used serial balloon inflations (1.5x12.0 mm, 2.0x12.0 mm, and 2.5x12.0 mm) over this wire with aggressive traction to try and pull back the undeployed stent into the aortic root. The stent did move slowly backwards.

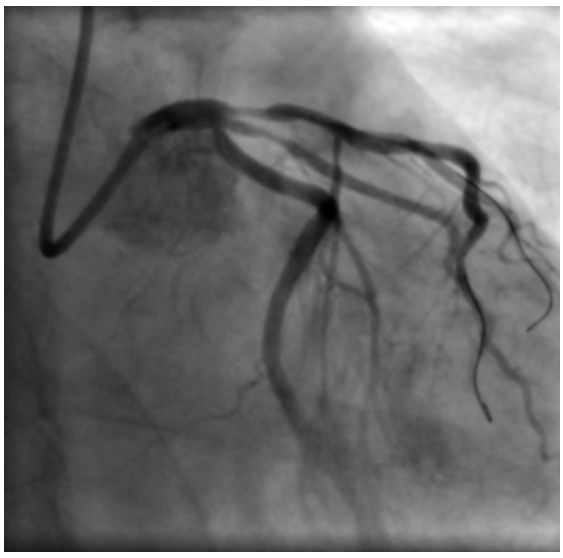

Figure 1: Original left anterior descending artery stenosis.

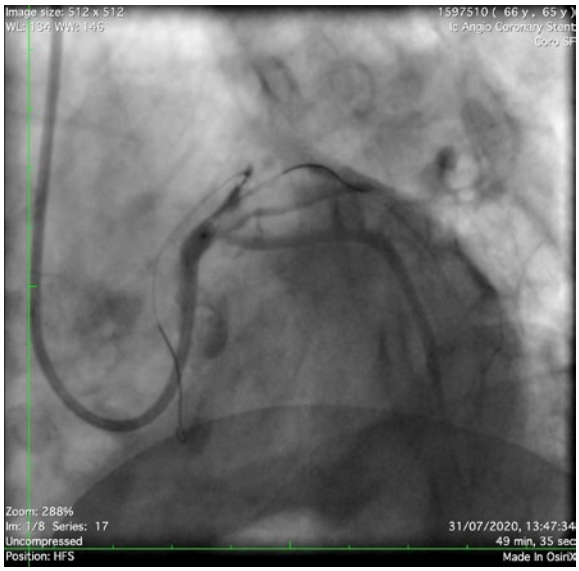

Figure 2: Failed left anterior descending artery stent deployment.

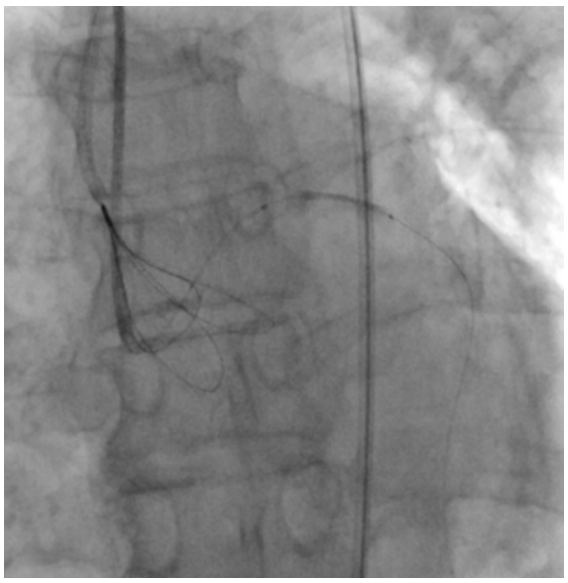

Figure 3: Attempted retrieval with an Nsnare™ Stent Retriever (Cook Medical, Bloomington, Indiana, USA).

The LAD was wired with the aid of a turnpike spiral microcatheter. The authors attempted to wire through the stent with a Pilot 200 (Abbott Vascular, Maidenhead, Berkshire, UK), and Confianza® Pro 12 (Asahi Intecc USA, Inc., Santa Ana, California, USA), but the turnpike spiral would not pass through.

The authors removed the wire and turnpike spiral and repositioned the guide. The guide manipulation moved the stent into the aortic root; the stent was then captured by an Nsnare in the aortic root and pulled into the Q3.5 guide.

Left femoral arterial access was obtained with an 8 Fr guide, with iliac crossover to maintain site control in case of access complication.

A Terumo stiff wire (Terumo Interventional Systems, Somerset, New Jersey, USA) was placed in the right femoral, and the guide was retracted gently into the 8 Fr femoral sheath and removed. A femoral angiogram from the left showed no site complications.

The patient was transiently hypotensive and required atropine and metaraminol, likely

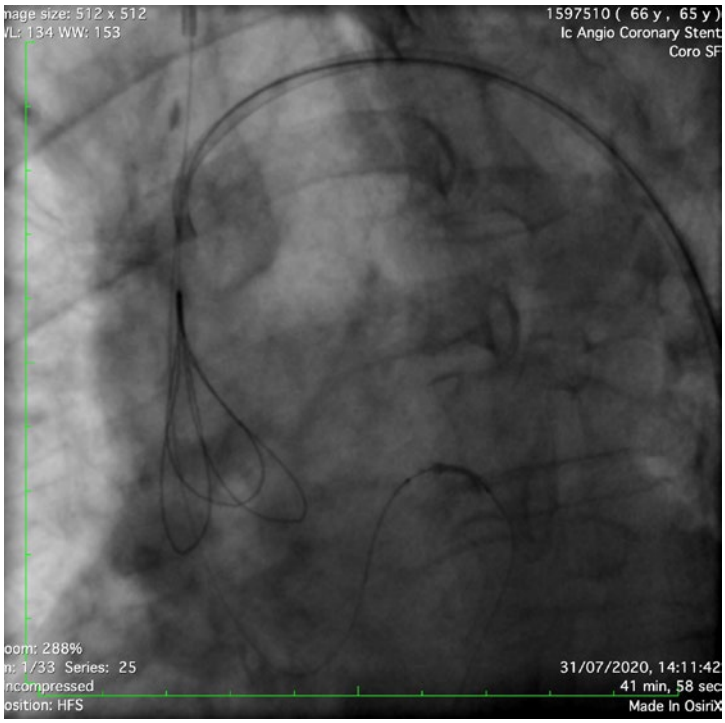

Figure 4: Further attempts at retrieval with an Nsnare™ Stent Retriever (Cook Medical, Bloomington, Indiana, USA).

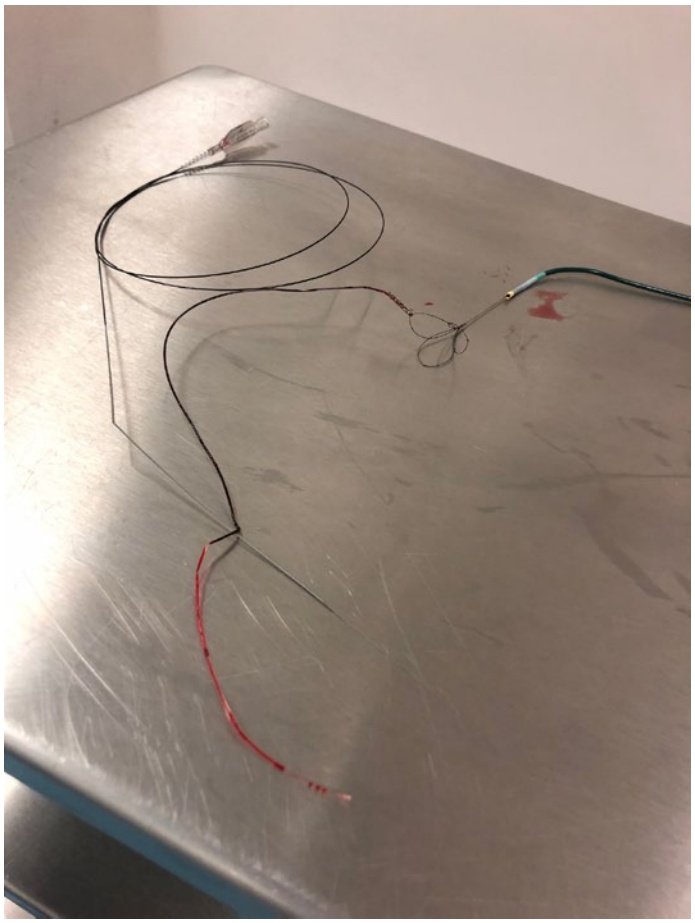

Figure 5: Fractured stent and shaft post-removal.

from a vagal response to pain at the site on sheath removal (Figure 5).

At this point, the authors returned to the LAD lesion. They passed a sion wire into the LAD. They placed a 3.0x28.0 mm XIENCE drug-eluting stent (Abbott Vascular) to the mid-LAD at 12 ats, and a 3.5 x 28 mm XIENCE drug-eluting stent to the proximal LAD or LM arteries at 16 ats. They assessed with intravascular ultrasound (IVUS) to guidepost dilatation, and post-dilated with a 3.5 mm OPN NC balloon (SIS [Swiss Interventional Systems] Medical, Frauenfeld, Switzerland) in the proximal LAD to 20 ats, and a 5.5x8.0 mm NC balloon in the LM to 20 ats.

There was a non-flow limiting dissection noted in the diagonal branch outflow with thrombolysis in myocardial infarction (TIMI) 3 flow throughout; therefore, the authors did not treat this.

They then removed the original Nsnare from the right radial without issue, as the spasm had resolved. The femoral arterial access sites were closed bilaterally with 8 Fr ANGIO-SEAL® (Terumo Interventional Systems) devices. A TR Band® (Terumo Interventional Systems) was applied to the right radial. A bedside transthoracic echocardiogram showed no pericardial effusion.

The entire procedure took over 6 hours.

Shortly after the end of the procedure, the patient reported a left arm weakness and mild speech slurring. They were emergently reviewed by the on-call stroke team who noted an National Institutes of Health Stroke Scale (NIHSS) score of 3. A CT-brain and CT-cerebral angiogram were arranged, which showed no acute abnormality. An MRI-brain scan did show widespread scattered embolic type infarcts, from which the patient made a complete functional recovery. Their peak troponin following this event was 954, and a transthoracic echocardiogram showed a preserved left ventricular ejection fraction of 55–60%, without regional wall motion abnormalities noted. The patient had a short course of antibiotics for aspiration concerns during the cardiac arrest and had inpatient IVUS-guided PCI to the right coronary artery 11 days after the initial procedure. The LAD or diagonal stents were also reassessed with further IVUS guided post-dilatation. The patient was discharged home well the following day.

DISCUSSION

PCI in the field of cardiology has significantly advanced in recent years, and has been proven to have superior outcomes to medical management or thrombolysis in the setting of ACS.[1,2] Despite equipment and technical improvements, complications, through downtrending, remain an ongoing clinical challenge as cardiologists encounter increasing patient comorbidities and lesion complexity.[3,4] Stent shaft fracture and retention of coronary interventional products are rare, but serious complications of percutaneous angioplasty can result in emergency surgical procedures, or death.[5] It is essential for interventional cardiologists to have a thorough understanding of all equipment being used in the catheterisation laboratory, an awareness of the potential for equipment complication to occur, and knowledge of how to deal with such complications. It is also imperative to continuously assess equipment in use in the catheterisation laboratory during a procedure, to ensure there has been no damage sustained that could impair function, or increase the risk of complications.

The incidence of stent loss has significantly reduced, with the development of second- and third-generation stents recently quoted at 1.3%.[6] Stent delivery shaft fracture is very rare, with only case reports noted. Issues contributing to such a complication can include physicians, such as excessive manipulation or pushing; patients, such as difficult delivery, tortuosity, and calcification; and equipment being possibly faulty from manufacture.

Retrieval techniques described in case reports include use the of snare and forceps devices, alongside the use of wire techniques such as the double helix for entrapment, the small balloon technique where a balloon is inflated distal to the stent and withdrawn, and the use of balloon inflation in the guide to compress and withdraw the retained components.[7-9] Interventional cardiologists should have basic knowledge of these techniques in the event of such a complication, as different situations are likely to require different techniques.

FOLLOW-UP

The patient has been contacted via telephone and is doing well in the outpatient setting, without residual neurological or cardiac symptoms.

CONCLUSIONS

This case highlights the challenges of managing this rare complication, and reminds us of the need for interventional cardiologists to remain upskilled in the management of unusual complications, as this can prevent the need for patients to proceed to emergency surgery.

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Same-Day Discharge After Transcatheter Aortic Valve Replacement

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Abstract

Transcatheter aortic valve replacement (TAVR) has been established as an alternative to surgical aortic valve replacement in select patients with severe aortic stenosis. Next-day discharge (NDD) after TAVR allow patients rapid mobilisation to return home. A minimalist pathway using NDD has been shown to be effective and safe in carefully selected patients. Following the COVID-19 pandemic and earlier reports of same-day discharge (SDD) after TAVR, in 2020 several institutions modified NDD protocols to carefully select patients for discharge the same day. These protocols maximised efficiency and resource utilisation while minimising COVID-19 exposures, hospital length of stay, and healthcare-associated costs, both to the institution and to the patient. In this literature review, the authors discuss the precedent for SDD after TAVR, investigate the pressure for efficiency amidst a global pandemic, and assess the safety and feasibility of SDD as seen across multiple healthcare systems.

NEXT-DAY DISCHARGE: THE CURRENT APPROACH

Transfemoral transcatheter aortic valve replacement (TAVR) is an alternative to surgical aortic valve replacement for most patients presenting with severe symptomatic aortic stenosis.[1-6] Hospital stays historically ranged from 3–11 days with median length of stay (LOS) 4 days (2012–2015).[7] In the 2020 Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) transcatheter valve therapy (TVT) Registry summary of 276,316 patients undergoing TAVR from 2011–2019, hospital stay had decreased to 2 days, with over 90% of patients discharged home.[8] Crucially, hospital LOS has gained significant weight in the management of TAVR, as more bundled fixed payment systems have been implemented across healthcare systems. Several

studies highlight the importance of streamlining the efficiency of TAVR with regards to expected cost burden reductions to the patient, as well as reduced overall in-hospital cost.[3,4] Current research suggests next-day discharge (NDD) after TAVR reduces length of hospital stay, without an increased risk of complications.[9] NDD has become more common, and over a quarter of patients are discharged 1 day after TAVR.

Consequently, over the last decade, 'minimalist' clinical pathways have been developed and implemented to facilitate safe discharge home at the earliest time after procedures. In 2019, the Vancouver Multidisciplinary, Multimodality, Minimalist (3M) Pathway for next-day discharge was validated using anatomic and functional screening criteria, along with peri- and post-procedure management guidelines to allow for NDD, while maintaining favourable safety and efficacy outcomes.[10] The 3M Pathway is composed of a minimalist peri-procedure approach, facilitated post-procedure recovery, and criteria-driven discharge (Figure 1).[10] Across 11 centres, 411 patients met the study inclusion criteria. 80.1 % of patients were discharged the next day per protocol, and all-cause mortality at 30 days was found to be 2.9% (95% confidence interval [CI]: 1.7%–5.1%). Secondary endpoints included a readmission rate of 9.2% within 30 days. The results from 3M were comparable to the two low-risk TAVR trials in the United States showing composite death from any cause at 1 year to be 1.0% and 2.3%, demonstrated favourable primary and secondary endpoint outcomes for patients discharged the day following TAVR, and establishing an evidence-based clinical pathway with excellent safety and efficacy outcomes.[10-15]

THE FIRST SAME-DAY DISCHARGE AFTER TRANSFEMORAL TRANSCATHETER AORTIC VALVE REPLACEMENT: SETTING THE PRECEDENT

In 2015, Généreux et al.[16] published the first case of a 65-year-old male with severe aortic stenosis, New York Heart Association (NYHA) III symptoms of congestive heart failure, who was safely discharged home the day of transfemoral TAVR. The patient's surgical history was significant for double coronary artery bypass grafting with percutaneous coronary intervention 10 years later. They presented with severe aortic stenosis (mean gradient of 46 mmHg, aortic valve area of 0.8 cm^2, and left ventricular ejection fraction of 40%), and a calculated STS predicted risk of mortality (PROM) of 6%. Elective transfemoral TAVR with a balloon expandable Sapien XT (Edwards Lifesciences, Irvine, California, USA) was performed percutaneously under conscious sedation with minimal instrumentation. The procedure was uneventful; the total procedure time was 37 minutes. Post-procedural transthoracic echocardiogram showed a mean gradient of 5 mmHg, and aortic valve area of 1.9 cm^2. Ambulation was allowed 6 hours after the procedure; telemetry showed no new conduction abnormality; complete blood count and electrocardiogram were comparable to pre-procedural. The patient was discharged home 10 hours post-procedure. The patient returned to normal daily activity on post-operative Day 2. No adverse events occurred during follow-up at 5-day and 30-day timepoints. This initial case demonstrated the possibility of same-day discharge (SDD) after TAVR, and of potential broader application to other similar patients.

SAME-DAY DISCHARGE AFTER TRANSFEMORAL TRANSCATHETER AORTIC VALVE REPLACEMENT: THE EXPERIENCE

As a result of the COVID-19 pandemic and the suspension of non-urgent surgical procedures, many institutions restricted access to elective cardiothoracic surgical and interventional cardiology procedures to reduce hospital admission and LOS, and limit both patient and healthcare worker exposure.[13,17-27] Limited inpatient bed capacity, staffing shortages, and scarce resources necessitated an evolution in the delivery of care, including the addition of telemedicine and acceleration of traditional clinical care pathways. Coupled with patient hesitancy to seek care, these circumstances intensified the need for efficiency in time to treatment and to discharge. Considering the reductions in peri-procedural complications and a growing shift towards use of conscious sedation during TAVR, demonstrated in the 2020 TVT Registry Summary, a few institutions developed standardised clinical care pathways

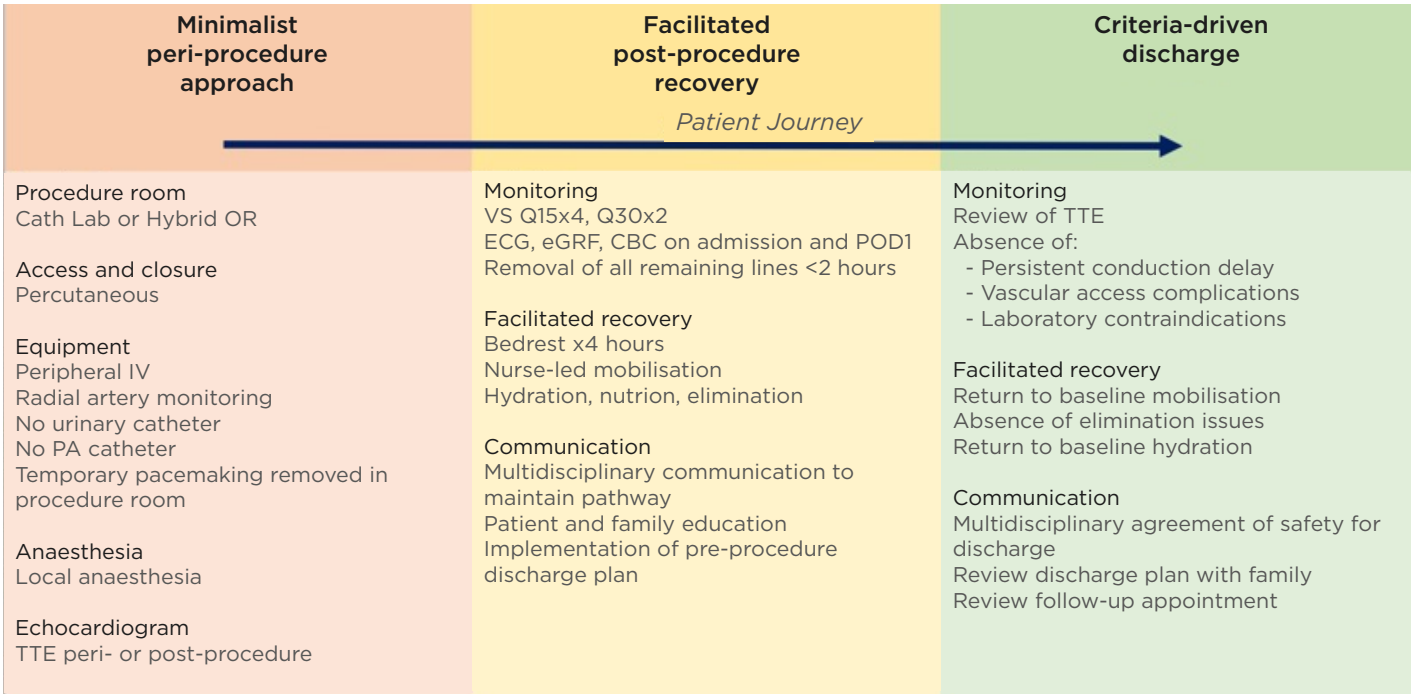

Figure 1: Vancouver multidisciplinary, multimodality, minimalist transcatheter aortic valve replacement clinical pathway.

Three components of the 3M TAVR Clinical Pathway: minimalist peri-procedure approach, facilitated post-procedure recovery, and criteria-driven discharge.

3M: multidisciplinary, multimodality minimalist; 3M TAVR: multidisciplinary, multimodality, minimalist transcatheter aortic valve replacement; CBC: complete blood count; eGFR: estimated glomerular filtration rate; IV: intravenous; OR: operating room; PA: pulmonary artery; POD1: post-operative Day 1; Q15: every 15 minutes; Q30: every 30 minutes; TTE: transthoracic echocardiogram; VS: vital signs[10]

for SDD after TAVR, following existing NDD evidence-based protocols.[10]

Single-centre case series established the safety of SDD after TAVR.[17-21,23,24,27] One of the earliest, from France, was published in 2020, demonstrating the safety of ambulatory TAVR in patients with pre-existing permanent pacemakers (PPM).[17] This was followed by a similar series in the United Kingdom of 13 elderly patients with PPMs, who underwent TAVR via a 'Daycase TAVR Protocol', demonstrating no complications out to 30 days.[18] Rai et al.[19] described six patients without baseline PPMs who were discharged home the same day as transfemoral TAVR, but were monitored with a real-time remote heart rhythm monitor for 14 days. One patient with a new-onset left bundle branch block underwent additional electrophysiology testing demonstrating normal conduction, and was discharged the same day as the TAVR. No complications were reported during the follow-up period. Of note, patients considered for SDD met the following criteria: ambulatory, capable of performing activities of daily living, and robust social support.[19] In the early experience with SDD after TAVR, remote monitoring was often utilised,[19-21] but was not considered routine.[16,23-27] By modifying the 3M protocol[10,13] and implementing best practices of the NDD protocol,[22] Pop et al.[23] carefully selected patients for SDD after TAVR. Their protocol excluded patients with pre-existing bundle branch or atrioventricular block. They found no difference in the 30-day cardiovascular readmission rate for 29 highly selected patients discharged within the same day of TAVR. Moreover, at 30-day follow up there were no new PPMs implanted in the SDD after TAVR patients. They concluded there were no observable differences in safety outcomes compared to the standard NDD protocol, thus further supporting the feasibility of SDD.

Similarly, the Emory Heart and Vascular Center, Atlanta, Georgia, USA, created a SDD TAVR

protocol, and published the outcomes in 2021.[24] After careful evaluation by the Heart Team, every patient scheduled to undergo TAVR via a transfemoral approach under nurse-led conscious sedation was considered for SDD. Pre-specified characteristics making SDD unsafe or not feasible resulted in the patient being deferred to the NDD protocol. The exclusion criteria were divided into four categories corresponding to the phases of care: demographics, procedural variables, post-procedure, and discharge planning (Figure 2). A single-centre retrospective analysis was completed to evaluate the outcomes of 29 SDD patients after uncomplicated minimalist TAVR, as compared to 128 NDD prior patients identified via propensity matching, who would have qualified for SDD based on the standardised SDD clinical care protocol.[24] Baseline demographic data was comparable between the two groups. Every patient in the SDD cohort was discharged on the day of their procedure after 6 hours of observation and meeting SDD criteria. No patients were discharged with remote monitoring. All-cause mortality at 30 days was zero in both cohorts, and interestingly, the rates of cardiovascular readmissions were higher in NDD cohort. Importantly, no SDD patient was readmitted with a new conduction abnormality or required a late pacemaker within 30 days.

The multicentre PROTECT TAVR study, an international observational study of patients who underwent TAVR with SDD at seven sites, found SDD post-TAVR to be safe and feasible in select patients at low risk for clinical events post-discharge.[25,26] Patient selection for SDD after TAVR was recommended by the local multidisciplinary heart team, but tended to follow an abbreviated 3M TAVR Clinical Pathway.[10] Patients with pre-existing conduction abnormalities were excluded unless they had a permanent pacemaker. During the procedure, standardised minimalist TAVR best practices were followed: procedure performed in a hybrid room, only local anesthaesia and minimal sedations utilised, avoidance of central venous access and

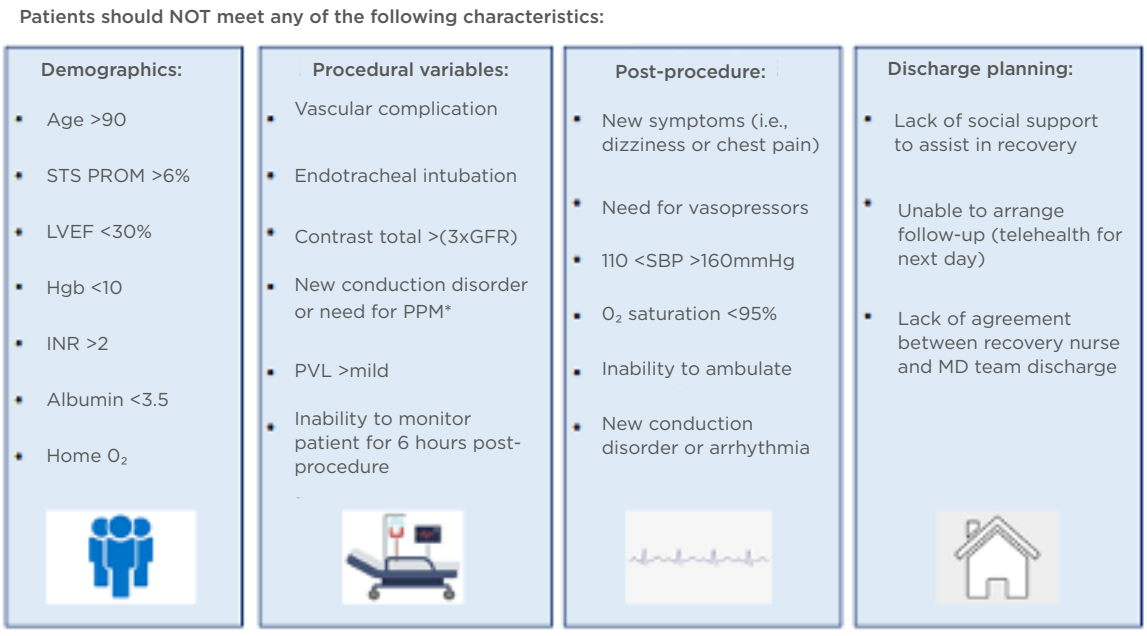

Figure 2: The Emory same day discharge protocol.[20]
Care pathway and protocol created to identify patients who could be safely discharged home the same day after uncomplicated, minimalist TAVR.

AV: atrioventricular; CHB: complete heart block; GFR: glomerular filtration rate; Hgb: haemoglobin; INR: international normalised ratio; LBBB: left bundle branch block; LVEF: left ventricular ejection fraction; O^2: oxygen; MD: multidisciplinary; PPM: permanent pacemaker; PVL: paravalvular leak; RBBB: right bundle branch block; SBP: systolic blood pressure; STS PROM: Society of Thoracic Surgeons Predictive Risk of Mortality score; TAVR: transcatheter aortic valve replacement.

indwelling urinary catheters, ultrasound guided percutaneous vascular access and pre-closure of the large bore sheath site, and reversal of heparin with protamine at the conclusion of the procedure. Patients were monitored in the cardiac catheterisation recovery area for a minimum of 4 hours, and then mobilised. Standard post-procedure transthoracic echocardiogram and electrocardiogram were completed on every patient prior to discharge, and patients were discharged to their family after 6 hours if all SDD criteria were met. Complications were few, with no major vascular complications, strokes, or cardiovascular deaths out to 30 days. One patient received a pacemaker post-procedure, but was still discharged the same day. There were no cases of new conduction abnormality requiring a pacemaker from discharge to 30-day follow up. The composite of cardiovascular death, myocardial infarction, stroke, all-cause readmission, new permanent pacemaker implantation, and major vascular complications at 30 days occurred in only 5.7% of patients (driven by readmission of six of 106 patients: 5.7%) and readmission for cardiovascular reasons was 2.3%.[26]

Recently, Krishnaswamy et al.[27] reported the Cleveland Clinic, Ohio, USA, experience with a SDD protocol compared to a NDD protocol for patients undergoing TAVR.[27] Patients were candidates for SDD after TAVR if they met six criteria: transfemoral TAVR under conscious sedation; 6-hour post-TAVR bedrest with rhythm monitoring; no major complications or need for additional observation; stable haemodynamics and electrocardiogram; comfortable ambulation post-procedure; and post-discharge social support to assist in recovery.[27] They too found low rates of complications for patients discharged on the day of the TAVR, with no deaths reported to 30 days. Notably, 5.3% of SDD patients developed a new left bundle branch block during the TAVR, all of which resolved during the observation period, and thus the patients were discharged later that same day. Predictors for successful SDD after TAVR included male sex, lower STS-PROM, and higher baseline haemoglobin level. Only seven of 114 SDD patients (6.1%) were readmitted within 30 days of the TAVR; notably, one patient was 103 years old, and two were admitted post-procedure Day 1 (one with a fever, and one with atrial fibrillation). Only one of the readmissions was for a new conduction abnormality that required implantation of a permanent pacemaker. The Cleveland Clinic protocol was less stringent, with no specific age or demographic exclusion criteria, than the Emory and PROTECT TAVR protocols, and may demonstrate SDD after TAVR is appropriate for a broader patient population.

THE CASE FOR SAME-DAY DISCHARGE AFTER TRANSFEMORAL TRANSCATHETER AORTIC VALVE REPLACEMENT: THE FUTURE

The safety of TAVR, along with the safety of NDD, have been well-established across a large spectrum of centres.[8,10-15,22,28] With this in mind, we must consider the risks inherent to SDD, particularly the inability to immediately assess and provide appropriate care for a patient with post-procedural complications. Cardiac event monitors did not prove necessary, and were not routinely included in most institutional SDD protocols. Although one of the most common complications after TAVR is need for permanent pacemaker, this was extremely rare in the patients on the SDD pathway, highlighting the need for careful pre-operative patient selection.[24-27] Moreover, late bleeding or vascular access site issues were also not demonstrated.

Careful selection of patients via evidence-based inclusion and exclusion criteria must be established to minimise the risks to patients after SDD. Universal criteria for SDD after TAVR have not been established, and institutional variability in these criteria has created ambiguity in appropriate selection of patients. Predictors for successful NDD after TAVR include male sex, young age, absence of atrial fibrillation, and lower serum creatinine.[19] Further, consideration must be given to patient's social support and geographic location relative to the home institution, as these factors may influence the risk-benefit ratio when choosing whether to safely discharge home on the same day of procedure.[24,29]

SDD after TAVR has emerged as a safe, efficient, and feasible option for carefully selected patients with symptomatic aortic stenosis, and limits the inpatient footprint and LOS. During COVID-19, SDD after TAVR ultimately led to improved resource utilisation, and a reduced nosocomial exposure risk to both patients

and healthcare staff.[20] While operating under the assumption that eliminating the overnight hospital stay is cost effective, additional research is needed to determine the true cost-saving impact of SDD TAVR. Recently, Cohen et al.[30] presented the cost analysis of TAVR versus SAVR from the low-risk TAVR PARTNER 3 data at 2 years, and demonstrated overall cost was lower for TAVR with a saving of $2,030 per patient, with an average LOS of 3 days.[30] Series assessing NDD have confirmed additional cost savings, and elimination of the inpatient stay may further improve cost effectiveness of TAVR. Consequently, SDD increased patient satisfaction, and enabled institutions to allocate resources justly amidst a global pandemic. The question remains if SDD TAVR will continue to be reimbursed, considering it is currently coded and billed as an inpatient procedure, thus requiring overnight admission.[31] This poses a challenge to hospitals, and ultimately may require a significant shift in TAVR billing codes at the national level. A paradigm shift will further promote innovation that may benefit patients, hospitals, and the broader national healthcare system. Ultimately, additional studies are needed to assess the impact of technological advances and healthcare delivery in the expansion of SDD TAVR.

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'Leave Nothing Behind' Strategy in Coronary and Peripheral Artery Disease: An Insight into Sirolimus-Coated Balloons

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Abstract

The long-term complications associated with stent implantation for the treatment of coronary and peripheral artery disease have prompted a search for more conservative treatments, and a 'leave nothing behind' strategy. Drug-coated balloons are an attractive alternative that combine the advantages of balloon angioplasty with inhibition of neointimal proliferation and restenosis. Paclitaxel has so far been the drug of choice in balloon coating, given its high lipophilicity and local tissue retention. Still, its use is limited by a narrow therapeutic window and safety concerns. Sirolimus-coated balloons entered the drug-coated balloon arena late because of the need to use specific technologies to overcome pharmacokinetic limitations. Their use was initially tested in in-stent restenosis and small-calibre native vessels, demonstrating results that overlapped with those obtained with paclitaxel-coated balloons in terms of efficacy. New indications for sirolimus-coated balloon angioplasty are emerging, such as acute coronary syndromes, coronary bifurcations, peripheral and coronary medium- to large-calibre native vessels, critical limb ischaemia, vasculogenic erectile dysfunction, and dysfunctional arteriovenous fistulas. Data in these areas are still limited to small, non-randomised studies, showing encouraging results.

INTRODUCTION

Plain old balloon angioplasty (POBA) paved the way for percutaneous coronary treatment, and represented the beginning of modern interventional cardiology. Subsequently, coronary stents were initially introduced as a bailout strategy for complications associated with POBA (mainly acute recoil and flow-limiting dissection), and dual antiplatelet therapy represents the gold standard in treating coronary artery disease to the present day. Drug-eluting stents (DES) have shown to be more effective in the prevention of restenosis and repeated revascularisation than bare metal stents.[1,2] Nevertheless, the events of late thrombosis or late stent fracture and cases of

restenosis observed with DES represent the main limitations in their use.[3,4] Hence, the attractiveness of drug-coated balloons (DCB) allows metal-free angioplasty, and limits barotrauma-induced intimal hyperplasia by delivering an antiproliferative drug that remains in the vessel wall for a limited time. Improvements in device characteristics and procedural techniques have limited acute complications related to balloon angioplasty in the use of DCB, which in any case can be treated with a stent bail-out strategy. The pharmacodynamic and pharmacokinetic properties of cytotoxic agents (taxanes), which are more favorable than those of cytostatic agents (limus) as an antiproliferative agent used in this technology,[5] have led to the spread of paclitaxel-eluting balloon. In recent years, pharmacological limitations related to sirolimus and its analogs in DCB have been overcome by introducing specific balloon-coating technologies. Thus, as already happened for DES, and given some concerns about taxanes as an antiproliferative drug, recently limus drugs have been investigated for their use in DCB,[6] both for the treatment of coronary and peripheral disease. At present, however, there is a lack of randomised data on their efficacy and safety profile, and comparison with taxane-eluting balloons and stents.

'LEAVE NOTHING BEHIND' STRATEGY

Improvements in coronary and peripheral stent design and the biocompatibility of the polymers and excipients used have reduced device-related cardiovascular events at midterm follow-up.[7] In the long term, however, DES appears to be associated with cardiovascular event rates comparable to those of bare-metal sents (BMS),[8] mainly related to the presence of an intravascular metallic device, which deters inflammation, intimal hyperplasia, and neoatherosclerosis. In addition, the duration of dual antiplatelet therapy can be reduced if a stent has not been released in the vessel, with benefit especially in patients at high bleeding risk. These considerations have led to incentives for developing 'leave nothing behind' strategies, such as the use of bioresorbable stents and DCB. After an initial setback related to the high rates of associated major cardiovascular events, the former has been completely modified in design and materials used, and still needs robust efficacy and safety data to allow a wide diffusion.[9] On the contrary, DCB have shown promising results in many trials and clinical studies, with more consistent data available with paclitaxel-coated balloons (PCB). In recent years, however, data are emerging on the use of sirolimus as a balloon-delivered drug, whose wider therapeutic window compared with paclitaxel could represent an advantage in efficacy and safety, as has already been occurred with drug-eluting stents.[10]

TAXUS VERSUS LIMUS

The performance of DCB depends on the type of drug used, its morphology, dosage, and added excipients, but also on factors related to the lesion treated and patient characteristics. These factors interact in determining the concentration of drug released, and affect release kinetics and storage mechanisms.[11]

The two main pharmacologic classes used are taxanes and limus. Taxanes, of which paclitaxel is the most widely used, are cytotoxic drugs that interfere with the M phase (mitosis) of the cell cycle by stabilising polymerised microtubules, arresting cells at the G1 phase, and resulting in a proapoptotic effect. In contrast, rapamycin and its analogs exert a cytostatic effect by blocking the activation of a protein kinase critical in signal transduction (mTOR), and preventing the cell from moving from the G1 phase to the S phase of the cell cycle (Figure 1).[12] The high lipophilicity with easy binding properties of paclitaxel has historically made it the drug of choice in DCB. However, paclitaxel is associated with high inflammation and toxic action at specific doses by cell apoptosis or necrosis,[13] resulting in a narrower therapeutic window than sirolimus. In addition, sirolimus distributes equally throughout all vessel wall layers, unlike paclitaxel, which accumulates predominantly in the adventitia with a relatively low transmural diffusion gradient.[5] To this should be added the recent meta-analysis by Katsanos et al.,[14] which showed higher mortality in patients undergoing lower limb revascularisation and treated with PCB than those treated with POBA, with a more significant effect on mortality in those receiving the highest doses of the drug. Despite the conceptual and methodological limitations of the work,[15] this evidence adds to previous findings showing lower mortality and superior clinical outcomes with everolimus-

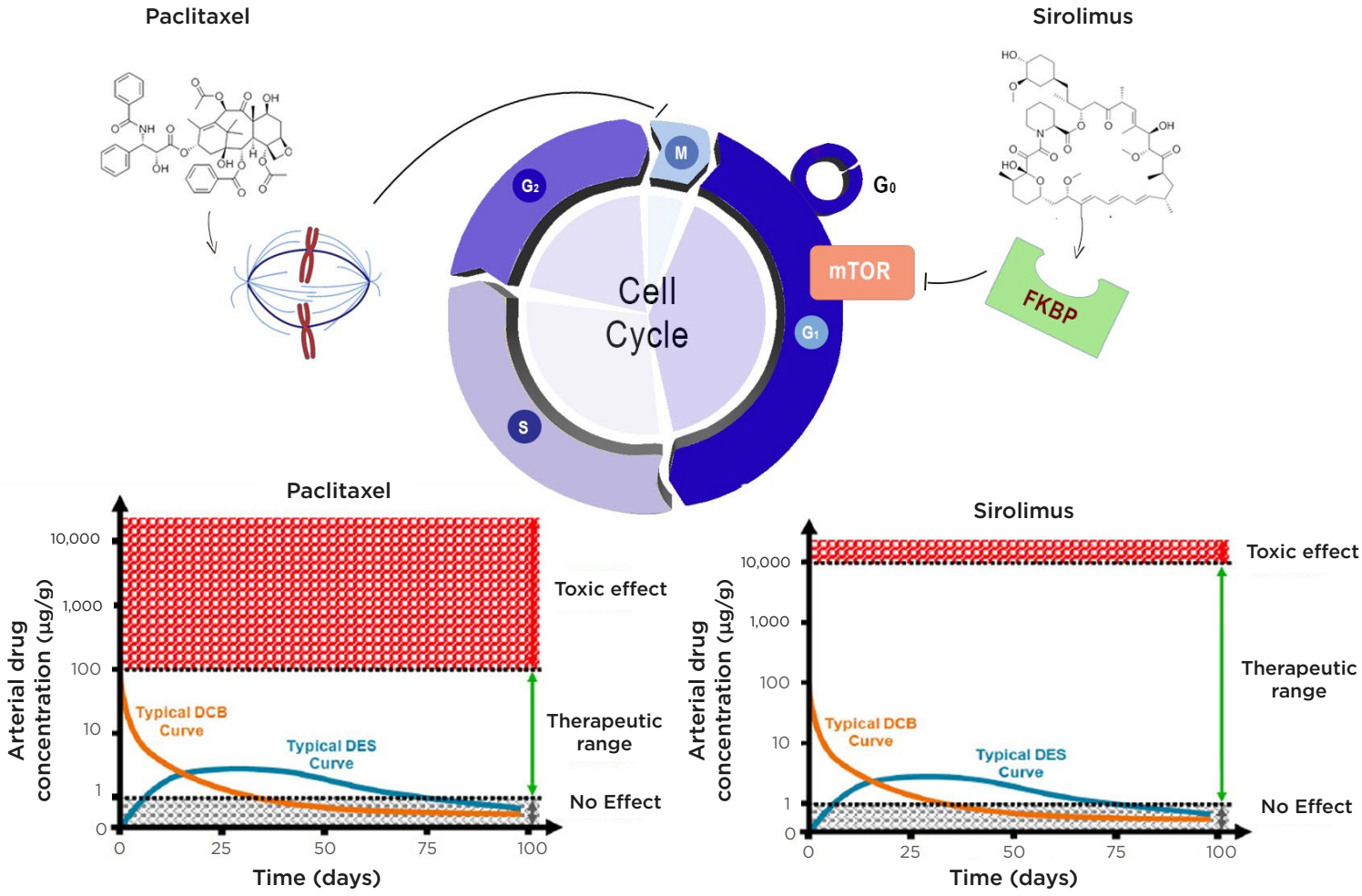

Figure 1: Effects of sirolimus and paclitaxel on cell cycle.

Paclitaxel and sirolimus act in two different phases of the cell cycle. The first interferes with microtubule organisation during cell division and blocks the cell in M phase. Sirolimus binds to the cytosolic protein FKBP and inhibits the mTOR pathway, which is involved in cell proliferation and the transition from the G1 to S phase of the cell cycle. The bottom graphs show the time course of drug concentrations in the arterial wall when released from a stent or balloon, and the different therapeutic windows of the two drugs.

DCB: drug-coated balloons; DEB: drug-eluting stents; FKNP: FK-binding protein; mTOR: mammalian target of rapamycin

eluting stents compared with taxus.[16] Therefore, in recent years, new technologies have been developed to overcome the pharmacological limitations of limus substances.

Few devices with a sirolimus coating are currently commercially available. In particular, MagicTouch (Concept Medical, Gujarat, India) uses Nanolute technology, which delivers polymer-free nanocarriers containing sirolimus surrounded by encapsulation of a phospholipid excipient.[17]

Conversely, the micro-reservoirs of the SELUTION SLR™ (Med Alliance, Nyon, Switzerland) DCB, through the proprietary cell adherent technology (CAT™), are designed to provide controlled and sustained release of sirolimus to maintain therapeutic concentrations over a prolonged period of time.[18] The Virtue® DCB (Caliber Therapeutics, New Hope, Pennsylvania, USA) is a microporous angioplasty balloon catheter carrying a sirolimus nanoparticle formulation. The drug is packaged with biodegradable polyester-based polymers.[19] New SeQuent® Please (B. Braun, Melsungen, Germany) coated balloons (SCB) uses a sirolimus coating in crystalline form, and butylated hydroxytoluene as an additive (Table 1).[20]

TECHNICAL CONSIDERATION FOR DRUG-COATED BALLOON ANGIOPLASTY

The success of DCB angioplasty is influenced by factors related to the technical execution of the procedure, which includes preparing the lesion, performing proper dilation, and monitoring the result obtained.

The Third Report of the International DCB Consensus Group provides technical guidance on the correct performance of DCB angioplasty.[21] In this setting, lesion preparation represents an essential step. Adequate pretreatment of the lesion allows better drug penetration into the vessel wall, and provides a better result in terms of lumen gain. Konishi et al.[22] showed that a smaller area of residual plaque after pre-dilatation is associated with a lower rate of target lesion failure.

Pre-dilatation can be performed with semi-compliant or non-compliant balloons, while the use of specific devices may be helpful in the presence of calcific lesions. In such cases, calcium may constitute a mechanical obstacle to the diffusion of the drug, so a debulking with a cutting or scoring balloon or with other devices (atherectomy, laser) allows a better antiproliferative efficacy of the DCB angioplasty. A balloon-to-vessel ratio of 1/1 is recommended for optimal preparation of the lesion. In some cases, it is advisable to start with balloons 0.5 mm smaller than the reference diameter, such as complex anatomy or severe in-stent restenosis (ISR), to avoid balloon slippage. Aggressive dilation at high atmospheres using balloons with a balloon-to-vessel ratio of 1/1 is also helpful to correct any stent underexpansion that may have caused restenosis.[23]

Predilatation should be considered optimal in the absence of major dissection, thrombolysis in myocardial infarction (TIMI) flow <III, or residual stenosis ≥30%.[21]

Each DCB brand has specific instructions for proper dilatation performance. In general, patient transit time (i.e., time from balloon insertion in the introducer sheath to balloon inflation) should be short, to avoid excessive drug loss during delivery. The inflation time varies depending on the DCB used, but should not be less than 30 seconds. The length of the balloon should be such that it covers 2–3 mm upstream and downstream of the predilated area. The authors recommend inflating the balloon slowly to reduce vessel barotrauma, stable pressure maintenance for approximately 30–60 seconds to allow optimal drug transfer, and gently and slowly deflating to reduce vessel recoil. The absence of C-type or more severe dissection and a TIMI 3 flow downstream determine the success of angioplasty with DCB.[21,23]

SIROLIMUS-COATED BALLOONS IN CORONARY ARTERY DISEASE

Currently, the use of DCB is indicated primarily in the treatment of ISR and atherosclerosis of small-calibre native vessels (<2.75 mm or <3.00 mm). Acute coronary syndromes, bifurcation lesions, and stenosis in medium-to-large calibre vessels represent new frontiers in the use of DCB. Available data are predominantly from PCB, but the introduction of new technologies for coating balloons with sirolimus has led to a proliferation of preclinical and clinical studies using SCB (Table 2).

In-Stent Restenosis

In the case of ISR, a DCB angioplasty has the advantages of not adding a scaffold that could alter the anatomy of the vessel, preserving any collateral branches originating from the stenosed stent, and allowing a shorter dual antiplatelet therapy regimen.[21] Histologically, ISR presents primarily as a phenomenon of intimal hyperplasia in BMS. On the other hand, in DES, it appears as a phenomenon of intimal hyperplasia associated with neoatherosclerosis. In the case of DES, if there are no mechanical problems (underexpansion, malapposition), the ISR phenomenon represents a failure to treat by antiproliferative drugs. The PACCOCATH ISR I[24] and ISAR DESIRE 3[25] studies were the first to demonstrate the possible use of DCBs in ISR. A meta-analysis of 10 studies comparing second-generation DES and PCBs showed similar efficacy in treating ISR, with lower all-cause mortality in the DES group, which can be explained by differences between the two groups in observational studies.[26] The DAEDALUS study pooled data from 10 randomised trials comparing angioplasty with PCB alone versus repeat stenting with DES alone to treat coronary ISR. At 3 years, repeat stenting

Table 1: Commercially available sirolimus-coated balloons.

Device	Company	Technology for drug delivery	Sirolimus dose (µg/mm²)
Virtue®	Caliber Therapeutics, New Hope, Pennsylvania, USA	Drug packaged in sum-micron nanoparticles lyophilised in the presence of lyoprotectants	N/A
Devoir	Minvasys SAS, Gennevilliers, France	Nanolute® technology: encapsulation of sirolimus in a protective lipophilic package	1.27
Selution™	Med Alliance, Nyon, Switzerland	Microreservoir (biodegradable polymer spheres containing sirolimus) embedded within an amphipathic membrane coated onto an angioplasty balloon (cell-adherent technology)	1.00
MagicTouch	Concept Medical, Gujarat, India	Nanolute® technology: encapsulation of sirolimus in a protective lipophilic package	1.27
SeQuent® Please coated balloons	B. Braun, Melsungen, Germany	Sirolimus in crystalline form	4.00

N/A: not applicable.

with DES was shown to be moderately superior to angioplasty with DCB in reducing the need for target lesion revascularisation (hazard ratio: 1.32; 95% confidence interval: 1.02–1.70; p=0.035).[27] A prespecified DAEDALUS analysis demonstrated similar efficacy and safety of DES and PCB in treating BMS-ISR, and a higher incidence of the safety endpoint (composite of all-cause death, myocardial infarction, or target lesion thrombosis at 3 years) in treating DES-ISR with PCB compared with repeat stenting.[28]

Currently, American guidelines do not consider the use of DCBs in the case of restenosis, but suggest the implantation of a new stent.[29] In contrast, European guidelines consider in Class IA both the use of DES and DCB.[30]

Data on the treatment of ISR with sirolimus DCB are still scarce. The SABRE trial is a single-arm feasibility study of 50 patients with Virtue SCB showing good procedural success of using a sirolimus DCB to treat ISR.[19] In the all-comer FASICO registry, 47% of indications for percutaneous coronary intervention (PCI) were ISR. MagicTouch SCB demonstrated 100% procedural success and excellent short-term efficacy and safety outcomes.[31] Clinical trials to date compared SCB versus PCB in a limited number of patients, showing overlapping outcomes.[32,33] During the Transcatheter Cardiovascular Therapeutics (TCT) conference 2021, Scheller presented data from two parallel trials (FIM Malaysian and German-Swiss) of SCB versus PCB to treat ISRA.[34] SeQuent Please SCB proved non-inferior to PCBs in terms of angiographic late lumen loss at 6 months (0.30 mm versus 0.30 mm, difference 0; 95% confidence interval: -0.24–0.24; threshold <0.35).[35]

De Novo Coronary Lesions

DCBs are progressively emerging as a treatment for native vessels stenosis. In small-calibre vessels, PCI with stent implantation is limited by high restenosis rates and adverse outcomes.[36]

Table 2: Main clinical studies using sirolimus-coated balloons.

First author/ study	Type of lesion	SCB	SCB comparator	Patients/ lesions (n)	LLL (mm; SCB versus PCB)	MACE (%)	TLR (%)	FU (months)	Procedural success (%)
SABRE[19]	ISR	Virtue	N/A	50	0.31±0.52	14.3	12.2	12	100
Ali et al.[32]	ISR	SeQuent SCB	PCB	25 versus 25/26 versus 25	0.31±0.62 versus 0.18±0.54 p=0.433	16.0 versus 12.0 p>0.99	16.0 versus 12.0 p>0.99	12	N/A
Briguori et al.[33]	ISR	Devoir	PCB	186 versus 186	N/A	N/A	15.5% versus 17.0 p=0.78	6	100
Scheller et al.[34]	ISR	SeQuent SCB	PCB	50 versus 51/52 versus 52	0.26 versus 0.25 (difference: -0.01; 95% CI: -0.24-0.23; threshold: < 0.35)	18.0 versus 14.0 p=0.596	16.0 versus 10.0 p=0.389	12	N/A
Loku Waduge et al.[42]	*de novo*	N/A	N/A	279/332	N/A	11.0	8.0	19	95
FASICO[31]	ISR/*de novo*	MagicTouch	N/A	32/34	N/A	9.4	9.4	6	100
FASICO NATIVES[44]	*de novo*	MagicTouch	N/A	27	0.09±0.34	0.0	N/A	6	74
EASTBOURNE[45]	ISR/*de novo*	MagicTouch	N/A	642	N/A	5.8	2.5	12	98.6
NANOLUTÈ[60]	ISR/*de novo*	MagicTouch	N/A	408/435	N/A	4.2	3.2	24	98.9
Wan Azman Wan Ahmad et al.[46]	*de novo*	SeQuent SCB	PCB	35 versus 35/37 versus 38	0.1±0.32 versus 0.01±0.33	6.0 versus 0.0 p=0.493	0.0 versus 0.0	12	N/A
SELFIE[43]	*de novo* (ACS)	MagicTouch	N/A	62	N/A	4.80	3.2	12	100

The table shows the main studies published to date in which SCBs have been used. Of these, only four have compared SCBs with PCBs and of these, most have used SeQuent SCBs. It can be seen that LLL and MACE tended to be higher in SRI studies than in studies with *de novo* lesions, although data variability is high. In addition, all studies have very high rates of treatment success.

ACS: acute coronary syndromes; FU: follow-up; ISR: in-stent restenosis; LLL: late lumen loss; MACE: major adverse cardiovascular events; N/A: not available; PCB: paclitaxel-coated balloon; SCB: sirolimus-coated balloon; TLR: target lesion revascularisation.

A series of non-randomised studies, registries, and randomised clinical trials have compared DCB with simple balloon angioplasty, BMS, and DES, with nonunique results. The PICCOLETO I trial[37] randomised patients with stable or unstable angina undergoing PCI of small coronary vessels (≤2.75 mm) to Dior PCB or Taxus DES. The trial was stopped due to increased major adverse cardiovascular events in the DCB group, and demonstrated the importance of preparation, even in small arteries, of a stenotic lesion before treatment and effective formulation of the antiproliferative drug. The most recent randomised clinical trials, adequately designed (BASKET SMALL 2,[38] PICCOLETO II[39]) have demonstrated the non-inferiority of PCB compared to stents. The results obtained in small-diameter vessels suggested using DCBs in *de novo* lesions in vessels >3 mm in calibre. The DEBUT study showed the efficacy of PCBs in treating *de novo* lesions in patients at high bleeding risk compared to BMS. In the study, 76% of PCBs used were >2.75 mm in diameter and 64% were >3 mm in diameter.[40]

The use of limus-coated balloons in native vessels is still in infancy. The BIO-RISE CHINA study showed the superiority of a biolimus-coated balloon over POBA in patients with small-vessel disease (reference vessel diameter <2.75 mm) for the primary endpoint of in-segment late lumen loss at 9 months.[41] The use of SCB in small vessel disease has demonstrated promising results in a retrospective study with a mean follow-up of 19 months[42] and a prospective registry.[43] At the angiographic follow up at 6 months of the FASICO NATIVES registry, enrolling patients treated with MagicTouch SCB with a reference vessel diameter of 2.32 ± 0.44 mm, late lumen loss was 0.09 ± 0.34 mm, and the percentage diameter stenosis was 31 ± 18.[44]

EASTBOURNE is a multicentre registry designed to test the long-term safety and efficacy of SCBs (MagicTouch) in a real-world population. Reference vessel diameter was 2.58 ± 0.76 mm. In 55% of cases, these were *de novo* lesions, and analysis at 12 months showed good immediate performance and a good safety profile. Of note, SCBs give a higher rate of target lesion revascularisation in ISR than in *de novo* lesions (5.4 versus 0.2%; p=0.0008).[45]

Few data are available on a direct comparison between SCBs and PCBs in the treatment of *de novo* lesions.

Wan Azman Wan Ahmad et al.[46] have recently presented data showing the non-inferiority of SCBs (SeQuent SCB, 4 µg/mm^2) compared with PCBs (SeQuent Please Neo) in vessels ≥2.5 mm. Paclitaxel demonstrated, however, a more remarkable ability to determine positive remodeling (late lumen enlargement 58% in PCB versus 32% in SCB; p=0.019). These results have sparked debate about the possible different efficacy of limus and taxanes in the stentless treatment of *de novo* lesions.

The TRANSFORM I (TReAtmeNt of Small Coronary Vessels: MagicTouch Sirolimus Coated Balloon) trial comparing SCB versus PCB[47] in small vessels (≤2.5 mm) and the TRANSFORM II (Sirolimus-coated Balloon Versus Drug-eluting Stent in Native Coronary Vessels) trial[48] (in vessels with diameter >2.0 mm and ≤3.0 mm) are still ongoing, and will bring crucial results in the field.

Bifurcation Lesions

In treating coronary bifurcation lesions, a provisional single-stent approach is superior to systematic two-stent techniques.[49] Use of PCB has been tested in the side branch with stent implantation in the main branch[50] and in a stentless strategy,[51,52] with good results of efficacy and safety.

Data with SCB are also limited in the treatment of bifurcations. Athulorala et al.[53] and Jones et al.[54] recently presented encouraging results of SCB use in the side-branch during provisional stenting technique in true bifurcations.

Acute Coronary Syndromes

The use of DCB has also been considered for the treatment of acute coronary syndromes. Sirolimus has demonstrated an essential role in reducing the degree of inflammation and migration of inflammatory cells, and stimulating the endothelium to the release of nitric oxide.[55] The use of DCB in treating acute coronary syndrome, and especially in ST-segment elevation myocardial infarction, has a rationale for several reasons: patients are on average younger compared with those with chronic coronary

syndromes, so the leave nothing behind strategy retains the possibility to intervene in different ways (coronary artery bypass graft, PCI with DES, or again with DCB) in case of progression of atherosclerosis or new acute events. In addition, the characteristics of the vulnerable plaques make them easy to treat with balloons, also allowing reduction in the duration of dual antiplatelet therapy.

Available data are mostly limited to PCB. After the negative results of DEB-AMI,[56] some evidence has shown that a DCB-only strategy in the acute setting is safe and feasible, with good clinical and angiographic outcomes at medium-term follow-up.[57–59] Randomised data on the use of SCBs in acute coronary syndromes are lacking. Data from the Nanolute[60] and SELFIE registries[43] show an excellent efficacy and safety profile of their use.

SIROLIMUS-COATED BALLOONS IN NON-CORONARY SITES

Sirolimus-Coated Balloons in Peripheral Artery Disease

Issues related to late complications of stent placement and the advantages of a leave nothing behind strategy have also been debated in the treatment of peripheral artery disease (PAD). DCBs have emerged as a new treatment option for obstructive PAD and critical limb ischaemia. European guidelines recommend using DCBs for ISR and short femoropopliteal lesions (i.e., <25 cm) as a Class B treatment option.[61]

As with coronary artery disease, the most consistent data are with PCB. Nine PCBs have been Conformité Européenne (CE)-marked for use in PAD, and three also have U.S. Food and Drug Administration (FDA) approval. Several randomised clinical trials have compared PCBs versus standard percutaneous transluminal angioplasty in PAD treatment, showing a superior efficacy and safety profile of PCBs compared with percutaneous transluminal angioplasty.[62-66] Mixed results were reported in critical limb ischaemia treatment, a stage of PAD often under-represented in randomised clinical trials.[67] Although registries and non-randomised studies have shown the use of DCB to be effective and safe,[68] some concerns about possible distal embolisation of paclitaxel in an area already damaged by ischaemia, and reports of microvasculitis and panniculitis after treatment with PCB, have limited the use of this technology.[69,70]

On this background, interest in SCB has grown. At present, three SCB have been approved for the treatment of lower limb arterial disease: MagicTouch, SELUTION, and Virtue.

The former was tested in the prospective single-arm XTOSI study. Fifty patients with femoropopliteal or below-the-knee lesions were treated with SCB, with 100% technical and procedural success. The primary endpoint (6 month primary patency) was achieved in 80% of patients. At 12 months, freedom from clinically-driven target lesion revascularisation was 89.7%, and amputation-free survival was 81.6%, with no early safety concerns.[71]

The efficacy and safety of SELUTION SCB were evaluated in treating femoropopliteal lesions in 50 patients in the SELUTION SLR first-in-human trial. The mean late lumen loss was 0.29 ± 0.84 mm at 6 months follow-up, significantly lower than the 1.04 mm objective performance criterion value ($p<0.001$).[72]

The treatment with the device determined a rate of primary patency by duplex ultrasound of 88.4%, with a significant improvement in the Rutherford category[73] ($p<0.001$), and in ankle brachial index measurements ($p<0.001$). Only one case of clinically-driven target lesion revascularisation was reported. In the prospective single-arm PRESTIGE study[74], the same device was tested in below-the-knee lesions determining critical limb-threatening ischaemia in a population of 25 patients. Primary tibial patency at 6 months was 81.5%, with a technical success rate of 100%.[74] All current SCB studies are limited by short- to medium-term follow-up.

Sirolimus-Coated Balloons in Erectile Dysfunction

Erectile dysfunction (ED) can have a vascular cause in 60–80% of cases when stenosis of the iliac-pudendal-penile arteries impairs perfusion of the male genital organ.[75]

Angioplasty with POBA is associated with recoil in a high percentage of patients,[76] while a high rate of restenosis was observed after

DES placement.[77,78] The PERFECT-4 study[79] enrolled 44 patients with ED and obstructive penile arterial lesions randomised to POBA or PCB angioplasty. There were no significant differences between the two treatments in the rate of restenosis at 8 months (40% versus 48%; p=0.569) and clinical success at 12 months (50% versus 59%; p=0.545), but both treatments were safe with no adverse events in the two groups. A meta-analysis on endovascular treatment of vasculogenic ED showed the procedure's safety, and highlighted the heterogeneity of the results of the various included studies.[79]

The authors' experience of DCB utilisation for endovascular treatment of ED comprises treatment of 194 consecutive patients with International Index of Erectile Function (IIEF-5) score <21, positive penile Doppler, and failure of drug treatment. Two hundred and thirty-eight lesions were treated, of which six (16%) were at the level of the internal iliac artery, 155 (65%) of the internal pudenda, 57 (30%) of the common penile artery, and 10 (4%) of the dorsal artery of the penis. The affected segment's length was 11.9 ± 6.6 mm, with a vessel's reference diameter of 2.2 ± 0.5 mm (minimum lumen diameter of 1.2 ± 0.6 mm). Relative stenosis was 73 ± 6.5%. A PCB was used in 141 lesions (59%), and SCB in 56 (24%). Procedural success (defined as residual stenosis <10% without signs of dissection) was 98%. Clinical success (defined by Δ IIEF-5 baseline score versus 3/6/8 months >5 points) occurred in 74.1% of patients treated with SCB, and 78.2% of patients treated with PCB (p=NS). At 8 months, clinical success was 68.9% in the SEB group, and 63.1% in the PCB group.[80]

The authors started to enroll patients with vasculogenic ED not responding to phosphodiesterase-5 inhibitors for >1 year and presenting with an IIEF-5 score <12, and a dynamic Doppler with Caverject® (Pfizer Inc., New York, USA) injection with peak systolic velocity <20 cm/sec in the multicentre, prospective, SUASION Registry.[81] Angioplasty was performed with SCB. Of 27 patients enrolled, more than 74% had an improvement of >5 in the IIEF-5 score, and 73% had a Doppler peak systolic velocity score increase of >10. At 6 months, this was 70.4% and 68.4%, respectively. Procedural success was 100%, and in a minority of cases (14%), a drug-eluting stent was required.

Sirolimus-Coated Balloons in Carotid Disease

The use of DCBs has shown promising results in the treatment of carotid ISR[82] where, however, experience with SCB is limited to a few cases described in the literature.[83] Piccoli et al.[84] used a pre-dilatation with PCBs before carotid stenting in patients with post-endarterectomy restenosis, demonstrating at a follow-up of 18 months no >50% restenosis, with only a transient ischaemic attack during DCB inflation, and one death during follow-up due to a myocardial infarction.[84] Similar experiences are not described with SCBs.

Sirolimus-Coated Balloons in Dysfunctional Arteriovenous Fistulas

DCB was used in stenotic arteriovenous (AV) fistulas for dialysis. PCBs are superior to standard angioplasty in treating dysfunctional fistulas at 6 months.[85-87] Angioplasty with SCBs is feasible and safe in treating dysfunctional or thrombosed AV fistulas with MagicTouch AVF SCBs.[88,89] Based on the results of these two pilot studies, the IMPRESSION trial comparing DCB angioplasty with MagicTouch AVF SCB versus POBA in dysfunctional AV fistulas was designed.[90] Recently, Tang et al.[91] reported the 6 month and 12 month results of the ISABELLA registry, a prospective, single-arm study testing the feasibility and safety of SELUTION SLR SCB in the treatment of failing AV fistulas in 40 patients.[91] Technical and procedural success was 100%, with no adverse events. Target lesion primary patency rate and circuit access patency rate at 6 months were 28/39 (71.8%) and 22/35 (62.9%), respectively, whereas at 12 months they decreased to 16/36 (44.4%) and 10/32 (31.3%), respectively. Among the interpretations provided by the authors to explain these results, there is probably an insufficient share of the eluted drug to allow a duration of long-term effects.

CONCLUSION AND FUTURE PERSPECTIVES

There is a familiar feeling among interventional cardiologists that sirolimus is better than paclitaxel as an antiproliferative drug used in stents or balloons. This perception stems from some safety considerations about paclitaxel and the action on vessel wall cells evident in preclinical studies.

The chemical and pharmacokinetic characteristics of sirolimus have limited its use and delayed its entry into the market, compared with paclitaxel as a DCB coating. This has resulted in far less efficacy and safety data on SCB than on DCB at present. Comparisons between the two types of DCB are limited to a few non-randomised data.[32,92] Angioplasty with SCB appears to be effective and safe in all settings in which it has been tested, with short- and medium-term follow-up in most cases. Paclitaxel has demonstrated promising results in terms of late luminal enlargement as it reaches the tunica adventitia. In this sense, expectations are predominantly for long-term outcomes of SCB in treating native vessels. The TRANSFORM I[47] and TRANSFORM II[48] trials will help shed light on this point. Given the specific technologies in drug delivery of different SCBs on the market, it is also necessary to confirm the presence of a class effect and overlapping results of the various platforms.

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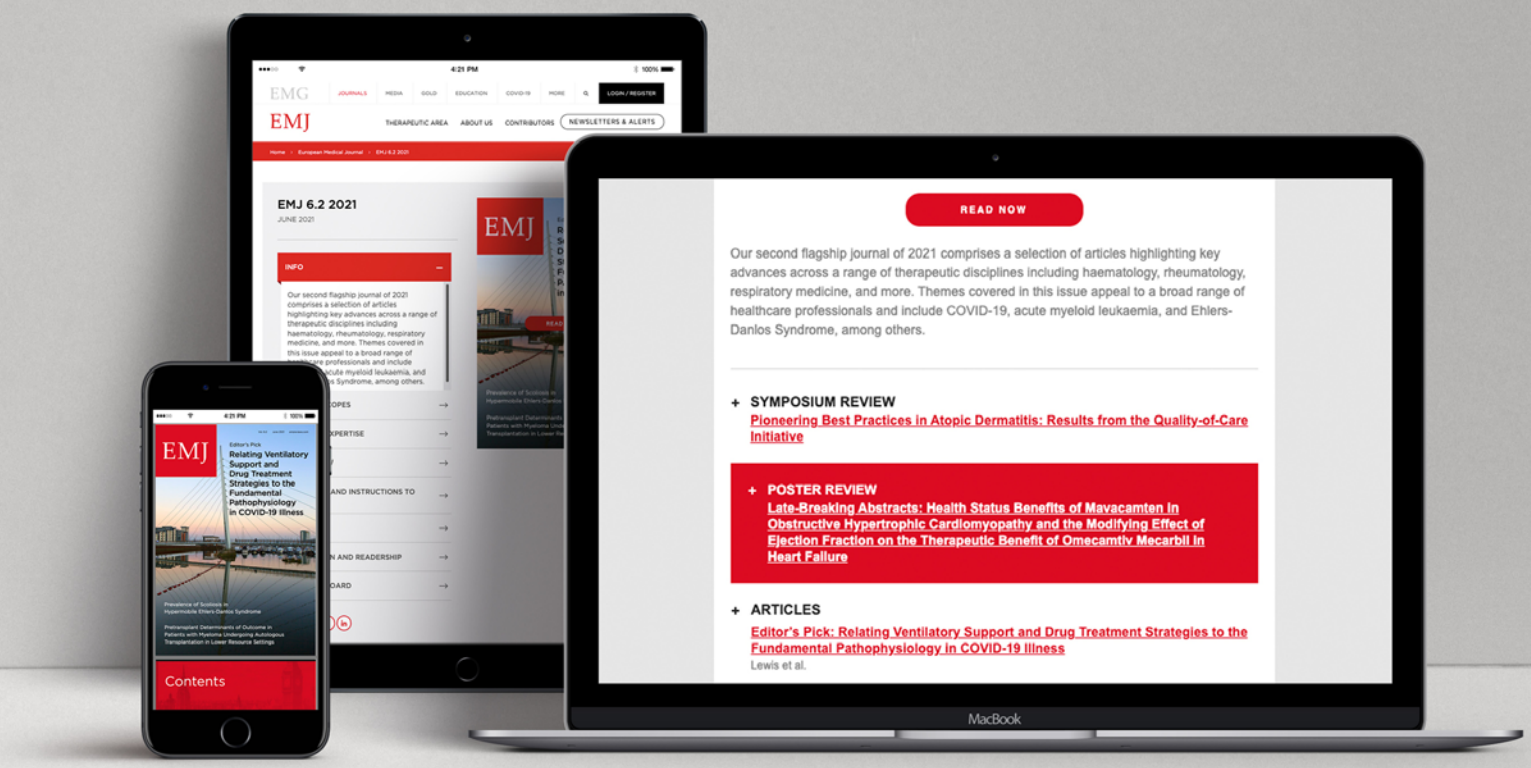

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