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REVIEW ARTICLE

Synovium Derived Mesenchymal Stromal Cells (Sy-MSCs): A Promising Therapeutic Paradigm in the Management of Knee Osteoarthritis

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Abstract

Synovium-derived mesenchymal stromal cell (Sy-MSC) is a newer member of the mesenchymal stromal cell families. The first successful demonstration of the mesenchymal stromal cell from the human synovial membrane was done in 2001 and since then its potential role for musculoskeletal regeneration has been keenly documented. The regenerative effects of Sy-MSCs are through paracrine signaling, direct cell–cell interactions, and extracellular vehicles. Sy-MSCs possess superior chondrogenicity than other sources of mesenchymal stromal cells. This article aims to outline the advancement of synovium-derived mesenchymal stromal cells along with a specific insight into the application for managing osteoarthritis knee.

Keywords Synovium · Mesenchymal stromal cell · Chondrogenicity · Osteoarthritis knee

Introduction

Osteoarthritis (OA) of the knee is a chronic degenerative condition of the articular cartilage which is associated with varying degrees of inflammatory synovitis and cartilage destruction of the joint [1]. The articular cartilage is avascular and aneural structure and hence the healing process is poor and results in fibrous tissue. OA knee primarily affects the elderly population which is a major cause of disability in older adults worldwide [2].

In India, the prevalence of osteoarthritis knee ranges from 22 to 39% with female preponderance [3]. The robust increase in the prevalence of OA knee is due to obesity and a sedentary lifestyle. Various modalities of treatment for cartilage rejuvenation are autologous chondrocyte implantation, microfracture, stem cell culture, and implantation as a part of regenerative orthobiologics [4].

Mesenchymal stromal cells (MSCs) are a rich cell source for regenerative medicine particularly in knee osteoarthritis for cartilage regeneration [5, 6]. MSCs are harvested from various tissues such as bone marrow, adipose tissues, skeletal muscles, placenta, umbilical cord, dental pulp, and synovium [7, 8]. Among these, the MSCs harvested from the synovial tissues had the greatest potential for differentiation into chondrogenic cells and their proliferation [9]. Analysis of cells harvested from fibrous and adipose synovium had a similar self-renewal and differentiation capability. Furthermore, in-vivo study demonstrated the differentiation of synovial MSCs into cartilage appropriate to the microenvironment for the repair of cartilage defects in rabbit knees [10].

Mesenchymal stromal cells are multipotent stem cells present in various sites of the body. They have direct and indirect mechanisms in their chondrogenic activity. They act as a stimulus to induce the differentiation of chondroprogenitors to convert into chondrocytes by growth factor secretion such as FGF and TGF-β [11]. They also reduce inflammatory joint disease progression by promoting T-cell class switch from pro to anti-inflammatory Th2 subtype.

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A popular treatment option to treat OA is orthobiologic therapies. More trials are needed to determine the best OA treatments among MSCs of bone marrow, adipose tissue, placenta, and synovium, even though the present research investigating their efficacy is informatory. This article throws light on the synovium-derived mesenchymal stromal cells (Sy-MSCs) in the cartilage regeneration in OA knees.

Cellular Therapy in OA Knee

Due to the robust development in the fields of regenerative and translational medicine, the usage of biological products to treat diseases has been of prime importance. Biocellular regenerative medicine aims to regenerate all cells and tissues and exert regenerative homeostasis in the local microenvironment. Cellular therapy is defined as the transplantation of either autologous or allogenic cells or modified cells to replace and regenerate the damaged tissues in a given area of interest. On par with cellular therapy, numerous researchers have demonstrated the usage of cellular elements in osteoarthritis in the past 2 decades.

Due to the intrinsic inability of cartilage to repair, the usage of biological products has become robust among practicing orthopedic surgeons and regenerative experts. Evidence on varied sources of mesenchymal stromal cells (MSC) for the management of osteoarthritis knees is available. The most common explored cellular source is bone marrow-derived MSCs (BM-MSCs) (bone marrow aspirate concentrate) followed by adipose-derived MSCs (ASCs) (adipose stromal cells, stromal vascular fraction, microvascular fragments, microfat, nanofat, and secretomes), and placenta-derived MSCs (P-MSCs) for cartilage regeneration.

Various studies have proved the efficacy, functional outcome, and safety regarding the usage of either BM-MSCs, ASCs, and P-MSCs for the management of osteoarthritis knees. A meta-analysis by Jeyaraman et al. demonstrated the superiority of ASCs in terms of the efficacy and safety profile in the management of osteoarthritis knees than BM-MSCs [12]. Due to the advancing age in the elderly population the yield of harvested MSCs from bone marrow sources is limited [13]. But considering the availability, sources of ASCs are 500 times more than that of BM-MSCs [14]. BM-MSCs have greater cartilage regeneration potential than AD-MSCs but due to the presence of various biological micromolecules and cytokines in the stromal vascular fraction from AD-MSCs, the cartilage regeneration can be accentuated [15]. Soltani et al. demonstrated that a single intra-articular injection of allogenic P-MSCs resulted in a better functional and clinical outcome at the end of the 6 months follow-up period [16]. Hsu et al. reported higher concentrations of glycosaminoglycan secretion with human P-MSCs which appear to be the better agent for chondrogenesis than human BM-MSCs. They concluded that the usage of a 3D culture system for P-MSCs would revolutionize cartilage tissue bioengineering [17].

The unexplored or minimally explored cellular source for cartilage regeneration is synovium-derived mesenchymal stromal cells (Sy-MSCs). In 2001, De Bari et al. demonstrated successful extraction of MSCs from human synovial membrane [18]. The synovial membrane is a specialized connective tissue composed of a double-layered membrane lining the synovial joints and tendon sheaths. The outer layer of the synovial membrane is composed of fibrous, adipose, and areolar components, and the inner layer is composed of sheets of cells (type A macrophage-like synoviocytes and type B fibroblast-like synoviocytes). The components of fibrous and adipose elements give rise to mesenchymal stromal cells named fibrous-synovial MSCs and adipose-synovial MSCs, respectively. Type A cells show positive expression for CD-68 and CD-14. They exhibit a rich expression of collagen III, V, and VI. Type B cells exhibit positive expression for CD-44 and VCAM-1 adhesion molecule [19].

Characterization of Sy-MSCs

Like BM-MSCs and ASCs, Sy-MSCs exhibit multipotent cellular efficacy and regenerative potential in both in-vivo and in-vitro. The benefits of MSCs transplantation depend on the viability and biological properties like controlled proliferation and differentiation, anti-apoptosis, anti-inflammatory, and immunomodulatory effects [20, 21]. The regenerative effects of Sy-MSCs are through paracrine signaling, direct cell–cell interactions, and extracellular vehicles [22]. The properties of various sources of MSCs are compared in Table 1.

Sy-MSCs have been revealed to be a multipotent cell source similar to BM-MSCs [23]. Sy-MSCs exhibit osteogenesis, chondrogenesis, and adipogenesis under lineage-specific culture medium [18, 24]. Due to the intrinsic ability for limited senescence, Sy-MSCs can be expanded in greater numbers in monolayer culture in-vitro. Human Sy-MSCs maintain the proliferative ability even after the 10th passage and maintain a linear curve in population doubling capacity. In a pre-clinical study with a rat model, Sy-MSCs exhibit higher CFU, proliferation, and chondrogenic differentiation kinetics and safety than the other sources of MSCs. The higher proliferative potential of Sy-MSCs is due to the telomerase activity which is usually undetectable in the somatic cells [25, 26].

Sy-MSCs co-cultured along with human serum demonstrated enhanced proliferation due to the presence of higher levels of PDGF in human serum which binds to PDGF receptor found in Sy-MSCs. Inversely, the decreased proliferative capacity of Sy-MSCs is noted in the presence of

Table 1 Characteristics of the varied sources of MSC therapy for OA knee

Sources of MSCs	Sources	Potency	Significance	Invasiveness	Ethical consideration
ESCs	Inner cell mass	Totipotent	Forms an entire organism and irreversible stem cells; ? allogenicity	+	+++
BM-MSCs	Iliac crest	Multipotent	↑ Potential to regenerate bone and cartilage; Easy to isolate stem cells; No culture required; Auto and allogenicity + +	−	+
AD-MSCs	Abdomen, medial aspect of thigh	Multipotent	↑ Potential to regenerate cartilage and soft tissues; Complex natured to isolate stem cells; Autologous + +; ??? Allogenicity	−	+
Sy-MSCs	Synovium around knee joint	Multipotent	↑ Potential to regenerate cartilage than bone; Culture required for exponentiation; auto and allogenicity + +	+	+
Pl-MSCs	Amniotic membrane, chorionic plate, chorionic villi, decidua	Pluripotent	Difficult to isolate inner cell mass; ↑ potential to regenerate bone, cartilage and soft tissues; auto and allogenicity + +	+	−
Um-MSCs	Umbilical cord, Wharton jelly	Pluripotent	Culture required for exponentiation; auto and allogenicity + +	+	−
AF-MSCs	Cytotrophoblast, syncytiotrophoblast	Pluripotent	Culture required for exponentiation; auto and allogenicity + +	+	−
PB-MSCs	Circulating mononuclear cells	Multipotent	Enhanced osteogenic and adipogenic potential	+	−

anti-PDGF antibodies [27, 28]. Shirasawa et al. exhibited maximal chondrogenic differentiation by inducing Sy-MSCs with BMP-2, TGF-β, and dexamethasone in pellet culture than BM-MSCs [29].

Various studies observed tenfold rise in synovial fluid-derived MSCs (SF-MSCs) in injured or osteoarthritic knees [30, 31]. These synovial fluid-derived MSCs show similar characterization to Sy-MSCs. SF-MSCs exhibit more clonogenicity and chondrogenicity and lower adipogenicity in-vitro than BM-MSCs. The source for SF-MSCs is from synovial shedding, infrapatellar fat pad, or articular cartilage. The number of SF-MSCs increases as the disease progresses [32].

Genotype and Phenotype

RT-PCR analysis of synovial tissue specimens exhibited the expression of extracellular matrix molecules, adhesion molecules, cytopeptides, and transcription factors in Sy-MSCs [33]. Immunohistochemical analysis of Sy-MSCs showed similar pattern as shown by BM-MSCs [34]. Sy-MSCs show positive expression for CD-10, -13, -44, -49a, -73, -90, -105, -147, and -166, and negative expression for CD-14, -20, -31, -34, -45, -62e, -68, -113, and -117 [35, 36]. Sy-MSCs show negative expression for alkaline phosphatase enzyme and HLA-DR antigens [8].

During the culture of Sy-MSCs, after first passage, immunophenotype exhibits a transformation from CD-34, -45, -62e, and HLA-DR antigens to CD-73, -90, and -105 which are expressed in higher quantities [34]. Such immunophenotypic transformation renders Sy-MSCs as a multipotent cellular population. With the higher expression of CD-90 in Sy-MSCs, the chondrogenic potential of Sy-MSCs are accentuated both in in-vitro and in-vivo [34].

In mice, Futami et al. observed more than 90% positive ratios for CD-29 and -44, less than 10% positive ratios for CD-106, and 50% or more positive ratios for CD-140a among Sy-MSCs and cells derived from bone marrow and muscles [37]. Osteogenesis is evidenced by the higher expression of the mRNA for RNUX2, osteopontin, and type 1 collagen levels in Sy-MSCs whereas adipogenesis is expressed by higher levels of the mRNA for Lpl, PPAR-α, C/EBP-α, and FABP4 levels in Sy-MSCs and the evidence of chondrogenesis is exhibited by the expression of Sox9, type II, and type X collagen in in-vitro Sy-MSCs [37].

Immunomodulation of Sy-MSCs

The immunomodulatory properties of Sy-MSCs enhance their usage in clinical applications [38, 39]. The pathways by which the immunomodulatory mechanisms of Sy-MSCs are regulated through.

T Lymphocyte System

Sy-MSCs mediate immunoregulation, either produced constitutively by MSCs or released following cross-talk with target cells. Nitric oxide and indoleamine 2,3-dioxygenase (IDO), which are only released by Sy-MSCs after triggering by IFNγ produced by target cells [40]. IDO induces the depletion of tryptophan from the local environment, which is an essential amino acid for lymphocyte proliferation. Sy-MSC-derived IDO was reported to be required to inhibit the proliferation of IFNγ-producing TH1 cells and, together with prostaglandin E2 (PGE2), to block NK-cell activity [40].

Activated CD8+ T lymphocyte by nitric oxide suppresses the proliferation of cytotoxic T cells, inhibits the production of INF-γ & TNF-α, and attenuates the cytotoxic effects. The activated CD4+ T lymphocyte by TGF-β, nitric oxide, hepatocyte growth factor, and PGE2 secreted by Sy-MSCs enhances lineage-specific differentiation and cellular proliferation [41]. Upon which the immunomodulatory activities are enhanced via T helper 2 cells through increased IL-4 levels and T regulatory cell through increased TGF-β and suppressed via T helper 1 cell through increased INF-γ levels and T helper 17 cells through increased levels of IL-17A as shown in Fig. 1 [42].

B Lymphocyte System

Sy-MSCs enhance antibody production through the activation of B lymphocytes by soluble factors secreted by them as shown in Fig. 1 [43].

NK Cells

Mesenchymal stromal cells inhibit cytokine production by NK cells when cultured or co-cultured in the media containing IL-2 or -15 [44]. MSCs hamper NK-cell cytolytic effects through soluble factors like HLA-G5, PGE2, IDO system, and also through downregulation of NK receptors like NKp30, NKp44, or NKG2D. Activated NK cells lyse MSCs. Upon exposure with INF-γ increases MHC-I expression on MSCs which conversely decreases the susceptibility to NK-cell-mediated lysis as shown in Fig. 2 [45, 46].

HLA-G5 System

The production of soluble HLA-G5 by Sy-MSCs has been shown to suppress T-cell proliferation, as well as NK-cell and T-cell cytotoxicity, and to promote the generation of regulatory T cells as shown in Fig. 2 [47, 48].

Harvesting and Delivery Methods of Sy-MSCs

Synovial stromal cells can be harvested from the synovial lining of knee [49], hip [50], or shoulder [51] joints. Fernandes et al. harvested synovial stromal cells arthroscopically from the knee through the anterolateral portal and processed them further to expand the cells for further differentiation and clinical applications [52].

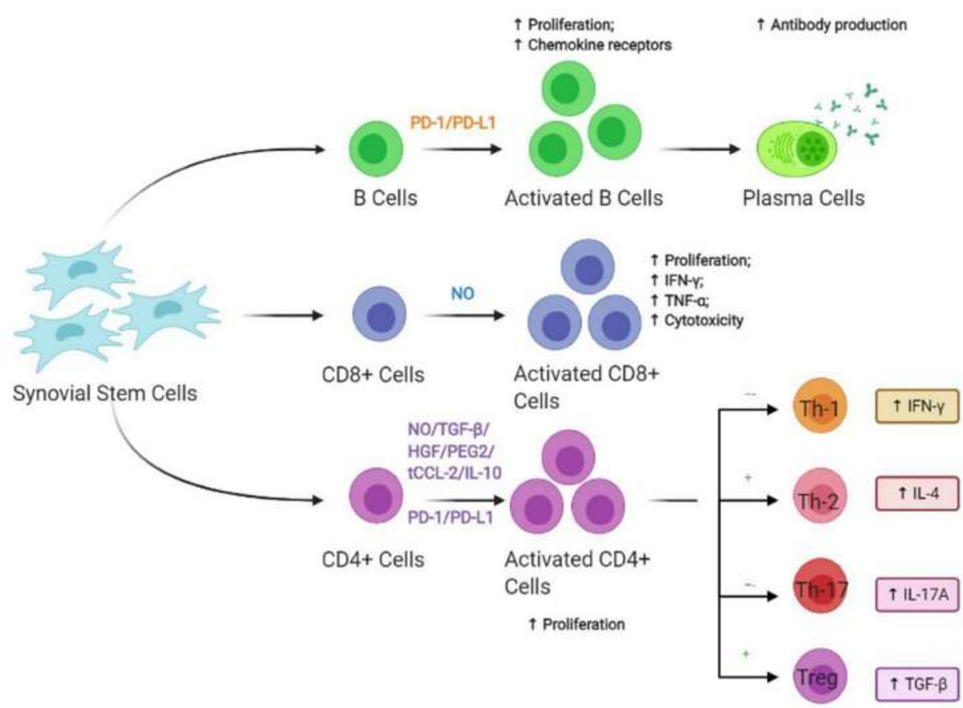


Fig. 1 Immunomodulatory effects of MSCs via T and B lymphocyte system. *CD* cluster differentiation; *IFN-γ* interferon-gamma; *IL* interleukin; *TGF-β* transforming growth factor-beta

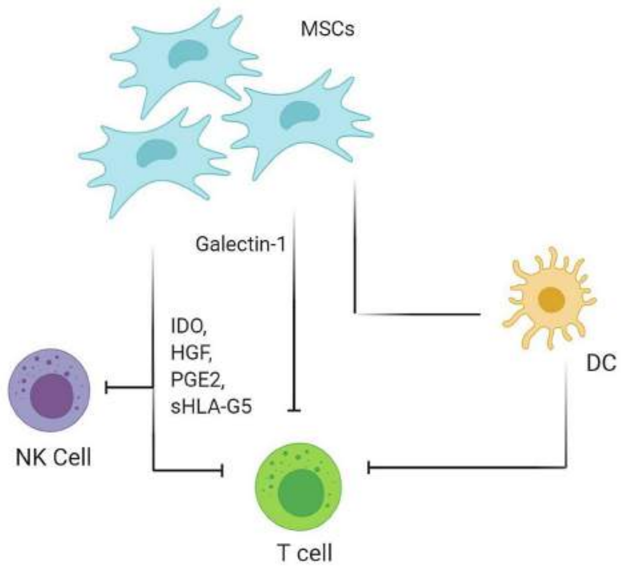


Fig. 2 Immunomodulatory effects of MSCs via NK cell and HLA-G5 system. *MSCs* mesenchymal stem cells; *NK cell* natural killer cell; *DC* dendritic cell; *IDO* indoleamine-pyrrole 2,3-dioxygenase; *HGF* hepatocyte growth factor; *PGE2* prostaglandin E2; *sHLA-G5* soluble human leukocyte antigen G5

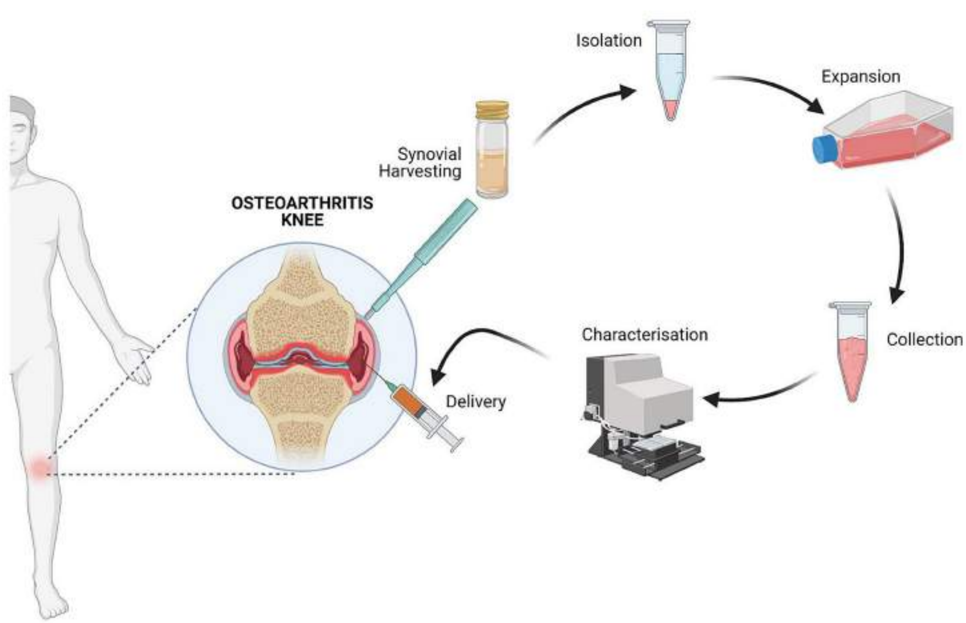
Li et al. [53] studied the feasibility of harvesting synovial stromal cells from arthroscopic flushing fluid from the knee joint for cartilage regeneration. Sy-MSCs were expanded in-vitro and induced for chondrogenic differentiation. These cells were delivered by xenogenic injection of MSC encapsulated by loading them into cross-linking polyPEGDA/HA hydrogel into full-thickness cartilage defects in cartilage groove. They observed a reduction in the defect area at the end of 2 months.

Researchers demonstrated that the repair of torn meniscus upon the suspension of Sy-MSCs on meniscus for 10 min. They further observed that the number of cells adhered to the pathological site underwent dynamic morphological changes over 24 h. These cells showed microspikes and pseudopodia for better adhesion onto the pathological meniscus [54].

Shimomura et al. [55] obtained Sy-MSCs arthroscopically and expanded in-vitro before transplantation to symptomatic chondral knee lesions. The intervention was delivered in two-stages, stage-I arthroscopic evaluation and synovial tissue biopsy from the anterior aspect of the knee followed by administration of the cultured Sy-MSCs after 4 weeks upon making a tissue-engineered construct of the size of the chondral lesion identified initially. All five patients achieved full defect filling at 48 weeks which was demonstrated by MRI during the follow-up. These cases showed no adverse events. Chondrogenesis was demonstrated histologically. Functionally these patients showed full clinical improvement by 24 months.

The evidence stated that the infrapatellar fat pad plays a major in the progression of the OA knee [56–58]. Targeting infrapatellar fat pad tissue with synovial stromal cells may reduce inflammation and fibrosis across the knee joint and proceeds with cartilage repair and regeneration [59–61]. The various steps involving Sy-MSC therapy for osteoarthritis knee are shown in Fig. 3.

Fig. 3 Steps involved in Sy-MSC therapy for osteoarthritis knee



Chondrogenicity of Sy-MSCs

The mesenchymal stromal cells possess the ability to differentiate into trilineage namely osteogenesis, chondrogenesis, and adipogenesis. Sy-MSCs possess superior chondrogenicity than other sources of mesenchymal stromal cells which were evidenced by (1) the origin of synoviocytes and chondrocytes from common progenitor pool [62], (2) the higher expression of CD-44 (hyaluronic acid receptor) and uridine diphosphoglucose dehydrogenase (UDPGD) [62], (3) formation of a continuous layer of the synovial membrane in the area of partial-thickness defects of the cartilage [63] (4) chondrocyte-like cells are present in synovial pannus in rheumatoid arthritis [64], and (5) the expression of type 1, 10, & 11 collagen, cartilage oligomeric matrix protein (COMP), SOX-9, and aggrecan in the synovial tissues [65]. Hence, Sy-MSCs have a greater proliferative effect in cartilage regeneration [19]. Besides cartilage regeneration, various studies demonstrated the regenerative potential of Sy-MSCs in terms of the tendon, ligament, muscle, and bone regeneration [66, 67].

Intracellular Signaling in Chondrogenic Differentiation

Various researchers have demonstrated the chondrogenic differentiation of MSCs in-vitro with the addition of external biological micromolecules such as growth factors (FGF, PDGF, TGF-β, EGF), bone morphogenetic proteins (BMPs), hedgehog, and Wnt glycoproteins. TGF-β superfamily (TGF-β2 and TGF-β3) has been demonstrated to be the potential inducer of chondrocytes in-vitro [68]. Among BMPs, BMP-2 and -7 are the potential inducers for chondrogenesis and extracellular matrix synthesis, respectively. The molecular interactions between ERK1/2 and SOX-9 stimulate chondrogenic differentiation of MSCs [62, 69]. To avoid the formation of fibrous cartilage, PTHrP or FGF-2 downregulates Col10a1 and Col2a1 during chondrogenesis and increases the deposition of type 2 collagen in the cartilage as shown in Fig. 4 [70].

SOX-9 expression helps in the survival and maintenance of chondrocytes in-vitro and in-vivo, expands ECM production and intracellular signaling among chondrocytes [71]. SOX-9 acts as a link protein for L-SOX-5 and SOX-6 transcription factors in maintaining chondrogenesis and also helps in the expression of chondrogenesis regulatory pathways (Wnt, Notch, and hedgehog signaling mechanisms) [72]. The other transcriptional factors that help in maintaining chondrogenesis are Runx2, Barx2, Nkx3.2/Bapx1, Msx1 and 2, β-catenin, Smads, Lef1, AP-1, and AP-2 [68, 73]. Apart from these transcriptional factors, the composition of extracellular matrix maintains chondrocyte morphology, phenotype, and genotype, differentiation, and maturation [74]. Among the various intracellular signals, Ser/Thr protein kinases, and Ser/Thr phosphoprotein phosphatases were the key regulators of chondrogenesis [75]. p38 and ERK1/2 are the key mitogen-activated protein kinases (MAPKs) that regulate chondrocyte signaling involved in the translation of extracellular stimulus into chondrocyte responses and gene expression for chondrocyte differentiation and proliferation [76].

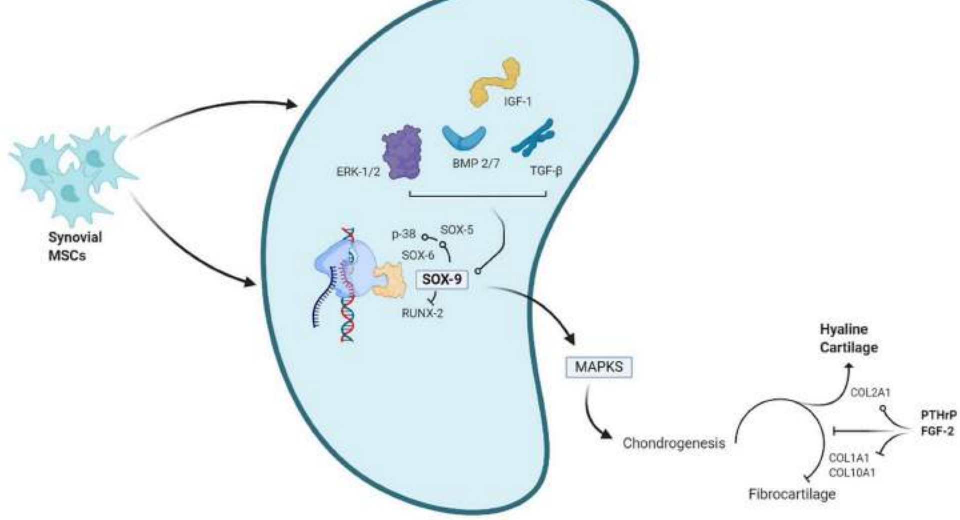


Fig. 4 Factors involved in selective chondrogenic differentiation of Sy-MSCs. *ERK* extracellular signal-regulated kinase; *IGF* insulin-like growth factor; *BMP* bone morphogenic protein, *TGF-β* transforming growth factor-beta; *SOX* SRY-related HMG box; *RUNX* runt-related transcription factor; *MAPKS* mitogen-activated protein kinase; *COL* collagen; *PTHrP* parathormone related peptide; *FGF* fibroblast growth factor

In-Vitro Chondrogenicity by Sy-MSCs

The source of MSCs differs in tissue differentiation and multipotent ability to obtain the tissue of interest [23, 26]. The murine MSCs derived from various sources exhibited that Sy-MSCs demonstrated a greater amount of cartilage matrix production in in-vitro pellet culture [26]. When matched with BM-MSCs, Sy-MSCs derived cartilage pellets were significantly larger [29]. De Bari et al. reported chondrogenic capability of Sy-MSCs was higher than periosteum-derived MSCs in-vitro [77].

The greater regenerative and chondrogenic potential was exhibited by MSCs derived from fibrous and adipose synovium. Though the amount of nucleated cell population was higher in fibrous synovium, MSCs from adipose synovium have more chondrogenic potential and accessibility to extract MSCs [78]. Koga et al. demonstrated an enormous cartilage matrix production after 4 weeks by synovium and bone marrow-derived MSCs when admixed with collagen gel transplanted into rabbit cartilage defects [79].

The fate of cellular therapy depends on specific cell–cell and cell–matrix interactions, which are controlled by extracellular and intracellular signaling molecules [80]. The components of culture media used for in-vitro chondrogenesis by Sy-MSCs include dexamethasone, ascorbic acid, ITS + premix, proline, sodium pyruvate, and TGF-β growth factor [18, 23]. TGF-β superfamily is known to stimulate chondrogenesis differentiation of MSCs. Due to the presence of TGF-β receptors, they undergo dimerization and phosphorylation-dependent signaling events, which are transduced by smad and non-smad pathways to the nucleus. In the nucleus, SOX-9 gets activated to induce the chondrogenic gene expression [80, 81].

Researchers studied the usage of TGF-β superfamily and BMPs in Sy-MSCs induced chondrogenesis. TGF-β1 induced chondrogenesis in the presence of Sy-MSCs pellets obtained from a rabbit model and dexamethasone [82]. Both Sy-MSCs pellets and TGF- β1 induced chondrogenic explant showed positive expression for collagen type II, which is an essential marker for chondrogenesis [82]. Shirasawa et al. demonstrated improved chondrogenesis with the combination of TGF- β3, dexamethasone, and BMP-2 with Sy-MSCs pellets [29].

A superior chondrogenic differentiation of Sy-MSCs has been observed with the simultaneous application of TGF-β1 and IGF-1 [83]. Along with chondrogenic differentiation, the higher amounts of glycosaminoglycan production were observed when Sy-MSCs were seeded along with 3D polyglycolic acid scaffolds and simultaneous application of TGF-β1 and IGF-1 [84]. Shintani et al. demonstrated the superior potential of BMP-2 and -7 in the induction of chondrogenesis than TGF-β1 [85]. A higher dose of BMP-7 in the presence of TGF-β1 demonstrated the enhanced chondrogenesis by Sy-MSCs [81]. Research is still going on to observe the appropriate concentrations of various growth factors for chondrogenesis by Sy-MSCs. The summary of the studies on in-vitro chondrogenicity by Sy-MSCs is given in Table 2.

In-Vivo Chondrogenicity by Sy-MSCs

Considering the common developmental lineage of the synovial membrane and articular cartilage, Sy-MSCs exhibit a greater capacity to accentuate chondrogenesis when applied to osteoarthritis models in animals. Ozeki et al. [49] in their study showed that Sy-MSCs halted the progression of collagenase-induced osteoarthritis in a rat model. They also evaluated the number of injections of Sy-MSCs needed for the management of osteoarthritis in their murine model. They have shown that the injected Sy-MSCs upregulated the expression of genes related to the chondroprotection such as PRG-4, BMP-2, and BMP-6 over 50-folds. Apart from chondroprotection, they also noted enhanced expression of TSG-6 responsible for immune-modulation and halt the inflammatory cascade [49].

Schmal et al. [86] compared the ability of the allogenic Sy-MSCs to repair the osteochondral lesions in the rabbit femur. They noted improved macroscopic regeneration in the Sy-MSC group compared to the controls. Pei et al. [87] in their study confirmed smooth hyaline cartilage from the regenerated cartilage after following it up for 6 months. Li et al. [88] qualified the cartilage quality of the osteochondral lesions repaired through Sy-MSCs in rabbit knees revealed greater tissue quality in the treated animals. Several studies investigated the effects of scaffolds in mediating the action of Sy-MSCs. Lee et al. [89] in their study investigated platelet-rich plasma to deliver the Sy-MSCs to regenerate full-thickness chondral lesions. The treated group showed significant microscopic and macroscopic scores at 6 months follow-up. Shimomura et al. [90] combined Sy-MSCs with hydroxyapatite (HA) and implanted them into full-thickness cartilage lesions in rabbits. They demonstrated that compared to the control group where only HA was used, subjects with Sy-MSCs and HA showed faster integration and improved osteochondral appearance while the controls demonstrated osteoarthritis-like features at 6-month follow-up. Various studies utilized porcine models to evaluate the porcine Sy-MSCs and found them effective in regenerating partial and full-thickness chondral lesions with improved ICRS score and macroscopic appearance [91].

With regards to human Sy-MSCs, Li et al. [53] utilized Sy-MSCs from arthroscopic washing fluid and studied their effect on murine models, and found superior results

Table 2 In-vivo chondrogenicity by Sy-MSCs

Author	Objective	Animal	Inference
Ozeki et al. [49]	Investigated the effects of single or repetitive intra-articular injections of Sy-MSCs	Rat osteoarthritis model	Periodic injections of Sy-MSCs maintained viable cells without losing their MSC properties in knees and inhibited osteoarthritis progression by secretion of trophic factors
Schmal et al. [86]	Compared the regenerative tissue quality following matrix-associated cell implantation using amplified chondrocytes compared to Sy-MSCs for cartilage lesions	Osteochondral lesions in rabbit femur	Cartilage regeneration following matrix-associated implantation using allogenic undifferentiated synovium-derived stem cells in a defect model in rabbits showed similar macroscopic results and collagen composition compared to amplified chondrocytes; however, biomechanical characteristics and histological scoring were inferior
Pei et al. [87]	Investigated engineered Sy-MSCs to repair allogeneic full-thickness femoral condyle cartilage	Osteochondral lesions in rabbit knees	Confirmed smooth hyaline cartilage from the regenerate cartilage after following it up for 6 months and hence allogeneic Sy-MSC based premature tissue constructs are a promising stem cell-based approach for cartilage defects
Li et al. [88]	To analyze cartilage repair tissue quality following Sy-MSCs transplantation in osteochondral defect	Osteochondral lesions in rabbit knees	Qualified the cartilage quality of the osteochondral lesions repaired through Sy-MSCs in rabbit knees revealed greater tissue quality in the treated animals
Lee et al. [89]	To determine the in-vivo effectiveness of Sy-MSCs encapsulated injectable PRP gel in the repair of damaged articular cartilage	Osteochondral lesions in rabbit knees	Platelet-rich plasma to deliver the Sy-MSCs to regenerate full-thickness chondral lesions. The treated group showed significant microscopic and macroscopic scores at 6 months follow-up
Shimomura et al. [90]	Combination therapy of Sy-MSCs with HA	Full-thickness cartilage lesions in rabbits	Subjects with Sy-MSCs and HA showed faster integration and improved osteochondral appearance while the controls demonstrated osteoarthritis-like features at 6-month follow-up
Li et al. [53]	Utilized Sy-MSCs from arthroscopic washing fluid loaded on to cross-linking hyper-branched polyPEGDA/HA hydrogel	Full-thickness cartilage defects generated in a murine model	Superior results obtained in repairing the chondral lesions compared to the controls or untreated groups. Human arthroscopic flushing fluid-MSCs are a novel and abundant MSC source that have high therapeutic value for cartilage regeneration
Shimomura et al. [55]	To assess the safety and efficacy of using a scaffold-free tissue-engineered construct (TEC) derived from autologous Sy-MSCs for effective cartilage repair	Osteochondral lesions of human knees	Autologous scaffold-free TEC derived from synovial MSCs may be used for regenerative cartilage repair via a sutureless and simple implantation procedure in osteochondral lesions of knee
Sekiya et al. [92]	To investigate the efficacy of Sy-MSC transplantation in cartilage defects	Femoral condyle chondral lesions of human knees	Transplantation of Sy-MSCs may be less invasive than mosaicplasty and autologous chondrocyte implantation and found superior in treating femoral osteochondral lesions

in repairing the chondral lesions compared to the controls or untreated groups. Shimomura et al. [55] performed autologous in-vitro cultured Sy-MSC transplantation obtained from an arthroscopic biopsy in 5 patients with a 1.5–3 cm^2 chondral lesion. All the patients demonstrated full defect filling at 48 weeks assessed by MRI without any adverse events. Tissue integration and chondrogenesis were also assessed histologically and found to be strongly stained for Sekiya et al. [92] used Sy-MSC transplantation for symptomatic femoral condyle chondral lesions in ten patients and noted significant improvement on MRI scores post-intervention. Histological evaluation showed hyaline cartilage and fibrous cartilage without any deterioration in the Tegner Activity Level Scale [93–96]. Summary of the studies on in-vitro chondrogenicity by Sy-MSCs is given in Table 3.

Engineered Chondrogenesis

The concept of "Engineered Chondrogenesis" came into existence to redifferentiate the de-differentiated chondrocytes in 3D culture systems [97]. Once de-differentiated chondrocytes are cultured in 3D culture systems, it is possible to recover the phenotypic and metabolic properties of chondrocytes. The limitations of 3D culture systems are due to the size of the tissue mass. 3D scaffolds either natural or synthetic that are made up of Sy-MSCs admixed with fibrin gel when cultured with chondrogenic media display a higher expression of cartilaginous characteristics with the expression of Sy-MSCs derived exosomes, proteins for type 2 collagen, aggrecan, and genes for SOX-9 expression [98].

The long-term benefits of 3D scaffolds are questionable, though the results of 3D scaffolds are encouraging. To overcome the potential risks, tissue-engineered constructs (TEC) composed of porcine Sy-MSCs and relevant ECMs generated in-vitro have been developed [99]. TEC cultured in a chondrogenic rich medium exhibits the higher expression of chondrogenic markers and their genes. TEC with human Sy-MSCs along with chondrogenic medium expressed the chondrogenic markers to a similar level as seen in TEC with porcine Sy-MSCs. With the presence of ascorbic acid, significant improvement in the mechanical strength of TEC is noted [100]. The adherence of more than 60% of cells was observed when Sy-MSCs were suspended on a rabbit cartilage defect. This phenomenon explains the direct adherence of Sy-MSCs to cartilage defects with minimal invasion and without the usage of periosteal coverage and scaffolds [101]. When physiological hydrostatic pressure is applied to Sy-MSCs in-vitro, it displays a significant expression of chondrogenic markers [102].

Future Perspectives

Kohno et al. [94] have shown that cellular yield and chondrogenic potential of Sy-MSCs were comparable in patients with rheumatoid arthritis and osteoarthritis and hence the indications for regenerative medicine using primary autologous Sy-MSCs are expanding. Overcoming the horizons of cellular therapy, exosomes derived from the Sy-MSC are being tried for their therapeutic potential in osteoarthritis. Zhu et al. [96] in their study showed the chondrocyte migration and proliferation when stimulated with Sy-MSC-derived exosomes. Being an inexhaustible autologous source, Sy-MSC-derived exosomes represent the future in the management of osteoarthritis and diseases of a similar kind.

Conclusion

Sy-MSCs demonstrates their regenerative mechanisms through paracrine signaling, direct cell–cell interactions, and extracellular vehicles. Sy-MSCs have been shown to possess superior chondrogenicity than other sources of mesenchymal stromal cells. Hence, Sy-MSCs remain a potential source of MSCs in the management of cartilage loss in osteoarthritis.

Table 3 In-vitro chondrogenicity by Sy-MSCs

Author	Objective	Animal/medium	Inference
Koga et al. [79]	Compared the in chondrogenic potential of rabbit MSCs	Cartilage defects in rabbits	Demonstrated an enormous cartilage matrix production after 4 weeks by synovium and bone marrow-derived MSCs when admixed with collagen gel transplanted into rabbit cartilage defects
Shirasawa et al. [29]	Investigated the optimal conditions for in-vitro chondrogenesis of human Sy-MSCs and compared with BM-MSCs	Six donors during knee operations for ligament injuries	Demonstrated improved chondrogenesis with the combination of TGF-β3, dexamethasone, and BMP-2 with Sy-MSCs pellets. Sy-MSCs have a greater chondrogenesis potential than BM-MSCs
Pei et al. [83]	To define cocktails of growth factors that support the growth and chondrogenic differentiation of Sy-MSCs in chemically defined medium	Dulbecco's modified Eagle's medium	Proposed a two-step protocol for the derivation of chondrogenic Sy-MSCs: a cocktail of TGF-β1, IGF-I, and FGF-2 is applied first to induce cell growth followed by a cocktail of TGF-β1 and IGF-I applied to induce chondrogenesis
Sakimura et al. [84]	To demonstrate the induction of chondrogenesis by TGF-β1 from Sy-MSCs in a 3D polyglycolic acid scaffold	Human synovial membranes from the knees of patients with osteoarthritis or rheumatoid arthritis	Along with chondrogenic differentiation, the higher amounts of glycosaminoglycan production were observed when Sy-MSCs were seeded along with 3D polyglycolic acid scaffolds and simultaneous application of TGF-β1 and IGF-1
Shintani et al. [85]	To compare the potential of BMP-2 and -7 and TGF-β1 to effect the chondrogenic differentiation of synovial explants	Synovial explants from the metacarpal joints of calves	Demonstrated the superior potential of BMP-2 and -7 in the induction of chondrogenesis than TGF-β1
Miyamoto et al. [81]	To investigate the effects of osteogenic protein-1 with or without TGF-β1 on chondrogenesis of human MSCs in-vitro	Synovial membrane of patients with rheumatoid arthritis undergoing TKR	A higher dose of BMP-7 in the presence of TGF-β1 demonstrated the enhanced chondrogenesis by Sy-MSCs

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed consent For this type of study informed consent is not required.

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ORIGINAL ARTICLE

Study of Cell Viability and Etiology of Contamination in Decalcified Bone Allograft: A Pilot Study

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Abstract

Background Bone allografts can elicit immune responses which is correlated with the presence of Human Leukocyte Antigen (HLA) and cellular DNA. It also has risk of causing occult infection arising out of contamination during its processing and storage. The presence of immunogenic materials like cells, cellular remnants and DNA in a decalcified bone allograft during different phases of processing has never been studied. Present study was conducted to explore- the cell viability using routine Hematoxylin and Eosin, presence of DNA using Feulgen staining and etiology of contamination in decalcified bone allograft during procurement, demineralization and ethanol preservation.

Methods The harvested bones from patients undergoing hemireplacement/THR/TKR were processed to prepare decalcified bone allografts. The samples during procurement (A), HCL treatment (B) and ethanol preservation (C) were sent for histopathological analysis (number of osteocytes in the maximum density field under 40x and the cells demonstrating presence of DNA on feulgen stain) and microbiological assessment (aerobic/anaerobic/fungal cultures).

Results Histopathological study demonstrated the presence of osteocytes and other cells like bone marrow, adipocytes, endothelial cells in the decal bone allograft. The average number of osteocytes gradually decreased from 55.47, 9.6, 0.86 in sample A, B, C, respectively. Feulgen staining confirmed the presence of DNA in osteocytes and other cells which decreased both qualitatively and quantitatively in subsequent stages of processing. Rate of contamination demonstrated at the procurement was 6.67% (*Staphylococcus aureus*). After treatment with HCl (demineralisation), 7.14% of non-contaminated allografts were found contaminated (*Staphylococcus epidermidis*). None of the remaining 13 non-contaminated allografts showed contamination after storage in ethanol. Overall 13% of the patients had positive cultures on microbiological assessment.

Conclusion The population of osteocytes in the harvested bone reduced significantly after processing with HCl and ethanol preservation. Presence of DNA, demonstrated by using Feulgen staining, was observed in bone marrow cells, adipocytes along with osteocytes which showed quantitative reduction on processing. Hence, antigenicity, conferred by cells and their DNA, reduced significantly after processing of decal bone. Contamination rate of banked decalcified allograft was 13%. Thus, culture and sensitivity tests should be carried out at each step of processing of decal bone allograft.

Keywords Allograft · Decal bone · Contamination · Bone bank · Feulgen staining · Bone morphogenic protein

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Introduction

Bonegrafts are required to reconstruct bone defects and augment bone healing [1].The autologous bonegraft is gold standard but with limited availability and additional donor site surgical complications as limiting factors [2]. Allografts can be used as a strut/buttress/to fill up cavities or as an augmentation in combination with autografts but with limited osteoconduction and osteoinduction properties [3]. They can be prepared from bone harvested following hemiarthroplasty/THA (head of femur) /femoral/tibial condyles following TKA or from freshly amputated limbs/cadavers.

Three types of bone allografts are Fresh frozen, Freeze-dried and Demineralised (or Decalcified) bone allografts.

Fresh Allografts are characterized by high resorptive activity and are associated with vigorous inflammatory as well as specific immune response. Due to development of better processing methods and understanding of immune responses, fresh bone allografts are rarely used now [4]. Frozen bone allografts, after harvesting, are stored as a sterile specimen at − 80 °C until transplanted. Freeze drying, where bone is freezed to make it dehydrated, alters the mechanical properties necessitating reconstitution (rehydration) of the graft while implantation. Decalcified/Demineralized bone allograft is promising/cost-effective as processing/preparation requires few chemicals and domestic refrigerator, making it economically viable and large volumes can be prepared/stored in a hospital/centres with limited resources.

Bone allografts can elicit immune responses in the hosts which may be triggered by the bone components, such as cells/collagen/fat/or matrix proteins, and is strongly correlated with the presence of Human Leukocyte Antigen (HLA)—a membrane bound immunological receptor [5]. Also, the cellular DNA may act as a trigger for a strong immune response through the cGAMP synthase enzyme [6]. The risk of occult infection due to contamination of allograft while harvesting/processing despite established tissue banking protocols is real [7, 8].

Present study was conducted to explore the cells/remnant DNA after processing of decalcified bone allograft using Feulgen staining to document the immunogenicity. The potential contamination of decalcified bone allograft, its microbiological culture during different phases (procurement, HCl treatment, ethanol preservation) of processing was analysed.

Fig. 1 Procured bone being washed with normal saline

Fig. 2 Removal of soft tissue attached to the procured bone using bone nibbler

Material and Methods

The prospective observational study was conducted at a tertiary care center, New Delhi (November 2018–June 2020). Bone samples were harvested in 15 cases from the femoral head of the eligible patients undergoing Hemiarthroplasty/Total hip replacement and femoral/tibial condyles after TKA after obtaining informed written consent. The exclusion criteria to harvest bones were patient having history of malignancy/active infection/autoimmune disorders/taken live vaccine within 4 weeks/positive serology for HIV/HBV/HCV/history of diabetes mellitus/endocrine disorders and narcotics use (persons who report to non-medically administered IV/SC/IM injection of addictive drugs like heroine).

A thorough physical examination (to look for unexplained generalized lymphadenopathy, needle tracks or other signs of parenteral drug abuse, oral thrush, genital ulcers, etc.) of the prospective bone donor was carried out to rule out any active infection in the body. Blood samples were sent for blood grouping, CBC, ESR, CRP, serology for HIV/Hepatitis C/Hepatitis B preoperatively. Decalcified bone allografts were processed under aseptic condition by 'sterile double jar technique' developed by Nather [9, 10].

The procured bone was profusely washed with normal saline to remove blood/fluids (Fig. 1) and cleaned of any attached soft tissues (Fig. 2). Bone was then washed with hydrogen peroxide (Fig. 3A, B) followed by an antibiotic solution(1gram Vancomycin/100 ml saline) and finally washed with copious saline.Small piece (of size 1 cm × 1 cm × 1 cm, made using manual osteotome) from the harvested bone was sent (SampleA) for aerobic/anaerobic/fungal cultures, and for histopathological examination and feulgen staining (DNA analysis).

Fig. 3 Treatment of procured bone with Hydrogen Peroxide

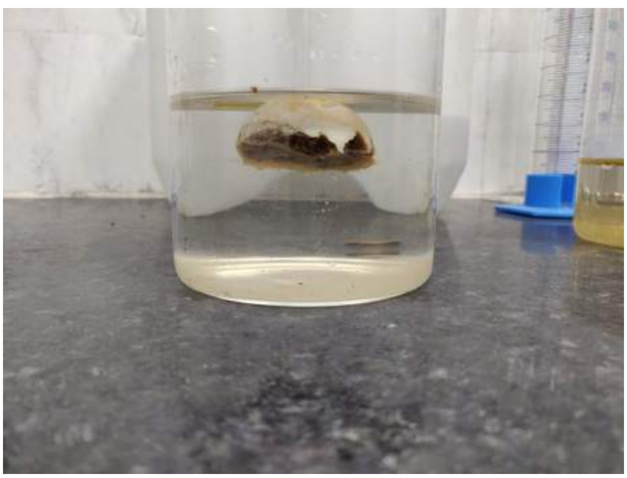

Fig. 4 After the end of decalcification process in 0.6 N HCl, femoral head starts floating in the HCl solution

Fig. 5 Decalcified bony specimens (preserved in 70% ethanol) kept in domestic refrigerator

The harvested bone was then placed in a sterile closed jar which was then put into a slightly larger outer jar and was sealed. The closed, sterile double jar covered with a sterile drape was labelled and was then transferred to the institute's bone bank. In the bone bank, the procured bone was then put into a sterile glass beaker containing freshly prepared 0.6 N HCl (53 ml of HCl + 947 ml of distilled water) to achieve the decalcification. The bone was kept in the acid solution till it starts floating on the surface of the solution (Fig. 4) which marked the end of the decalcification.

Decalcified bony specimen was then taken out from the jar under all aseptic precautions and was washed with copious volume of distilled water to neutralize the remaining acid. The bone samples (Sample B) were sent for aerobic/anaerobic/fungal culture and histopathology/DNA analysis. The decalcified harvested bone was then preserved in 70–90% ethanol in the domestic refrigerator (Fig. 5). At the completion of 3 months of ethanol preservation, two small bony pieces from the harvested bone were again sent (Sample C) for aerobic/anaerobic/fungal culture and histopathology/DNA analysis. The donor was again followed-up at 6 months post-harvesting for serological (HIV, HBV, HCV) testing and the donors who tested positive, were rejected.Only grafts of seronegative donors were stored for later clinical use.

The samples were inoculated in appropriate culture media and kept for overnight incubation for aerobic isolation, 72 hrs for anaerobic bacterial isolation and 28 days for fungal isolation. The presence and identification of bacteria & fungus was documented and recorded. Estimation of bioburden (cfu/gm), as done in samples of endotracheal aspirates, urine, etc., was not done as the estimation is not possible in sterile samples like bone/blood/CSF.

For histopathological analysis, 5–7 micron thick sections were cut from the specimen and stained with haematoxylin and eosin stain (H&E) to study organic, inorganic, cellular components, lacunae and number of osteocytes. A trinocular microscope (Nikon Eclipse 80i) was utilized to count the number of osteocytes. They were counted manually under 40x in 3 fields of maximum cell density and then the average was taken. All other cells (hematopoietic bone marrow cells, endothelial cells, adipocytes etc.) demonstrating the presence of DNA on feulgen staining were studied.

Results

4 bone donors were male while 11 were female. The average age was 64 (40–75) years. 9 Patients underwent hemiarthroplasty for fracture neck of femur ($n=8$)/fracture intertrochanteric femur ($n=1$). 6 Patients of OA knee underwent TKA.

Histopathological Analysis

All samples showed numerous lacunae filled with variable number of osteocytes, which were apparent both on H&E and Feulgen staining. On histopathological study, the average number of osteocytes detected (under 40x) in maximum density area gradually decreased from 55.47 to 9.6 to 0.86 in sample A,B,C, respectively. This signifies the quantitative decrease in osteocytes due to processing of decalcified bone allograft.

Feulgen staining confirmed the presence of DNA in all types of our tissue samples (Sample A, B, C). The staining technique was first standardized using sections from the reactive lymph node (Fig. 6a). Sample A showed characteristics lamellar pattern of bone and purplish-red Feulgen staining in osteocytes, bone marrow cells and endothelial cells in all patients (Fig. 6b). In Sample B, the lacunae were occasionally filled with osteocytes and feulgen staining showed presence of DNA in osteocytes, bone marrow, adipocytes, endothelial cells (Fig. 6c), though staining was much less, quantitatively as well as qualitatively, as compared to Sample A. Sample C showed homogenous bony architecture and lamellar pattern with empty lacunae and marrow spaces (Fig. 6d). Only 7/15 sample C showed remnant of nucleus.

Microbiological Culture

2/15(13%) of the patients had positive cultures on microbiological assessment. First patient (Case 5) had all the three sample A, B & C, positive for both aerobic and anaerobic cultures but with no growth on fungal culture. The organism isolated was *Staphylococcus aureus* in aerobic and gram-positive cocci in anaerobic (no species was identified further). Second patient (Case 8) had no growth in sample A but had positive growth in sample B and C in aerobic culture and the organism isolated was *Staphylococcus epidermidis.*

Thus, contamination demonstrated at the procurement was 6.67% (*Staphylococcus aureus*).After treatment with HCl (demineralisation), 7.14% of non-contaminated allografts were found contaminated (*Staphylococcus epidermidis*). None of the remaining 13 non-contaminated allografts showed contamination after storage in ethanol.

Discussion

The process of incorporation of autogenous bonegrafts is characterized by formation of new bone over a necrotic graft bed through the dual processes of resorption and substitution. The host response includes local hematoma formation, inflammatory and/or immune reaction to the graft material, processes of cell proliferation, osteoinduction, migration, differentiation and revascularization, resulting in new bone formation and union between graft and host. In fresh allografts, the processes of incorporation is qualitatively similar to those of autograft, but it occurs more slowly and is accompanied by extensive host response mediated by macrophages and lymphocytes via cell membrane receptors(MHC complex).

To reduce immunogenicity and encourage incorporation, allografts are processed (frozen/freeze dried/demineralised) [11]. Resorption, osteoconduction and osteoinduction proceed more rapidly with processed allografts, although remodelling and revascularisation are inferior as compared to autografts. When an allograft is processed via demineralisation, acid extraction of the graft leaves behind growth factors (BMP etc.), non-collagenous protein, and collagen while removing the mineral phase of the bone. This demineralised bone provides a suitable framework allowing instant permeability to reparative mesenchymal cells and neo-capillaries. The close contact between these cells of the host and the 'exposed' bone matrix induces the former to osteoblastic activity, and in successful implants, the original graft is gradually replaced.

The demineralisation in the preparation of decalcified bone allograft is carried out by 0.6 N HCl. The matrix retains high levels of BMP which is responsible for its osteoinductive property [12, 13]. When this decalcified graft is placed at the fracture site, there is osteoclastic and phagocytic resorption of calcium hydroxyapatite and cellular debris. This makes the graft porous through which neovascularization propagates. In decal bone, resorption of demineralized

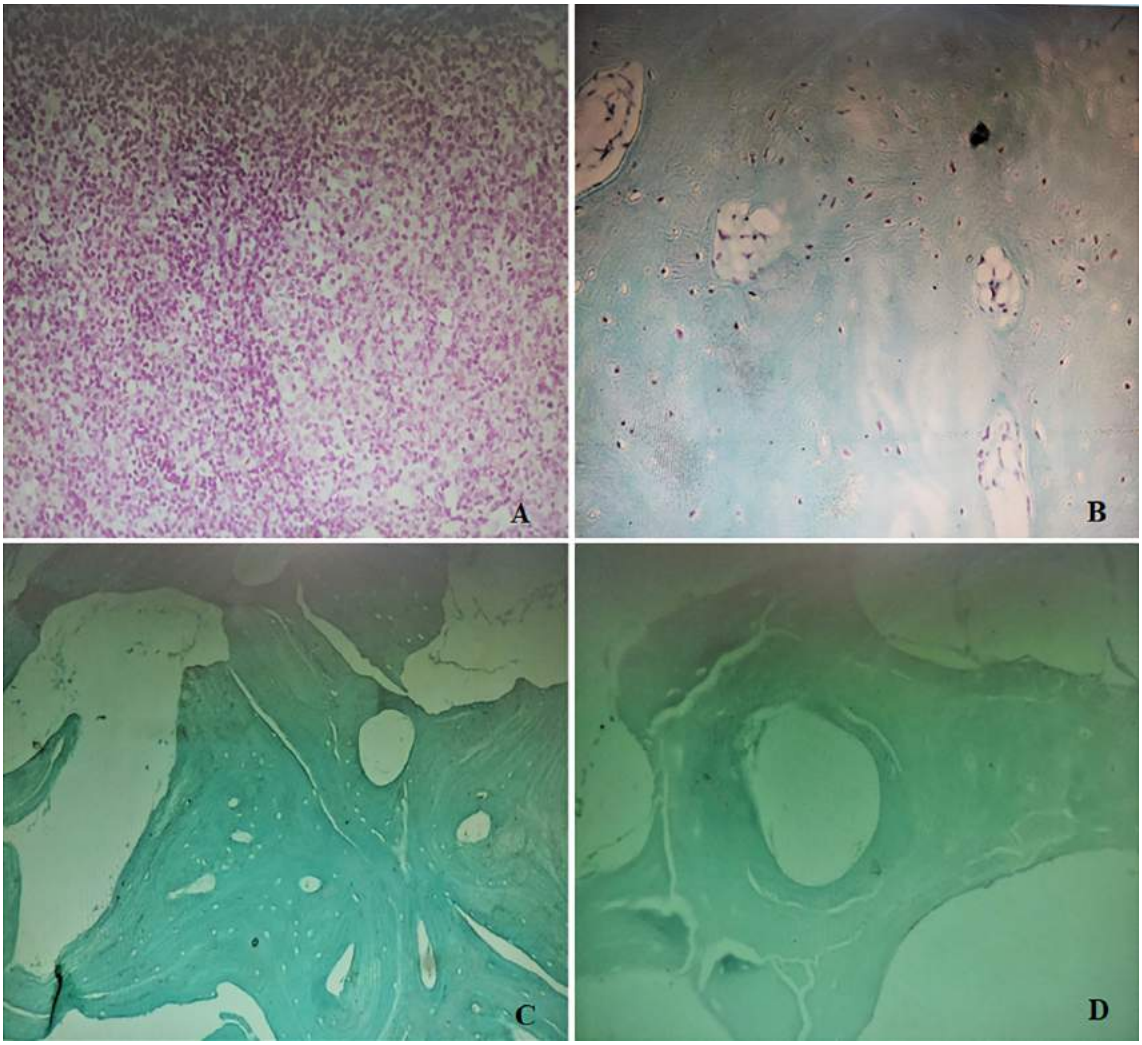

Fig. 6 FEULGEN STAINING (Magnification 40x): **a** Control of feulgen stain on a lymph node biopsy. **b** Feulgen staining after harvesting of bone (numerous osteocytes visible in their respective lacunae along with staining of nuclear material). **c** Feulgen staining after HCl treatment (lamellar structure preserved; osteocytes and lacunae rarely visible). **d** Feulgen staining after ethanol preservation (bony tissue homogenized; no cell, lacunae or nuclear material visible)

matrix is faster because of the prior removal of nearly half of minerals in the laboratory. Thus, decal bone provides an easily permeable scaffolding structure that permits creeping substitution [14].

This study used decalcified/demineralised bone allograft which is ethanol preserved and stored in refrigerator. They are economical and large volumes can be stored in a peripheral set up. But the question of contamination and its immunogenicity still remains.

Immunogenicity

Incorporation of a graft is influenced by the immunogenicity of the graft [15]. Even a decal bone once transplanted in the recipient would also evoke an immunogenic reaction [16]. Such an immunogenic reaction to a bone allograft is of "low threshold" and may last for a longer period; it is unlike allografting of solid organs where the immunogenic reaction is a sudden surge or "spike." This antigenicity of bone can be reduced by processing the allograft by cryopreservation/demineralisation/irradiation, etc.

The number of osteocytes detected (under 40x) in the 15 patient's samples, gradually decreased from an average of 55 per high density field in Sample A to less than 10 in Sample B and to less than 1 in Sample C. Death of osteocytes during decalcification process and storage in ethanol leads to decrease in the number of osteocytes and thereby decrease in the membrane bound immunological receptors, thus reducing immunogenicity, which could otherwise be triggered by the presence of human leukocyte antigen (HLA) on the cell membrane [15]. This is in accordance with a study on immunogenicity of decal bone, in which cellularity (CD4 and CD8 cells) in perigraft area was assessed by fine-needle aspiration cytology and it was concluded that decal bone did not excite an appreciably significant immunological response and partially decalcified allografts are a good substitute of autogenous bone grafts in clinical practice [17].

Also, various authors have described the immunological outcomes of allografting a decal bone over the years (Table 1) none of which have resulted in any local or systemic immune reaction.

Some studies on other types of bone allografts have shown that some viable cells may persist despite the decontamination process, supporting the literature reports on the presence of anti-HLA antibodies in patients receiving allogeneic bone transplants [18–20].

The cellular DNA also may induce an immune reaction as cytosolic DNA may be the trigger of a strong immune response through the cGAMP synthase enzyme [6]. In our study, purplish-red feulgen staining**,** demonstrating the DNA content, was observed in all the decal bone allograft samples at the time of harvesting both in osteocytes and in bone marrow cells, which on subsequent processing by HCl was scarcely visible and after the preservation in ethanol was visible in negligible cells.

Although we did not find any study in the literature commenting on the DNA content of a processed decalcified bone, but Coutinho LF et al. (2017) evaluated the samples of fresh frozen bone grafts from three tissue banks in Brazil and demonstrated that light microscopy images from all the bone samples studied, showed presence of osteocyte-like cells in all groups and intense Feulgen staining, demonstrated the presence of DNA in all bone samples, even after tissue processing [21]. Further, the ultrastructural analysis also showed red blood cells in lacunae within the bone tissue.

Therefore, we can say, that although we were able to demonstrate cells and DNA (Feulgen staining) in the processed decalcified bone allograft but as none of the scientists utilizing decal bone allograft in the past has reported any local or systemic immunogenic reaction in the recipient's body, the ability of these residual cells and nuclear material to provoke immunogenic reaction in recipient's body is limited and insignificant.

Table 1 Results of allografting decal bone in various studies

S. no	Author	Sample size (*n*)	Year	Any local/systemic immune reaction
1	Tuli, Srivastava et al. [36]	25	1988	None
2	Goel, Tuli et al. [14]	46	1992	None
3	Jain, Kumar et al. [16]	20	2015	None
4	Gupta, Keshav et al. [22]	42	2016	None

Contamination

Various studies that have used decalcified bone as an allograft have reported post-operative infection as one of the complications [14, 16, 22]. Contamination during harvesting of the graft from donor and graft handling procedure is reported to range from 1 to 37% depending on the source and method used to culture the micro-organism [23–30]. At the time of procurement, we found 1 out of 15 allografts (6.67%) to be contaminated by aerobic species (*Staphylococcus aureus*). The growth of gram positive cocci in anaerobic culture was identified but specific species was not isolated. No study has reported the contamination rate in a decalcified bone allograft, during harvesting. Although, Chiu CK found the contamination rate of 9.3% in deep frozen/freeze dried allografts, during the time of retrieval of the donor bones (femoral heads) [31]. They found *Staphylococcus epidermidis* as the main contaminating agent during harvesting followed by *Staphylococcus aureus.* After the treatment with HCl, only one allograft out of 14 non-contaminated allografts was found to be contaminated. Thus, contamination rate after treatment with HCl was 7.14% and the contaminating species was *Staphylococcus epidermidis*. *Staphylococcus aureus* grows within a range of pH 4–10 [32]. It is reported that alcohol treatment does not affect the survival of these organisms [33, 34]. In both of our samples, organism survived the ethanol treatment, hence further study are required to resolve the issue.

Staphylococcus epidermidis is a Gram-positive bacterium, and is part of the normal skin flora. Such skin contaminants isolated from bone cultures of possible donors can be possibly due to inadequate decontamination of the patients skin pre-operatively and subsequent manipulation of sample during operative procedures. But, sterile cultures at the time of harvesting (Sample A) and presence of contaminants during the processing phase (Sample B and C) was an unusual but an important finding in this patient. The possible explanation could be peri-operative antibiotic coverage to the patient might have eliminated the organism in Sample A or the amount of bone tissue sent for the culture in Sample A might be insufficient and/or unusual delay in transportation of sample vials from operating theatre to the microbiology laboratory. *Staphylococcus epidermidis* could not be isolated on first culture (Sample A) probably due to any of the above-mentioned reasons. Subsequently the organism probably has survived the decalcification (HCl) and preservation (ethanol), and multiplied and subsequently recovered on cultures of Sample B and Sample C.

The sensitivity and specificity of Nucleic acid amplification technology(NAAT)is superior to culture isolation,

Table 2 Organism isolated post-operatively after allografting decal bone

S. no.	Author	Sample size (*n*)	Year	Isolated organism (in post-operative period)
1	Tuli, Srivastava et al. [36]	25	1988	N/A
2	Goel, Tuli et al. [14]	46	1992	*E. coli*, *Klebsella*, *Proteus* (10.86%)
3	Garg, Dev et al. [37]	16	1997	N/A
4	Jain, Kumar et al. [16]	20	2015	*S. aureus* (5%)
5	Gupta, Keshav et al. [22]	42	2016	*S. aureus* (7.14%)

hence if NAAT would have been applied to SampleA it probably could have identified the bacteria present in low concentration. Interesting thing to note here is, this patient-who had undergone Total Knee Replacement for osteoarthritis of knee, complained of persistent non-purulent serous discharge from the surgical site in follow-up. Multiple cultures of the discharge did not yield organism on culture, which could be explained by the patient being under coverage of intravenous broad-spectrum antibiotics in post-operative period. Although, after 1 month, patient recovered completely. *Staphylococcus epidermidis* is not an uncommon organism isolated in bone allograft cultures. L Sims studied the intraoperative cultures of 996 allograft bones and found that 43 (4.3%) had positive cultures and identified *Staphylococcus epidermidis* as the most common (22%) contaminating agent [35].

Authors have utilized decalcified bone (decal bone) allografts in various procedures like in repairing benign cystic lesions of bone, in repairing lytic lesions of bone, filling large osteoperiosteal gaps and repairing delayed union/atrophic non-union of bones [14, 22, 36, 37]. These authors reported complications arising out of allografting decal bone including post-operative infection (Table 2).

Hence, we recommend that the culture and sensitivity tests should be carried out at each step of processing viz. procurement, after decalcification (HCl)and after ethanol preservation so that any sample of contaminated allograft can be excluded well before clinical use.

Conclusion

The population of osteocytes in the harvested bone reduced significantly after processing with HCl and ethanol. Presence of DNA was also demonstrated by Feulgen staining in bone marrow cells, adipocytes etc. along with osteocytes in these samples which showed quantitative reduction on processing. Hence, antigenicity, conferred by cells and their DNA is reduced significantly after processing of decal bone.

Contamination rate of banked decalcified allograft was found to be13% with isolated species as *Staphylococcus epidermidis* and *Staphylococcus aureus*.

This study established a histopathological evidence of the safety of decalcified bone allograft in terms of its antigenicity as done previously by other authors for fresh frozen allografts [21]. Decalcified bone allograft is a feasible option for limited resource countries as its processing and storage requires few chemicals and domestic refrigerator, making it economically viable and large volumes can be prepared/stored in a hospital/centres with limited resources. This would help to fulfil the unmet needs of bone allografts. However, to negate the risk of disease transmission, microbiological cultures must be carried out at each step of processing of decal bone allograft.

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Declarations

Conflict of interest There is no conflict of interest of above-mentioned authors in this study.

Compliance with Ethical Standards The authors declare that the above manuscript is in compliance with ethical standards for research, and have no potential sources of conflict of interest associated with its publication.

Ethics Approval All procedures were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards

Informed consent All participants involved were recruited only from UCMS and GTB Hospital, Delhi, after getting an appropriate ethical clearance from the institutional board and after taking an informed consent. The authors also certify that informed consent was obtained from all the human participants in this study.

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ORIGINAL ARTICLE

Role of WNT Agonists, BMP and VEGF Antagonists in Rescuing Osteoarthritic Knee Cartilage in a Rat Model

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Abstract

Introduction The superficial zone of articular cartilage (AC) is vital for its function and biomechanics. The damaged AC gets vascularized and undergoes hypertrophy and ossification. Studies have highlighted these two as the major causative factors in osteoarthritis (OA). We aimed at preventing the OA progression in a rat knee instability model by inhibiting the vascular ingrowth and ossification using VEGF and BMP antagonist. A WNT agonist was also used to promote AC regeneration because of its protective effect on the superficial layer.

Methods Rat knee OA was created by surgical excision of the medial meniscus and medial collateral ligament. Forty rats were divided into two groups of twenty each for surgical control and tests (surgery + intra-articular injection of drugs every two weeks). Ten animals from each group were sacrificed at four and eight weeks. Histology was mainly used to evaluate the outcome.

Results A surgical OA model was successfully created with higher histological scores for operated knees, both in short- ($P=0.0001$) and long-term ($P=0.001$). Modified Mankin score was lesser in the test animals as compared to control ($P=0.17$) in the short-term, but the trend was reversed in the long-term ($P=0.13$). Subgroup analysis revealed that repeated injections in the anterolateral compartment contributed to higher scores in the lateral ($P=0.03$) and anterior ($P=0.03$) compartment of the knee in the long-term.

Conclusion The combinatorial approach was effective in controlling the OA in short-term. Further studies are needed to test the sustained drug delivery system to improve the outcome.

Keywords Surgical model · Rat model · Osteoarthritis · Intraarticular injection · Histopathology · Micro-CT

Sanjay K. Chilbule and Karthikeyan Rajagopal have contributed equally to this study and should be considered as first co-authors.

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Introduction

Worldwide, osteoarthritis is estimated to be the most prevalent cause of disability. It is often secondary to the causes such as trauma, inflammation or malalignment of the limb [1]. Such secondary osteoarthritis is characterised by a progressive loss of articular cartilage, osteophyte formation, thickening of subchondral bone, and subchondral cyst formation [2].

Underlying osteoarthritis involves inflammation and angiogenesis, modulating chondrocytes' functions, contributing to abnormal tissue growth and perfusion, ossification, and endochondral bone development [3]. Normal articular cartilage is avascular, but osteoarthritic cartilage is invaded by blood vessels from the subchondral bone and surrounding synovium [4]. This vascular invasion into the aneural cartilage promotes nerve ingrowth and causes joint pain.

The vascular endothelial growth factor is higher in the osteoarthritic cartilage, which promotes the expression of matrix metalloproteinases (MMPs), interleukin-1 (IL-1), tumour necrosis factor alpha (TNF α) and nitric oxide (NO) [5]. It has been considered a therapeutic target, and its suppression inhibits osteophyte formation and progression of osteoarthritis [5]. Bevacizumab, one of the monoclonal antibodies to VEGF, is being used widely in malignancies and retina to decrease neovascularization [6]. Studies, both in chondrocytes and animal models, support the notion that inhibiting angiogenesis will provide effective therapeutic strategies for treating osteoarthritis [5, 7].

The bone morphogenetic protein (BMP) action on the mesenchymal stem cells (MSC) is anabolic and promotes the expression of cartilage-specific matrix [8]. However, during cartilage repair, its action is catabolic [9]. It is activated during cartilage injury and acting on the damaged cartilage's chondrocytes; the SMAD 1/5/8 signalling route causes hypertrophy and increased expression of MMPs [9, 10]. The overall effect is damaged matrix and osteophyte formation.

Wnt signalling is vital for AC maintenance, especially in increasing the AC's superficial zone's cellularity and thickness. The superficial layer provides a smooth gliding surface and resists the shear stress generated during movement. Its damage initiates degenerative changes in the cartilage, and loss leads to severe osteoarthritis. Wnt signalling inhibition in Col2a1-ICAT-transgenic mice has caused severe degeneration of AC and late osteoarthritis [11]. Therefore, we hypothesised that Wnt signalling's activation would protect the AC from mechanical stress and prevent osteoarthritis progression.

This study targeted the three known mediators of the osteoarthritic process, namely BMP signalling, VEGF and Wnt pathway. We used a combination of three drugs, Bevacizumab, to reduce neovascularization associated with VEGF, dorsomorphin to decrease BMP-directed hypertrophic transformation of the articular cartilage and BIO to activate the Wnt signalling pathway. These drugs were introduced intra-articularly into a surgically created rat knee model of osteoarthritis with the hypothesis that the combination will delay osteoarthritis.

Materials and Methods

This study was approved by the institutional review board (IRB) and the animal ethics committee (IAEC). A surgically induced unstable knee model of osteoarthritis was created. The test group received an intra-articular injection of the three selected drugs at the time of surgery, and in the long-term group, three further doses at two weeks interval. There were 20 animals each in the short-term (four weeks) and long-term (eight weeks), ten each as test and control. Ten animals were deemed sufficient for any surgical response variability in each group [12, 13]. At sacrifice, the knees were harvested and cartilage degeneration on histology assessed by Mankin score.

Animal Experiments

Six-to-seven-month-old male Sprague–Dawley rats were procured from and underwent further experimentation at the centre's small animal facility. A temperature-controlled environment with the restricted entry (22 ± 3 °C), with 55 ± 5% relative humidity and a 12-h light/dark cycle was maintained and rats were fed on SAFE® D131 (Safe Diets, Augy, France) and filtered water ad libitum. They roamed free in the cages after the surgical intervention.

Creation of the Surgical Model

Anaesthesia induction was carried out using inhalational anaesthesia with 2.5–3% isoflurane with oxygen 1–2 L/min. Ketamine (90 mg/kg) and xylazine (10 mg/kg) were injected intraperitoneally (IP) to provide sedation during the surgery and postoperative period. Preoperative ciprofloxacin 10 mg/kg IP was injected and was repeated on the next postoperative day. Meloxicam 1 mg/kg IP was given preoperatively and postoperatively for two days for pain control. Under sterile precautions, in biosafety level (BSL) II, surgical procedures were carried out with the animal in the supine position after shaving and preparing the lower limb with 10% povidone–iodine and 70% ethanol. Through a medial parapatellar approach, the medial collateral ligament (MCL) was severed. And medial meniscectomy was done. The joint capsule and skin were closed in layers using absorbable subcuticular sutures.

Animals were sacrificed at the end of four or eight weeks using the CO_2 asphyxiation protocol [14].

Animal Groups

Four animals were used to create a surgical osteoarthritis model and standardisation of injection protocols with two rats in the surgical (S) and surgery with drugs group (SD). One rat each for S and SD was sacrificed at four weeks (short-term) and eight weeks (long-term) postoperative to standardise the evaluation protocols.

Subsequently, forty rats underwent surgery to create right knee instability. Animals were segregated into two groups; S and SD group with 20 in each. The left knee acted as internal control with no intervention. The contralateral knee in the S group is marked as N (normal knee) and ND (normal knee in drug-treated) in the SD group. Ten animals from each group were sacrificed at four and eight weeks after the surgical intervention. The knee joints were harvested and processed for histology.

Intraarticular Drug Administration

The intra-articular drugs were calculated from either human dose (for therapeutic applications) or concentrations used in previously published murine studies adjusting to the rat's body weight. The following drugs and doses were used:

(1) 6-Bromoindirubin-3′-oxime (BIO from Tocris, Minneapolis, MN, USA), a WNT agonist, was used in the dose of 0.2 mg/kg based on the publication by Wang et al. for osteoporosis in rats [15].
(2) Bevacizumab (Inj Avastin, Roche, Basel, Switzerland), a recombinant humanised monoclonal anti-VEGF antibody, used in ophthalmology to decrease the neovascularisation, retina and colonic/ lung carcinoma. Based on a dose of 2.5 mg for an eye volume of 6 ml, we calculated a dose of 0.4 mg/per ml of knee volume or body weight and arrived at a final dose of 0.2 mg after measuring the rat knee's maximum distension to be 0.5 ml. A final dose of 0.2 mg diluted in 100 µl was selected [6].
(3) Dorsomorphine Hydrochloride (dorsomorphin from Tocris, Minneapolis, MN, USA), a BMP antagonist, was used in the dose—5 mg/kg based on dose for mice used by Pochori et al. [16].

Each SD group animal received 168 µl (100 µl Avastin + 28 µl BIO + 40 µl dorsomorphin) of drugs in the joint immediately after surgery and closure as the first dose, and in the long-term group at two, four and six weeks, under inhalational anaesthesia using isoflurane. Injections were carried out using a 31-gauge needle in the anterolateral compartment of the knee and was deemed not to cause overdistension.

Histopathological Assessment of Osteoarthritis

Histopathology of articular cartilage was assessed by one of the authors, an experienced pathologist specialising in orthopaedics and experienced in assessing in vivo cartilage regeneration. During assessments of modified Mankin score for osteoarthritis, he and his assistant were blinded to the study groups.

Five-micron sections were taken from the anterior and posterior halves of the medial and lateral condyle to get four representative sections from the joint. The joints were then histologically scored on Safranin-O-stained slides for the four quadrants, anteromedial, anterolateral, posteromedial and posterolateral. Modified Mankin's score is used for the evaluation, which is previously validated for assessment of cartilage regeneration in osteoarthritis [17, 18]. Tibia and femur were assessed separately and an average of the four scores taken for the outcome. The mean of the scores from the four areas was considered as the score for each joint. Subgroup analysis for the medial, lateral, anterior and posterior compartment was done using the mean of the scores achieved for these respective areas.

Radiological Evaluation

High-resolution micro computerised tomography (HR-micro CT) was carried out using IVIS® Spectrum CT imaging system (PerkinElmer Santa Clara, CA, USA) on the gross specimens of the knee joints soon after the animal sacrifice ($n = 2$ in each group, a total of eight animals). These provided an additional qualitative assessment of osteoarthritic joints.

The outcome of the test group (SD) was compared with the normal opposite knee (N and ND) and surgical controls (S) using an unpaired *t*-test. Each quadrant score of SD was compared with the S group using an unpaired *t*-test. The incidence of osteoarthritis after treatment was compared with the control using Fisher's exact test.

Results

Osteoarthritis Model

A surgical model for osteoarthritis was successfully established in the operated rat knees (Fig. 1A–L). At two weeks after the surgical defect, the histological assessment showed the early sign of osteoarthritis, i.e. loss of glycosaminoglycans in the operated knee (Fig. 1C). There was a marked inflammatory pannus associated with angiogenesis and osteophytes at the cartilage margin at four weeks (Fig. 1D–H). At eight weeks, articular cartilage underwent further degeneration and developed severe osteoarthritis. Severe cartilage destruction and eburnation accompanying subchondral cyst and growth plate aberration were seen (Fig. 1H–L). Overall, the results were qualitatively supported by the micro-CT and the coronal, axial and sagittal sectional images illustrated the osteophyte formation and reduced joint space in the operated knee (Fig. 1M–P). Grading of osteoarthritis development using modified Mankin scores also confirmed that there was a statistically significant difference in the Mankin scores of the operated knee (S) and the opposite knee (N) in short- (5.6 ± 1.07 vs 3.0 ± 0.8, $P = 0.0001$) and long-term (5.5 ± 0.8 vs 3.9 ± 0.9, $P = 0.001$) in the control group (Fig. 2A).

Characteristics of the Surgical Model Compared to the Opposite Normal Side

In the animal model, there were osteoarthritic changes in the control group's normal knees (N). These scores were

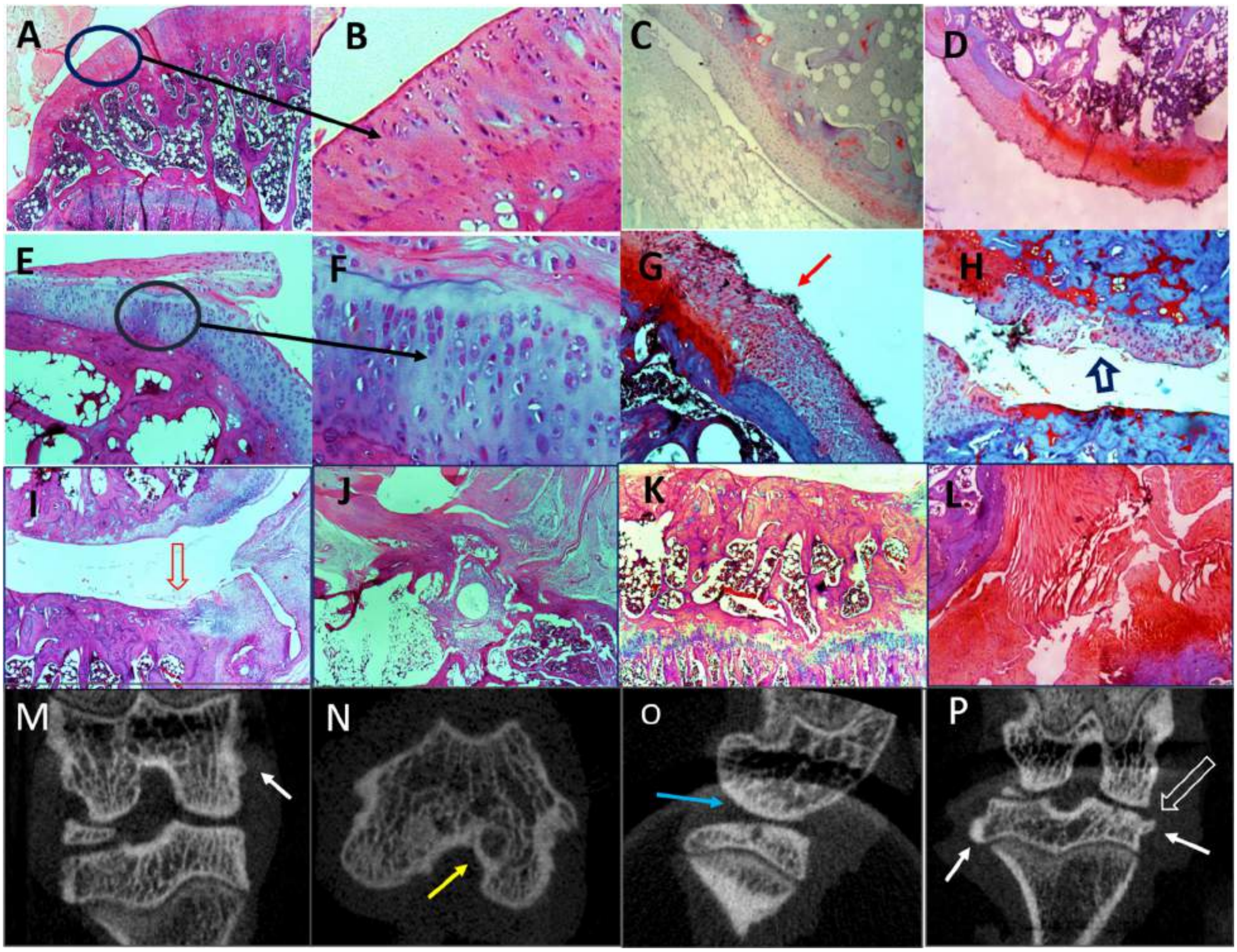

Fig. 1 **A–P** Depicts the histological and radiological features of instability induced osteoarthritis in the rat knee following medial collateral ligament section and medial meniscus excision. **A** Light microscopic image (HE, 10×) shows normal articular cartilage showing normal chondrocyte distribution and **B** morphology seen in magnified view (HE, 40×). **C** One of the earliest features of OA (2 weeks) is a loss of glucosaminoglycan (GAG) from the articular cartilage seen best as lack of safranin O staining (SO, 10×). **D** At four-week follow-up, marked inflammatory pannus is observed growing centripetally and covering the articular surface (SO, 10×). **E, F** Another feature of early OA is hypercellularity (HE, 10×) with conspicuous cloning of chondrocytes in magnified view (HE, 40×). **G** Angiogenesis starts with the inflammatory pannus marked by a red solid arrow (SO, 10×). **H** At the same time, osteophytes appear at articular cartilage margins (SO, 10×). With the progression of OA, cartilage develops **H** clefts and **I** eburnation due to the loss of cartilage exposing subchondral bone marked by a red open arrow (HE, 10×). **J** At eight-week, the subchondral cyst is observed which are also one of an important feature of OA, especially in late OA. **K** Growth plate aberration is also seen in the late stages of OA (HE, 10×). **L** Intra-articular fibrotic tissue leads to arthrofibrosis limiting the joint movements which reduce pain (SO, 10×). **M** Coronal section with the micro-CT shows the early osteophytes (white solid arrow) with maintained joint space. **N** Appearance of a subchondral cyst (yellow solid arrow). **O** Coronal cut shows reduced joint space and subchondral sclerosis (blue solid arrow) at 8 weeks. **P** Late OA shows reduced joint space with multiple osteophytes. (*HE* haematoxylin and eosin, *SO* Safranin O)

higher in the long-term than the short-term (3.9 ± 0.9 vs 3.0 ± 0.8, $P = 0.17$). We compared the scores between medial and lateral compartments separately as rats tend to varus knee. When comparing the medial vs lateral compartments, there was a tendency for the N group (normal unoperated side of surgical controls) to have higher scores in the medial than lateral both in the short- and long-term (Fig. 2B).

Characteristics of the Surgical Model Group (S)

The S (Surgical control) group scores between short- and long-term (5.6 ± 1.07 vs 5.5 ± 0.8, $P = 0.98$) were not significantly different (Fig. 2A). There was also no significant difference in the scores of the medial and lateral condyles of the operated knees in the short-term (6.2 ± 2.2 vs 4.9 ± 1.09, $P = 0.11$). However, in the long-term (6.8 ± 2.1 vs 4.2 ± 1.7,

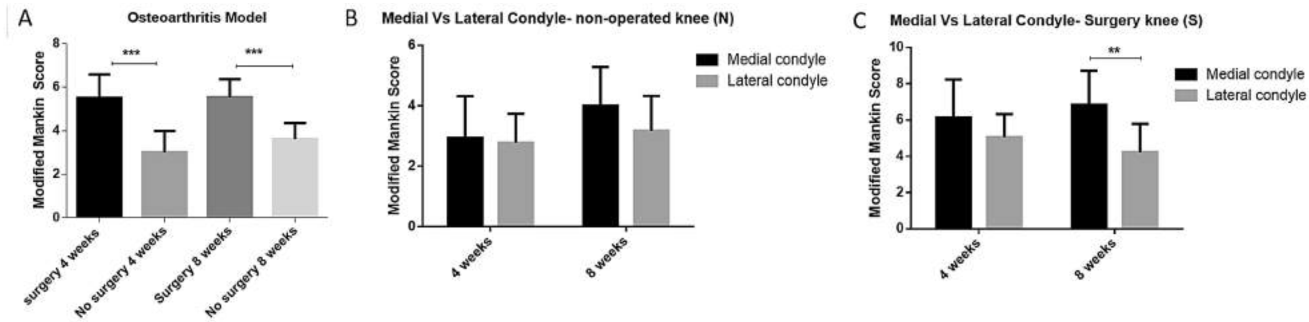

Fig. 2 The bar diagrams represent the histological grading of osteoarthritis in the **A** surgical control; operated knee (S) vs normal non-operated knee (N) at short and long follow-up. Comparison of mean Mankin score between the medial vs lateral compartment in **B** normal non-operated knee (N) and **C** operated knee (S) of the control animals. The results show a significant increase overall score and specifically in the medial compartment in the short- and long-term after surgery

$P=0.01$) significantly more osteoarthritic changes were found in the medial compartment suggesting higher medial compartment osteoarthritis (Fig. 2C) in the surgically damaged compartment.

Effect of the Wnt/BMP/VEGF Modifiers (Surgery + Drug [SD] vs Surgery Alone [S] Group)

In the short-term group's histopathological assessment of the articular cartilage, the mean Mankin score was lesser in the SD group than the S group (4.9 ± 0.8 vs 5.6 ± 1.07, $P=0.17$) though not significant. In the long-term, the mean Mankin score in the SD and S groups were not significantly different (6.6 ± 2.06 vs 5.5 ± 0.8, $P=0.13$) (Fig. 3A).

In the SD group, the knees' osteoarthritis score deteriorated significantly between short- and long-term (4.9 ± 0.8 vs 6.6 ± 2.06, $P=0.02$) (Fig. 3A).

In the short-term evaluation, the combined medial compartment (anteromedial and posteromedial) scores of the SD group (4.7 ± 1.2 vs 6.2 ± 2.2, $P=0.03$) were significantly lower than the S group suggesting a beneficial effect on the compartment not directly receiving the injections (Fig. 3B). However, the therapeutic effect was not maintained in the long-term follow-up, (6.74 ± 2.3 vs 6.85 ± 1.8 $P=0.89$),

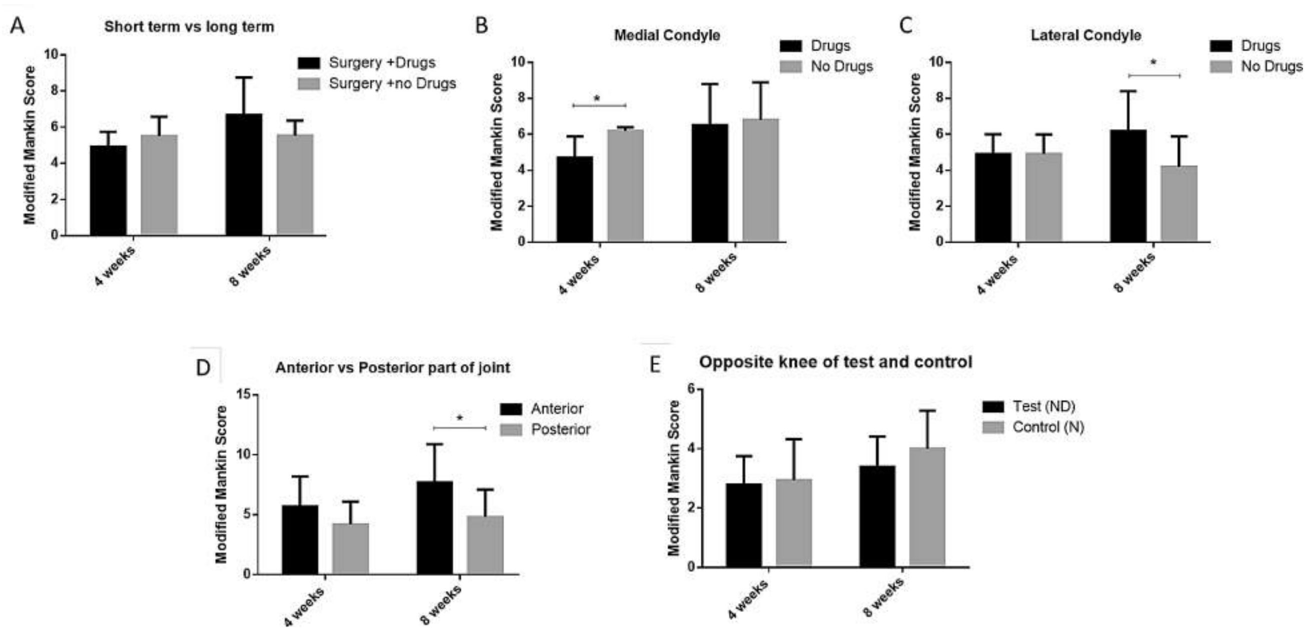

Fig. 3 The bar diagrams represent osteoarthritis histological grading in the **A** test and control joints at short- and long-term follow-up. The mean Mankin score in the **B** medial, **C** lateral, and **D** anterior vs posterior compartment of the knee in test and control animal. **E** The level of osteoarthritis in the non-operated knee of test and control. The medial and posterior compartments in the short-term and posterior compartment in the long-term have been protected from OA by the drugs in the test group

(Fig. 3B) with higher lateral joint scores in the SD vs S group (6.64 ± 2.2 vs 4.23 ± 1.57, $P = 0.02$) (Fig. 3C).

Overall, the articular cartilage over the anterior compartment had more osteoarthritic damage than the posterior compartment, especially in the long-term (7.7 ± 3.2 vs 5.6 ± 2.4, $P = 0.03$) (Fig. 3D).

Characteristics of the Normal Side in the Test (ND) and Control (N)

Due to the injury and the pain in the right knee, the animal tends to bear its weight in the opposite limb, which results in increase stress and cartilage damage in the contralateral joint [19, 20]. The analysis showed that the opposite knee in the test group (ND) scored lesser in both short- (2.79 ± 0.96 vs 2.94 ± 1.38, $P = 0.62$) and long-term (3.39 ± 1.02 vs 4.01 ± 1.29, $P = 0.32$) follow-up compared to the opposite knee (N) of the surgical control (Fig. 3E). It implies that the pain response is minimal in the drugs infused joint.

Micro-CT analysis of two animals in the test group (SD group) at eight weeks showed a marked reduction in the size and number of osteophytes and well-preserved joint space similar to the normal non-operated knee (N). There was no subchondral sclerosis and cyst in the test joints (Fig. 4A–F).

Histological analysis showed varied results; six out of ten in the short term and three out of ten in the long-term in the test group showed a well-preserved near normal cartilage (Mankin score < 5) with good staining for GAG, while the remaining animals exhibited loss of GAG staining at four weeks and complete cartilage destruction similar to the control animal at the eight weeks follow-up (Fig. 5A–F). In the control group the well-preserved joints were seen in two out of 10 short- and two out of 10 in long-term. The odds ratio of the drugs rescuing the OA were six times higher than the control ($P = 0.16$).

Discussion

This study was based on a combinatorial approach using a cocktail of three drugs to target the damaged articular cartilage destined to become osteoarthritis. The three targets chosen to prevent articular cartilage degeneration were VEGF, Wnt and BMP pathways. Our study's overall outcome showed that in the short-term the osteoarthritis was partially rescued in the medial compartment and posterior compartments by the combination of BMP and VEGF antagonists and Wnt agonist, and in the long-term, there was a limited progression. Typically, the medial compartment of the knee was more susceptible to damage in the tested model due to excision of the medial meniscus and division of the medial collateral ligament. Nevertheless, our therapeutic intervention showed lesser osteoarthritis and protected the medial joint from the damage in the short-term after insult and slowed the osteoarthritis progression but could not altogether reverse it in the long-term.

Wnt signalling is essential for cartilage homeostasis and chondrocyte survival; besides, it protects the AC from mechanical stress. Previous studies demonstrated that activation of the Wnt pathway following the mechanical injury stimulated the matrix secretion and prevented further cartilage degeneration [21, 22]. However, Wnt signalling's continuous activation by overexpression of ß-catenin leads to osteoarthritic phenotypes with increased expression of matrix-degrading proteinases [23]. Thus, Wnt signalling can confer both protective and destructive effect on AC. The transient or homeostatic level activation of Wnt signalling is desirable for the cartilage, and it imparts reparative changes [24, 25]. In this study, the drugs were infused every two weeks once and it showed a therapeutic effect in the short-term. This strategy is in line with a previous observation that the two weeks after transient activation of Wnt signalling thickened the AC and induced the regenerative effect [25]. The long-term animals received two additional doses of the drug but failed to show further improvement. Therefore, further studies are intended to check the effect of a single dose vs single-dose/month of drugs on osteoarthritis progression.

Administration of dorsomorphin (BMP antagonist) on the 14th day of chondrogenic differentiation inhibits hypertrophic markers such as COL10A1 and MMPs, suggesting that BMPs promote hypertrophy chondrocytes [9]. This small molecule, a pyrimidine compound, is a BMP antagonist and inhibits the BMP type I receptors ALK2, ALK3 and ALK6 [9, 26]. It blocks BMP-mediated SMAD1/5/8 phosphorylation, target gene transcription and osteogenic differentiation [9, 26]. SMAD pathway activates the expression of RUNX, MMPs, aggrecanase and alkaline phosphatase [27], thus supporting our hypothesis that it will inhibit osteophyte and rescue the arthritic joints.

Damaged articular cartilage or mechanical compression causes VEGF expression through the activation of hypoxia-inducible factor 1 [27]. The VEGF increases neovascularisation of the cartilage, hypertrophic changes, osteophyte formation and eventually osteoarthritis. VEGF also activates catabolic pathways leading to matrix degradation, releasing inflammatory cytokines, setting up a vicious cycle [28]. Bevacizumab is a humanised monoclonal antibody that inhibits vascular endothelial growth factor A (VEGF-A) [29]. This drug improves the environment for cartilage repair in damaged joints by blocking angiogenesis [30]. A safety study of intraarticular injection of Bevacizumab has shown improved histology and matrix protein gene expression in a rabbit model of osteoarthritis knee [30, 31].

The rat osteoarthritis model is most commonly used to elucidate the pathology and therapeutic effect of disease-modifying osteoarthritis drugs. Although the rat leg's

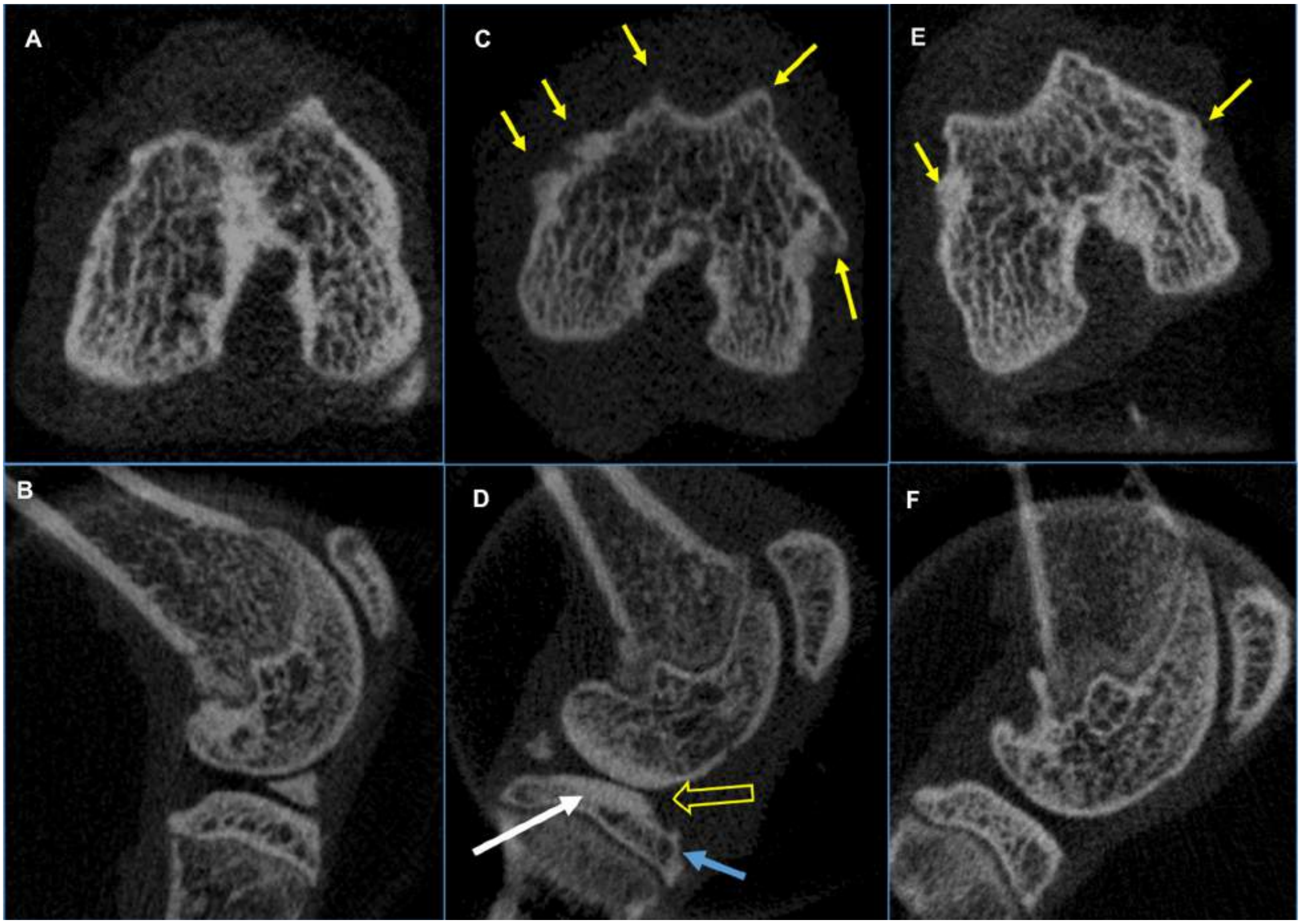

Fig. 4 Micro-CT images of the rat knees (right side) with axial and sagittal sections. **A** A normal knee at day 1 showing the absence of cardinal features of osteoarthritis such as osteophytes, subchondral sclerosis, subchondral cysts. **B** A well-maintained joint space is seen in the sagittal view. **C, D** depict the corresponding sections from the S group rats (surgical control) at 8 weeks. **C** Axial cuts shows the osteophytes on medial and lateral condyles and edges of the patella-femoral trochlear groove (solid arrow). **D** Sagittal cut shows a striking reduction of joint space (open yellow arrow) with marked subchondral sclerosis (solid white arrow) and subchondral cyst (solid blue arrow) especially on the weight-bearing parts of the tibiofemoral joint. **E** and **F** images represent the test joint at 8 weeks (OA model + drugs). **E** Osteophytes are smaller and fewer in number in both the condyles. **F** Joint space is normal; there is an absence of subchondral sclerosis and cysts and osteophytes

biomechanics is different from the bipeds, it mimics the osteoarthritis progression and pain response observed in human [20, 32]. The rat osteoarthritis model is created by either surgical intervention or chemically induced methods. In this study, we surgically damaged the medial meniscus and medial collateral ligament (MCL), resulting in severe osteoarthritis at eight weeks follow-up. A previous study comparing different surgical models illustrated that the transection of patellar ligament formed a severe osteoarthritis with cartilage destruction and osteophyte formation, whereas the transection of either MCL or meniscectomy leads to moderate osteoarthritis [33]. The injury on both meniscus and MCL imposed a continuous severe insult on the cartilage due to severe instability, leading to an irreversible destructive change in the cartilage. That explains why our strategy did not exhibit significant long-term improvement. It is ideal to use a mild osteoarthritis animal model, which can be created by ACL injury alone or a chemically induced knee instability method, to study any strategy's therapeutic effect [33, 34].

Limitations

Repeated injections by themselves caused trauma and could have influenced the outcome in the test group adversely [35]. This could be avoided in future by using drug-eluting microbeads, and other systems for sustained drug delivery such as hydrogels have been implanted or injected into the joint cavity to avoid confounders [36].

The long-term assessment (eight-week time point) though desired, is not suitable for this model as the joint trauma

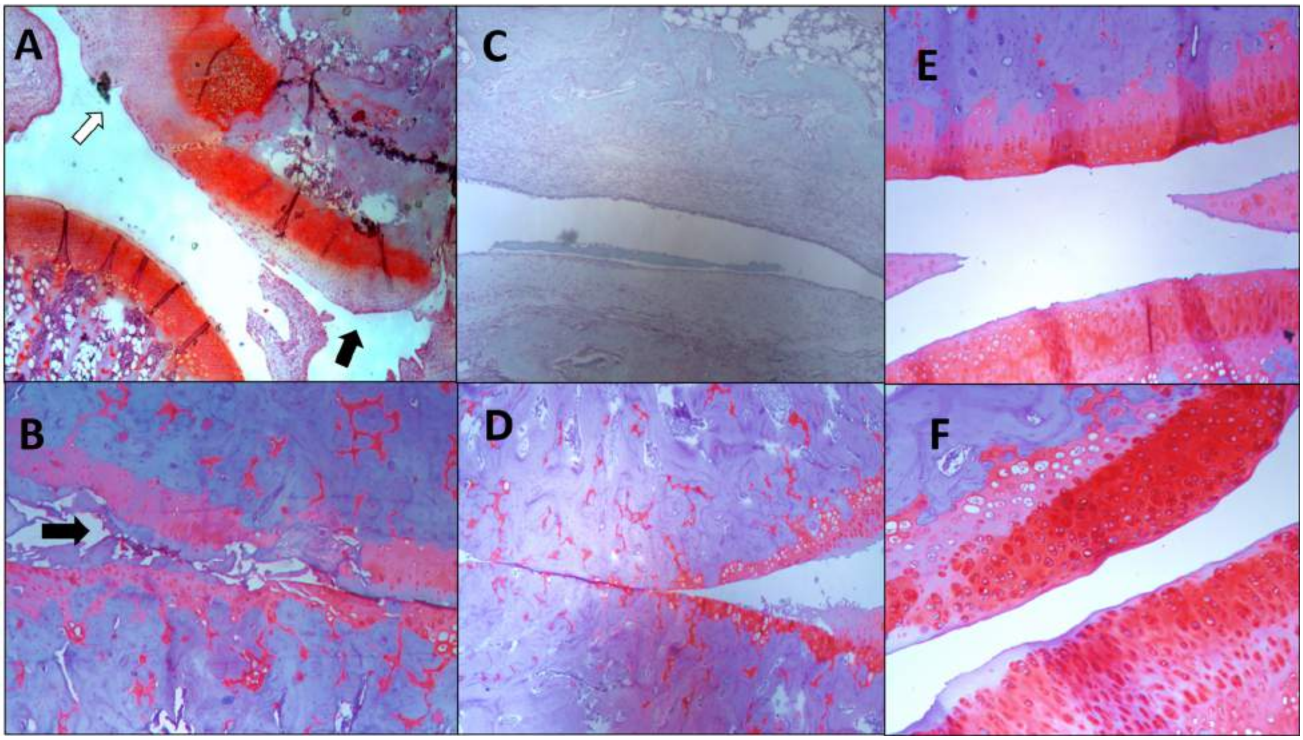

Fig. 5 The light microscopic images represent the test's articular cartilage and control groups knees stained with Safranin O dye. **A** The short-term outcome in S group knees showing inflammatory pannus (solid black arrow) over articular cartilage with the loss of GAG and eburnation. **B** At eight weeks with extensive destruction of the joint, complete joint space loss and exposed subchondral bone (black arrow). **C** Worst outcome in test (SD group) animal in the short-term shows complete loss of cartilage with inflammatory pannus covering the subchondral bone. **D** Worst outcome in the long-term with extensive destruction, complete loss of joint space and eburnation. **E** The best outcome in test animal in the short-term with near-normal articular cartilage (lateral condyle) in the joint. **F** Good GAG content, hypercellularity and cloning of chondrocytes with a small amount of pannus, but otherwise well-maintained superficial layer and normal architecture is seen, which shows the best outcome in the long-term (safranin O stain, 10×)

continues and there is a complete, irreversible loss of cartilage as it is a sustained insult. In a severe instability type model, only short- and extremely short-term results (one and two weeks) should be assessed to get meaningful data. In the recent past, people have used either a meniscectomy or an ACL injury model to decrease osteoarthritis for testing drugs [37, 38].

In conclusion, the strategy of inhibiting BMP signalling using dorsomorphin, anti-VEGF drug bevacizumab, and activation of the Wnt pathway using drugs temporarily arrested osteoarthritis progression in rat surgical osteoarthritis knee model. Further experimentation is suggested with a refined animal model and delivery systems for drugs.

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Author contribution SC and KR have contributed equally to this study and should be considered first co-authors. VM designed the study. VM, SC, KR, VD conducted the animal experiments. NW performed the histopathological analysis. VM, SC, KR, VD analysed the data. VM, SC, KR prepared the manuscript. All five authors participated in this study and their contribution was essential to successfully complete this study.

Declarations

Conflict of interest All the authors declared that there is no conflict of interest.

Ethical approval This study was conducted after obtaining approval from the institutional review board, Christian Medical College, Vellore (IRB No: 7573) and the experimentation on rats were performed after institutional animal ethics committee (IAEC No: 29/2011) clearance.

Informed consent There is no human subject participated in this study. Therefore, informed consent is not required.

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ORIGINAL ARTICLE

Effect of Fracture Reduction with Different Medial Cortical Support on Stability After Cephalomedullary Nail Fixation of Unstable Pertrochanteric Fractures: A Biomechanical Analysis

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Abstract

Background This study evaluated the biomechanics of the proximal femoral nail antirotation-II (PFNA-II) in AO/OTA 31A2.2 intertrochanteric fractures based on the fracture reduction quality.

Methods Unstable intertrochanteric fractures were created according to the AO classification and repaired by proximal femoral nail antirotation-II (PFNA-II) using one of three medial cortical support groups. The specimens were tested using cyclic axial loading. The following parameters were recorded: force and stiffness at failure, maximum vertical and horizontal displacement, neck-shaft angle, and location and patten of failure.

Results In the cyclic loading test, the force at failure in the anatomical reduction (AR) group was greater than that of the positive medial cortical support (PMCS) group (984.22 ± 12.63 vs. 936.95 ± 16.78) N ($P < 0.05$) and negative medial cortical support (NMCS) group (918.04 ± 28.86) N ($P < 0.05$). The stiffness in the AR group was 4.77 and 31.9% higher than that in the PMCS group ($P > 0.05$) and NMCS group ($P < 0.05$). The maximum vertical displacement was the largest in the NMCS group. The maximum horizontal displacement in the NMCS group was 28.6 and 19.1% larger than that in the AR group ($P > 0.05$) and PMCS group ($P < 0.05$). The neck-shaft angle in the NMCS group was smaller than that in the anatomic reduction group ($P < 0.05$) and positive support group ($P < 0.05$).

Conclusion For the unstable AO/OTA 31A2.2 intertrochanteric fracture, there were significant differences in their mechanical stability among AR, PMCS and NMCS. The NMCS is not recommended during the intraoperative reduction.

Keywords Intertrochanteric fracture · Positive medial cortex support · Negative medial cortex support · Biomechanics

Introduction

The incidence of intertrochanteric fractures has increased significantly along with the accelerated aging of the population [1], and the morbidity is 1.32% among people over 85 years old [2]. In elderly patients, early operation within 24–48 h and function exercise can significantly reduce the complications and mortality [3]. For the intertrochanteric fracture patients without obvious operation contraindications, surgical treatment is still the first choice.

Compared with other surgical procedures, intramedullary nail fixation has obvious biomechanical advantages, due to its less invasiveness. It is suitable for most intertrochanteric fractures and more widely applied clinically. However, there are many hip muscles, and the mechanical structure is complex. To achieve anatomical reduction (AR), multiple reductions are often needed, and the operation time will be prolonged. In addition, the elderly patients often

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have other underlying chronic diseases, such as pneumonia and decreased cardiac function. To ensure the safety of the surgery, the operation time should be shortened as much as possible. A balance between the operation time, safety, reduction quality and biomechanics is needed. The reduction quality is one of most important factors affecting the stability of internal fixation of the intertrochanteric hip fracture [4]. If the stability is poor, the head-neck fragment will continue to telescope along the axis of the implant (lag screw/helical blade), resulting in the shortening of the proximal femur, and loss of the neck-shaft angle and varus. In these cases, the phenomenon of cut-in or cut-out and the functional influence will appear, and the hip function will be affected [5–7]. There are various criteria for assessing the reduction quality of intertrochanteric fractures, and the most widely used criteria were proposed by Baumgaertner et al. [8–11]. The Baumgaertner criteria define a displacement of any fragment of less than 4 mm (between 3 and 5 mm) as a good reduction quality, but the displacement direction of the fracture fragments is not considered at all. We were the first to test the effect of the displacement direction of the fracture fragments on stability from the perspective of biomechanics. The purpose of this study was to compare the biomechanical stability of different medial cortical support patterns after the proximal femoral nail antirotation-II (PFNA-II) fixation for unstable AO/OTA 31A2.2 intertrochanteric fractures. We aim to provide the theoretical basis for its clinical application to reduce postoperative complications and improve the outcome of the surgery.

Materials and Methods

Sample Preparation

A total of 18 synthetic proximal osteoporotic femurs [12, 13] were divided into 3 different medial cortical support groups in intertrochanteric fracture models (AO/OTA 31A2.2) [14, 15], namely anatomical reduction (AR), positive medial cortical support (PMCS) and negative medial cortical support (NMCS).

The fracture models were simulated according to the 2018 AO/OTA classification of 31A2.2 fracture models of intertrochanteric fractures. The intertrochanteric fractures were created using custom templates. According to the definition of lateral wall by Hsu [16], a horizontal line was drawn 3 cm below the innominate tubercle of the greater trochanter. At the intersection of this horizontal line and the lateral cortex, a 45° angle line was drawn intersecting the fracture line at point A with a lateral wall thickness of 2 cm. Another horizontal line was drawn at the lowest point of the lesser trochanter and the intersection of this line and the anteromedial wall of the femur was designated as B. The AO/OTA 31A2.2 fracture model was made by drawing a straight-line F across the two points of A/B and removing the large area of the lesser trochanter and part of the posterior wall (Fig. 1).

All fracture models were made by the same senior surgeon. PMCS is defined as the medial cortex of the head–neck fragment displaced and located slightly superomedially to

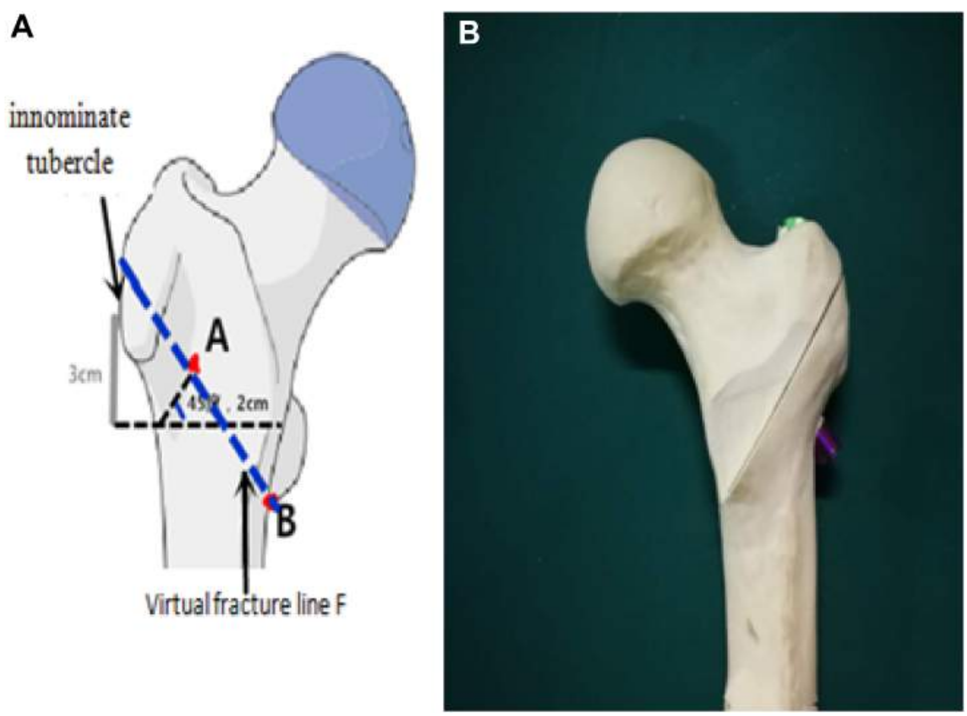

Fig. 1 Schematic diagram of fracture model; **A** anterior view; **B** posterior view

the medial cortex of the femur shaft in the anteroposterior (AP) view. NMCS is the opposite of the PMCS, and is defined as the medial cortex of the head–neck fragment located lateral to the medial cortex of the femur shaft in the AP view. Every displacement is defined as a cortical distance of 3.64 mm. All the fractures were fixed using the PFNA-II (170 mm, diameter: 9 mm, titanium alloys; Double Medical Technology Inc., Xiamen, China). The lag screw was placed and fluoroscopy was used to ensure that the lag screw position was in the inferior third of the femoral neck in the PA view and in the center of the femoral neck in the lateral view, and the tip-to-apex distance (TAD) was between 20 and 25 mm [17–19]. All PFNA-II nails were statically locked with a distal locking screw.

Test Protocol

The model was place on the Instron 3365 testing machine (Instron, Norwood, MA, USA) with the distal part embedded. The position of the model was simulated with one leg standing (Fig. 2). The models were oriented at 15° of adduction in the coronal plane and aligned vertically in the sagittal plane [20, 21]. The femoral head was inserted proximally into an acetabulum-type cup and was free to rotate inside the cup.

All three different medial cortical support groups were subjected to the cyclic loading test according to a previous study [13]. In the cyclic loading test, the number of cycles varies, but the commonly used 10,000 cycles protocol attempts to simulate the walking of a patient over a 6-week period until healing occurs. The upper load of 1400 N is considered to be the equivalent of the weight of a 70-kg person.

The test protocol included a preload of 200 N that was increased to the maximum force at a rate of 100 N at each cycle [22, 23] until failure or until a force of 1400 N is reached [24] at a displacement rate of 10 mm/min. The force at failure was defined as that at which there was a visible failure of the internal fixation (screw blade cutting out, screw blade withdrawing, screw blade broken or fracture reduction loss or new bone fracture), or a drop of the applied force or an inability to increase the force value with increasing standard travel.

The displacement and neck-shaft angle data were collected using the GOM Inspect Professional Dynamic Capture 3D system (GOM GmbH, Braunschweig, Germany) (Fig. 2). The load data were taken from the force gauge of the testing machine. The stiffness of the construct was calculated using the load/standard travel curve from the last three conditioning cycles.

After testing, the specimens were examined for the location of the fractures, distal screw migration or bending of the implant.

Statistical Analysis

The SPSS 23.0 statistical software (IBM Corp., Armonk, NY, USA) was used to analyze the data. One-way analysis of variance (ANOVA) was used to analyze the comparison among the data of multiple groups, and the least significant difference (LSD) post hoc test was used to compare the data of the two groups. Student tests were used to analyze the comparison between the two groups. The difference was considered statistically significant when the P value was less than 0.05.

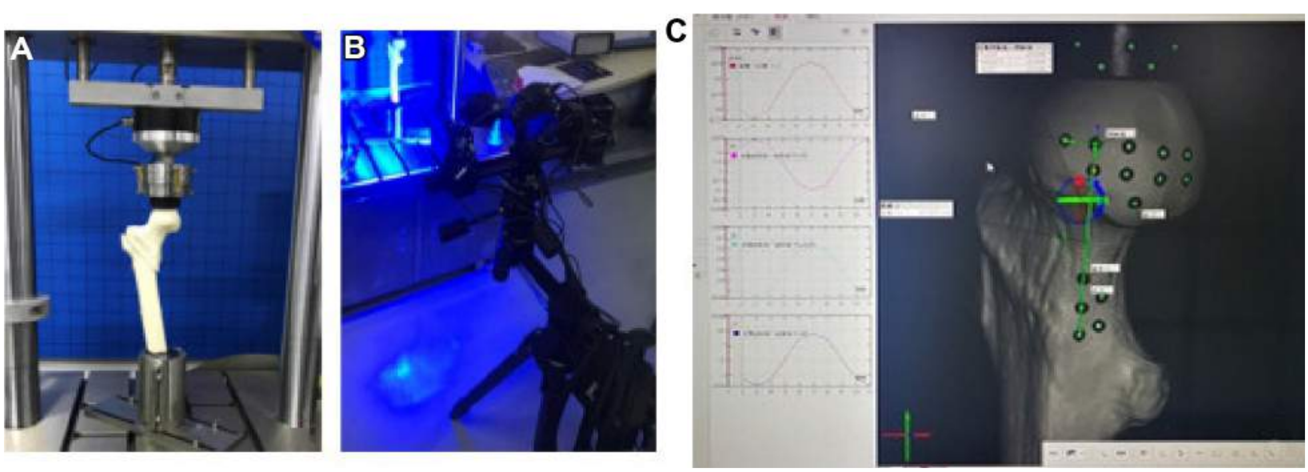

Fig. 2 **A** Axial stiffness mechanical test was taken under the Instron (Model 3365) testing machine (Instron, Norwood, MA, USA); **B** The data were collected by the GOM Inspect Professional Dynamic Capture 3D system (GOM GmbH, Braunschweig, Germany); **C** Screenshot of an optical view with vertical and horizontal axis of data acquisition

Table 1 Results of the testing protocol

Fixation	Force at failure (N)	Stiffness standard (N/mm)	Vertical displacement (mm)	horizontal displacement (mm)	Neck-shaft angle (°)
AR	984.22 ± 12.63	115.3 ± 5.8	21.04 ± 4.63	15.82 ± 3.48	121.84 ± 2.89
PMCS	936.95 ± 16.78	109.8 ± 4.1	21.71 ± 5.92	17.93 ± 4.89	121.12 ± 3.79
NMCS	918.04 ± 28.86	78.5 ± 10.8	22.95 ± 4.98	22.17 ± 4.82	119.77 ± 3.31

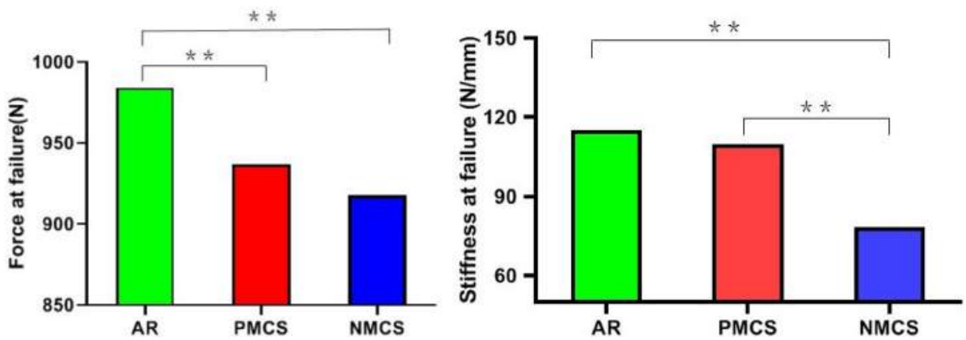

Fig. 3 The force at failure of AR group was 4.8% and 6.72% larger than that of PMCS and NMCS groups, respectively. The stiffness at failure of AR group was 4.77% and 31.9%larger than that of PMCS and NMCS groups, respectively. **Significant ($P < 0.05$)

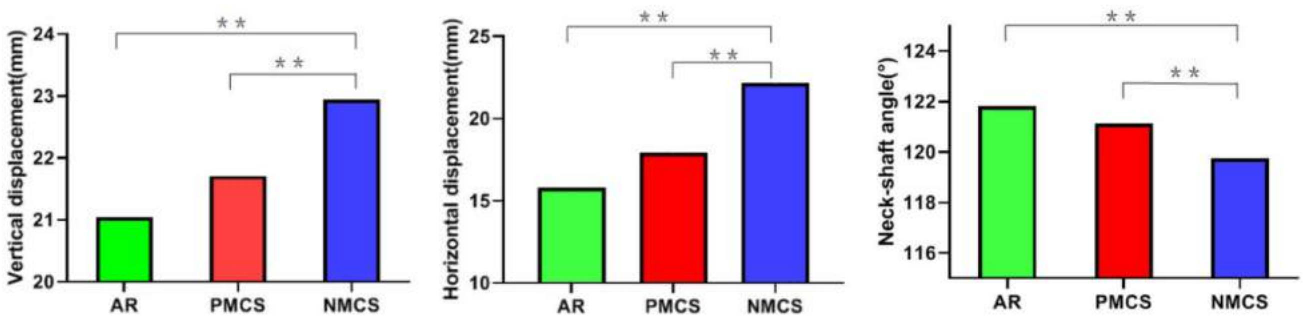

Fig. 4 The vertical displacement of NMCS group was 8.32% and 5.4% larger than that of AR and PMCS groups, respectively. The horizontal displacement of NMCS group was 28.64% and 19.12%larger than that of AM and PMCS groups, respectively. The neck-shaft angle of AR group was 0.6% and 1.7% larger than that of PMCS and NMCS groups, respectively.**Significant ($P < 0.05$)

Results

The detail results are shown in Table 1.

In the cyclic loading test, the force at failure of the AR group was 4.8 and 6.72% larger than that of the PMCS and NMCS groups, respectively ($P < 0.05$). However, there was no statistical difference between the PMCS and NMCS groups ($P > 0.05$), (Fig. 3).

The stiffness at failure of the AR group was 4.77 and 31.9% higher than that in the PMCS group ($P > 0.05$) and NMCS group ($P < 0.05$), (Fig. 3). The vertical displacement of the NMCS group was 8.32 and 5.4% larger than that of the AR and PMCS groups, respectively ($P < 0.05$), (Figs. 4, 5). The horizontal displacement of the NMCS group was 28.64 and 19.12% larger than that of the AR and PMCS groups, respectively ($P < 0.05$) (Fig. 4). The

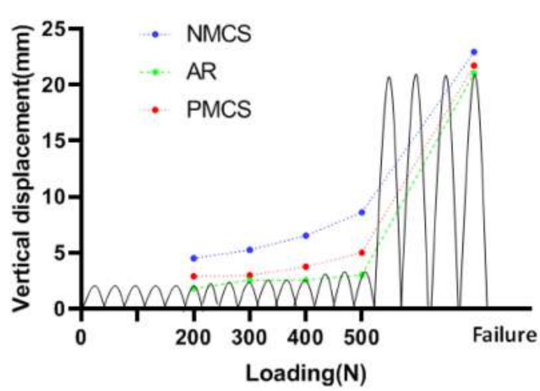

Fig. 5 The cyclic loading test was used to ensure the force and stiffness at failure, the maximum vertical and horizontal displacement, the neck-shaft angle

neck-shaft angle of the AR group was 0.6 and 1.7% larger than that of the PMCS and NMCS groups, respectively ($P < 0.05$) (Fig. 4). However, there was no statistical difference between the AR group and PMCS in the stiffness at failure, the maximum vertical and horizontal displacement, and the neck-shaft angle ($P > 0.05$).

The breakage of the head–neck fragment occurred in seven cases, split fracture at the zone of the distal screw in two cases, and breakage in the distal femur area in eight cases, and one case of breakage in both the zone of the distal screw and distal femur area.

Discussion

The results of this study revealed that although the AR, PMCS, and NMCS are all methods that achieve good reduction quality according to the Baumgaertner criteria, there are significant differences in their mechanical stability. The PMCS method is not inferior to the AR method, and both are superior to the NMCS method. The Baumgaertner criteria only consider the displacement distance of the fracture fragments, but we should also consider and add the displacement direction of the fracture fragment to these criteria. All the forces at failure in the AR, PMCS and NMCS groups were less than 1400 N, which is consistent with the results obtained by Ceynowa [13]. Accordingly, whether early weight-bearing is needed after the treatment of unstable AO/OTA 31A2.2 intertrochanteric fractures should be carefully considered.

In 1980, Kaufer first described five factors that affect the stability of internal fixation of the intertrochanteric hip fracture, namely bone quality, fracture geometry, reduction quality, implant type and implant placement [4]. For implant type selection, compared with extramedullary fixation, intramedullary fixation has many advantages, such as central fixation with better biomechanics to reduce the risk of collapse and less invasive procedure [17–19]. As a result, the intramedullary nail is much more widely used. Before intramedullary nail insertion, the reduction of the fracture should be the most important procedure. AR is the goal of all fracture treatments. However, sometimes, it is not easy to achieve AR in intertrochanteric fractures in a short time during the surgery, which will undoubtedly increase the operation time and the risk of complications. Since the elderly patients often suffer from some chronic medical condition, the incidence of perioperative complications and mortality is high. To reduce the operation time and the incidence of intraoperative complications, we had to compromise the reduction quality to ensure the safety of the operation. At present, in clinical practice, we most commonly use the Baumgaertner criteria to evaluate the reduction quality in intertrochanteric fractures. According to the proposed criteria, the reduction quality of the intertrochanteric fractures is divided into three grades: good, acceptable, and bad. Less than 4 mm displacement of any fragments is considered as good reduction quality, but the displacement direction of the fracture fragment is not considered. However, it seems that the displacement direction of the fracture fragment after reduction also affects the stability and clinical outcomes [25–27]. Therefore, in this study, we further divided the reduction quality into AR, PMCS and NMCS and found that the biomechanical performance of these three kinds of reduction models with "good" reduction quality was quite different.

In the cyclic loading test, the stiffness in the PMCS and AR groups was much higher than that in the NMCS group, and there was a statistically significant difference. Stiffness refers to the ability of a component to resist deformation. The change in the reduction quality can alter the whole stiffness. The ability to resist deformation in the AR and PMCS groups is higher than that in the NMCS group. The reason is that when the experimental model is loaded, the head and neck fracture fragment will have a slight tendency of varus deformity, the medial cortex of the distal intertrochanteric fracture can support the proximal cortical fragment to resist deformation in the PMCS and AR groups. For the negative cortical support reduction model, the medial cortical support is absent. The lack of this kind of support reduces its ability to resist varus deformity. The head–neck fragment was under more force, as a result the breakage of the head-neck fragment was found the most in the PMCS group. Different reduction quality had different location and patten of failure. The varus deformity of the head and neck fracture fragments also implies a decrease of the neck-shaft angle. The changes in the neck-shaft angle were also the largest in the NMCS group. On the other hand, the NMCS group had the largest vertical and horizonal displacement in each cycle. When the load of the sine wave load increases, the head and neck fracture fragment moves down more in the negative cortical support group than that in the positive cortical support group and the AR group, as a result the spiral blade may cut more bone of the femoral head and neck fracture fragment. Therefore, the screw blade in the NMCS is more likely to destroy the normal bone of the femoral head as mentioned by Ceynowa [13], especially in patients with osteoporosis. Thus, the shortening and varus deformity of the proximal femur will result in a poor mechanical environment in the intertrochanteric fracture site, increased stress of the internal fixation device, increased incidence of the internal fixation failure (cut-out, cut-in), fracture non-union and other complications [27, 28].

In this study, we only considered the effect of the medial cortical support in the coronal plane. We believe that there should be similar differences in mechanical stability in the sagittal plane. In the unstable intertrochanteric fractures, the posterior medial side of the intertrochanteric region is mostly comminuted and displaced, while the anterior medial region is mostly thicker with a simple fracture line. Therefore, the cortical support reduction of the "anteromedial corner" proposed by Professor Chang is extremely important [27]. The stability of the fracture reduction should be determined from both the AP and lateral views to avoid intertrochanteric fracture reduction without cortical support reduction. The head and neck fragments will slide excessively to the medullary cavity which will affect the stability of the fracture site under axial compression, leading to varus or internal fixation failure. In addition, the AR model in our study is hand-made and idealized. However, due to the resolution of the fluoroscopy machine, a cortical displacement of less than 2 mm cannot be distinguished by the naked eye. It is difficult to distinguish the accurate AR, slight PMCS and slight NMCS during the surgery. Thus, during the surgery, the surgeon should make a much more careful evaluation.

This study has several limitations. First, no lateral bending stiffness tests and torsional stiffness tests were performed. Second, in the current treatment, InterTAN, PFNA-II, Gamma3 are all widely used as intramedullary fixation devices, but we only used the PFNA-II to perform the biomechanical test. In the future, the stability of the positive cortical support reduction model can be compared using different implants.

Conclusion

For the unstable AO/OTA 31A2.2 intertrochanteric fracture fixed using PFNA-II, the mechanical stability of the PMCS is not inferior to AR, but significantly superior to the NMCS. If we have to shorten the operation time and reduce the operation risk, the PMCS, after the reduction of intertrochanteric fracture is also an acceptable option. In addition, we should refine the evaluation criteria of the reduction quality and appraise the relative position of the medial cortex of the fracture fragment after reduction to provide an optimal mechanical environment for early functional exercise and fracture healing.

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Declarations

Conflict of Interest The authors have no conflicts of interest to disclose. The authors alone are responsible for the content and writing of the paper. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed Consent For this type of study, informed consent is not required.

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ORIGINAL ARTICLE

Implications of the Overlapping Degree Between Proximal Fibula and Tibia for Placing the Optimal Syndesmotic Screw: A Virtual Cadaveric Study

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Abstract

Background To determine the optimal direction of the syndesmotic screw and to introduce a consistent landmark for practical application by analyzing three-dimensional (3D) modeling and virtual implantation.

Methods A total of 105 cadaveric lower legs (50 males and 55 females; average height, 160.6 ± 7.1 cm) were used to reconstruct a 3D model by using the Mimics® software and the joint morphology was evaluated. Syndesmotic cylinders (Ø3.5 mm/Length 100 mm) were transversely placed in the proximal end of the incisura fibularis for simulating screw fixation. The tibial proximal cylinder, which was tangent to the posterior tibial condyles, was traced and the angle between the two cylinders was measured as the tibial torsion angle (TTA). After rotating the syndesmotic cylinder parallel to the ground, the overlapping degree between the proximal fibula and tibia was assessed as a radiologic indicator.

Results Concerning tibial torsion, the TTA was an average of 36.7° (range, 17.2°–54.4°; SD, 8.78) When the syndesmotic cylinder was rotated to be parallel to the ground, the proximal fibula had nonlinear or linear overlap with the lateral border of the tibia, regardless of the joint morphology. In this non-overlapping view, three Weber's indices for normal fibular length could be better visualized than the mortise view.

Conclusion The syndesmotic cylinder in the proximal end of the incisura fibularis could be consistently placed parallel to the ground by internally rotating the tibia until there was a nonlinear or linear overlap between the proximal fibula and the tibia, regardless of the joint morphology.

Keywords Ankle · Syndesmotic injury · Screw fixation · Three-dimensional modeling

Abbreviations

3D	Three-dimensional
CT	Computed tomography
DICOM	Digital imaging and communications in medicine
KISTI	Korea institute of science and technology information

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KISTI Korea institute of science and technology information
PTFJ Proximal tibiofibular joint
TTA Tibial torsion angle

Background

Syndesmotic injury/instability often occurs concurrently with ankle fractures and has been treated solely with a trans-syndesmotic screw until recently. However, the dynamic suture-button technique has become more conventional owing to the possible advantages over the typical transsyndesmotic screws [1]. Regardless of the fixation options, the optimal trajectory of the guideline for positioning the definitive implant is the most important factor in preventing iatrogenic malreduction [2, 3]. Concerning the management of syndesmotic instability, first of all, surgeons intraoperatively verify the reduction adequacy by conventional radiography, including plain and fluoroscopic methods, without special equipment. The radiography of syndesmotic joints has traditionally been described in the anteroposterior (AP), lateral, and mortise views [4]. On the mortise view, the medial joint radiographic clear space between the talar dome and the distal tibia is within 2 mm. The leg must be rotated internally 15°–20°, thereby aligning the intermalleolar line parallel to the detector and usually results in the fifth toe being directly in line with the center of the calcaneum [5, 6].

As is well known, AP and mortise radiographs are inaccurate for determining the accuracy of syndesmotic reduction, and postoperative computed tomography (CT) provides a better evaluation of the syndesmosis than radiographs [7]. Often, the intraoperative fluoroscopic images demonstrate acceptable fibular position radiographically, but on the CT scan, the fibula is perched slightly anteriorly or posteriorly in the tibial incisura. Besides, considering the tibial torsion, which is an important anatomical parameter in clinical practice and displays variability among individuals [8], the rotational degree of the injured ankle cannot be determined and should be individualized by preoperative measurement of the non-injured contralateral leg. Therefore, a recent study reported the consistent landmark of the tibial tubercle as the TT view to assess the reduction adequacy of syndesmotic joint and make the optimal screw trajectory during the surgery [9]. However, some orthopedic surgeons cited the potential limitations of clinical relevance due to the anatomic variation of tibial tubercles in the academic communication and congress of foot and ankle surgery.

Therefore, our next study sought to determine whether the usefulness of the tibial tubercle as an intraoperative landmark could be confirmed using other consistent and reliable structures. Based on the clinical experience of syndesmotic injury management, the authors have been using the overlapping degree between the proximal fibula and the lateral margin of the tibia as a consistent and reliable indicator to decide the adequacy of the leg's internal rotation. The principal objectives of this cadaveric study were to verify the clinical relevance of the overlapping degree between the proximal fibula and the tibia, assess the morphology of the syndesmotic joint and implications of optimal fixation, and compare the practical usefulness between the tibial tubercle and the overlapping degree by analyzing three-dimensional (3D) models and virtual implantation of a syndesmotic screw in a 3D model.

Materials and Methods

Digital data of the human body were collected from the Korea Institute of Science and Technology Information and used by agreement. We used CT images of adult cadavers who underwent continuous 1.0 mm slice CT scans (Pronto, Hitachi, Japan) in the supine position. Based on a review of their records, cadavers with joint or tibiofibular bone problems were excluded. A total of 105cadavers (50 males and 55 females) were enrolled. Their mean age at death was 52.4 years (range, 21–60 years; SD, 9.12) and their mean height was 160.58 cm (range, 146–176 cm; SD, 7.23). CT data in Digital Imaging and Communications in Medicine (DICOM) format were imported into Mimics® software (Materialise Interactive Medical Image Control System; Materialise, Antwerp, Belgium) to reconstruct 3D models, which included the tibia, fibula, and talus. After generating the 3D models, the CT scanning plane was reoriented to produce anatomical axial and coronal images parallel to the tibial plafond in the neutral rotation using the Mimics® software (Fig. 1).

An actual-size 3D cylinder model (Ǿ3.5 mm, length 100 mm) was created using 3D CAD software (SolidWorks 2019®, MA, USA) for simulating syndesmotic screw fixation in the distal tibiofibular joint. After obtaining 3D reconstructions of the bones and implant, virtual implantation of syndesmotic screws (syndesmotic cylinder) was performed via four synchronized windows composed of the axial plane and coronal, sagittal, and 3D biplanar images [10–13]. In the true coronal plane, a provisional line 1 mm in diameter at the proximal end of the incisura fibularis was placed for determining the height of the screw. In the axial plane, the provisional line was adjusted for bisecting the fibula and incisura fibularis and defined as the ideal syndesmotic cylinder trajectory [9]. Then, after the syndesmotic cylinder was definitively placed along the provisional line, it was fine-tuned and verified several times by an experienced surgeon (first author, coauthors, and corresponding author). Next, for considering tibial torsion and its variability [8, 14], the tibial proximal cylinder (Ø3.5 mm/Length 150 mm), which was

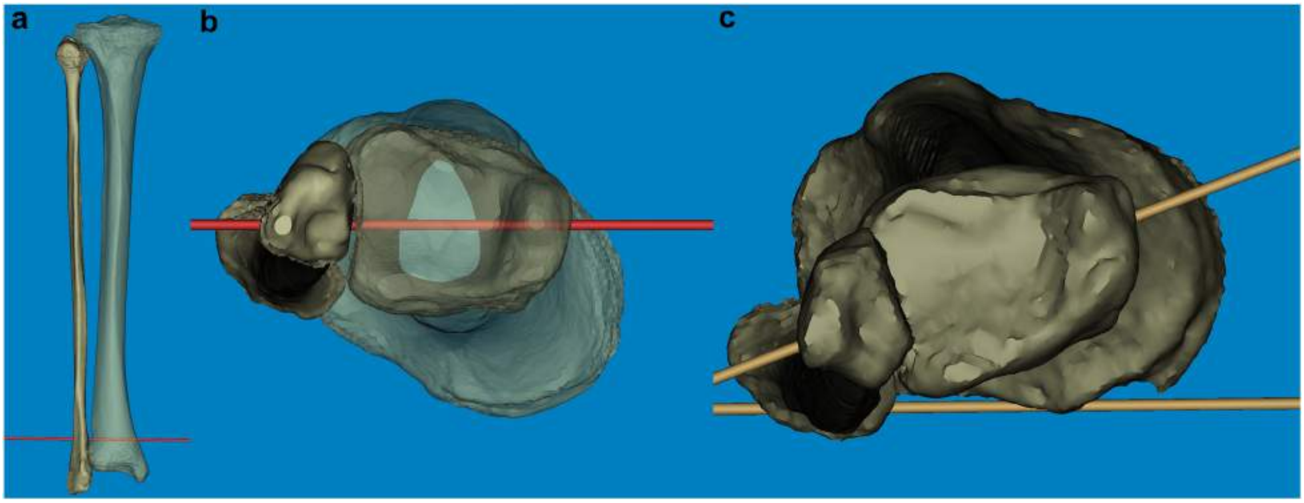

Fig. 1 **A** After generating 3D models of the tibia and fibula, the syndesmotic cylinder was inserted in the proximal end of the incisura fibularis. **B** In the cephalad view of the 3D biplanar image, the trajectory of the cylinder was the bisecting line of the fibula and the incisura. **C** The tibial proximal cylinder, which was tangent to the posterior tibial condyles, was traced and the angle between the two cylinders was measured for individual comparison

tangent to the posterior tibial condyles, was traced and the angle between the proximal cylinder and syndesmotic screw was measured for individual comparisons (Fig. 1).

Using the features of free 360° rotations with magnification in any plane, the morphology of the syndesmotic joint was assessed. The 3D models were rotated until the syndesmotic cylinder was parallel to the ground without any tilt, and this projection was defined as the syndesmotic AP projection. In the syndesmotic AP projection, the overlapping degree between the proximal fibula and the lateral border of the tibia was assessed for utilizing as a practical and consistent landmark. In addition, we evaluated various indicators, including the relationship between the adjacent bones, a non-irregular Shenton's line, and Weber's indices [4], and compared them with the conventional projection of the ankle mortise.

All measurements are presented as mean and range or binary variables, including the overlapping point, tibial torsion, and others. All statistical analyses were performed using the SPSS statistical software package for Windows version 25.0 (SPSS Inc., Chicago, IL, USA). P values < 0.05 were considered to be statistically significant.

Results

Concerning tibial torsion, the TTA was an average of 36.7° (range, 17.2°–54.4°; SD, 8.78). The TTA in men (38.6° ± 8.66°) and women (35.0° ± 8.60°) in women was significantly different ($p = 0.038$). Regardless of individual variation in tibial torsion, the 3D biplanar images consistently showed that the proximal fibula was nonlinearly or linearly overlapping with the tibia in the syndesmotic AP projection of all models (Fig. 2, non-overlap). However, there was a clear space in the proximal tibiofibular joint in the true coronal scanning plane image. Concerning the tibial tubercle, it was directed superiorly and nearly vertical to the ground floor in the syndesmotic AP projection (Fig. 2).

Regarding the syndesmotic joint type, there were 44 cases of flat joints and 61 cases of crescent joints. The position of the distal fibula in the incisura was symmetric in 75 cases and asymmetric in 30 cases (29.4%). Upon comparing both legs, there were 20 cases of side differences (19.6%) in the distal fibula position (Fig. 3). Based on the side differences in the syndesmotic joint, there was no significance among continuous variables of the height of the cadaver ($p = 0.502$), the height of the incisura fibularis ($p = 0.497$), and TTA ($p = 0.383$). The logistic regression analysis revealed that the joint type was $p = 0.498$ and symmetry was $p = 0.018$. When the Hosmer–Lemeshow goodness-of-fit test was performed with side difference as the dependent variable ($p = 0.613$), the joint symmetry was significantly different, and the odds ratio was 3.50 (95% CI: 1.235–9.936; $p = 0.018$). Thus, joint symmetry had a significant impact on side difference; if the syndesmosis was symmetric in the incisura fibularis, the risk of a side difference was increased 3.5-fold.

The height of the incisura fibularis was an average of 26.6 mm (range, 21.1–32.7 mm; SD, 2.51). According to sex, the height of the incisura fibularis was 26.2 ± 2.76 mm in men and 27.07 ± 2.21 mm in women and the difference was not statistically significant ($p = 0.067$). The height of the cadaver was 161.1 ± 7.56 cm in flat type joints and 160.2 ± 7.00 cm in crescent type joints, and there was no statistical significance ($p = 0.560$). The height of the

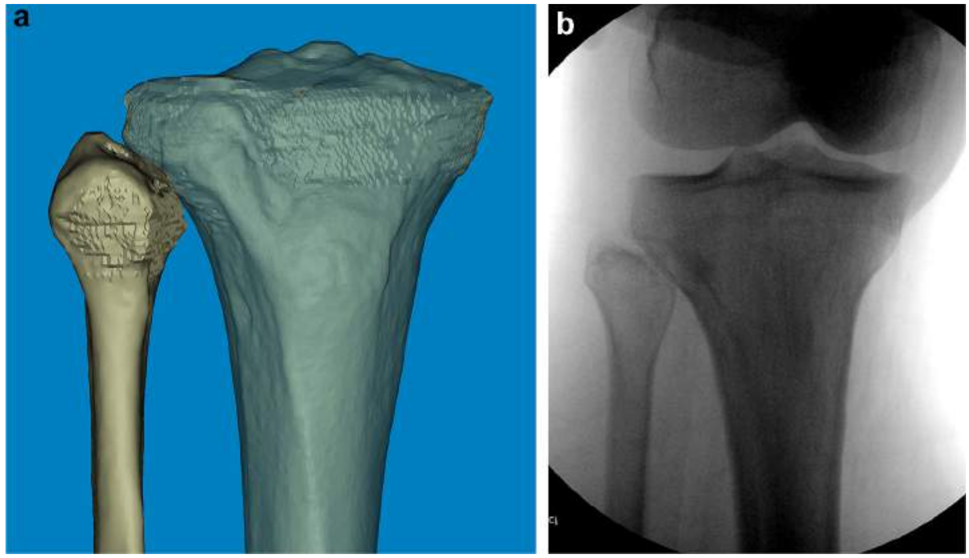

Fig. 2 **A** The overlapping degree in the 3D biplanar images showed that the proximal fibular was linearly or nonlinearly overlapping with the tibia in the syndesmotic anteroposterior (AP) projection. **B** The fluoroscopic image showed a non-overlapping degree in the syndesmotic AP projection

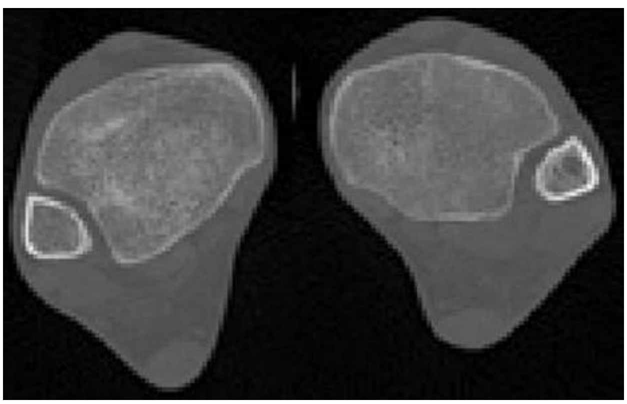

Fig. 3 Upon comparing both legs, there was a side difference. The right leg was positioned symmetrically to the distal fibula in the incisura, whereas the left leg was asymmetric

incisura fibularis was 26.1 ± 2.46 mm in flat type joints and 27.04 ± 2.50 mm in crescent types, and the difference was not statistically significant ($p = 0.053$). The degree of TTA was 36.8° ± 7.52° in flat type joints and 36.6° ± 9.63° in crescent types, and the difference was not statistically significant ($p = 0.930$).

When the CT scanning plane was reformatted along with the syndesmotic cylinder in the coronal plane, various indicators of a normal ankle joint were clearly identified in all models. Compared with the mortise view, the non-irregular Shenton's line of the ankle was better visualized as the medial spike of the distal fibula pointed exactly to the level of the joint space (Fig. 4). The coronal plane image of the whole tibia and fibula demonstrated that the lateral border of the talus was always placed more medial than lateral to the distal tibia and the entire relationship

Fig. 4 When the computed tomography scanning plane was reformatted along the syndesmotic cylinder similar to the syndesmotic anteroposterior projection, the non-irregular Shenton's line of the ankle was better visualized as the medial spike of the distal fibula pointed exactly to the level of the joint space

between the fibula and the tibia in the incisura fibularis was easily identified (Fig. 4).

Discussion

Regarding the management of syndesmotic injury, it is widely known that there are two practical issues to diagnosing subtle instability and how to evaluate the intra- and postoperative reduction adequacy without special software and equipment. By this computational anatomy and simulation study, we identified the consistent radiologic indicators that might be used for assessing the intraoperative reduction adequacy according to variability in the tibial torsion and the depth of the incisura fibularis. As a result, this study found practical and interesting information that could be produced without special equipment. (1) The ideal screw trajectory was parallel to the ground if the leg was internally rotated such that the proximal fibular was nonlinearly or linearly overlapping with the tibia, regardless of individual variation in the tibial torsion and joint morphology. (2) Given the relatively high frequency of side differences (19.6%) and asymmetry (29.4%) of the syndesmotic joint, careful preoperative consideration of the opposite syndesmotic joint should be undertaken to guide the reduction adequacy. Thus, the intraoperative relationship, wherein the lateral border of the talus must always be just medial to the anterior tubercle in the syndesmotic AP projection, could help in the intraoperative assessment of reduction adequacy. (3) Eccentric movement of the fibula may not be occurred by the compressive force because our proposed trajectory and the position of the syndesmotic screw was the bisecting line of the fibula and incisura fibularis.

At the beginning of the study on the syndesmotic joint, the tibial tubercle (TT view) was used to determine the degree of internal rotation [9]. However, an inadequate screw trajectory was sometimes caused by insufficient internal rotation or excessive internal rotation (Fig. 5). Thus, first, the overlapping degree between the proximal fibula and the tibia was clinically applied to determine the syndesmotic screw trajectory, wherein our surgical experience proved useful and practical [15]. Henceforth, we performed the computational simulation study and demonstrated superiority over the tibial tubercle as a consistent landmark with less variation (Fig. 6). As mentioned in a previous study [9], through the syndesmotic AP projection, the screw trajectory and height, reduction adequacy, and relationship to the incisura fibularis could all be identified in real-time under standard fluoroscopic imaging and verified the positional change of the talus through the compressive force of the screw. Considering that subtle syndesmotic widening and fibular malreduction are notoriously difficult to measure by means of standard radiographic views[10, 16], our proposed technique might be of practical use without special or additional equipment.

This study also revealed interesting points by additionally measuring symmetry and the side differences in ankle syndesmosis, which had relatively high occurrences of 29.4% and 19.6%, respectively. Considering that the ankle joints with symmetry were 3.4 times more likely to have side differences, care should be taken when the opposite normal ankle joint is used to guide the reduction adequacy. The morphologic features of the syndesmotic joint showed that 41.9% were flat joints and the incisura fibularis, with a mean of 26.6 mm, was not significantly different according to joint type ($p=0.053$) and sex ($p=0.067$). Furthermore, its proximal end could be consistently utilized as a screw insertion point, regardless of variations. If the screw was inserted in the proximal end of the incisura fibularis through the syndesmotic AP projection, it is expected to have an ideal trajectory, which was the bisecting line of the fibula and the incisura fibularis.

However, our computational analysis had several fundamental limitations. All measurements were from normal ankle joints and thus could have a rather descriptive character compared with the existing studies. Considering that accuracy and precision are the most important parameters for the evaluation of quantitative measurements for

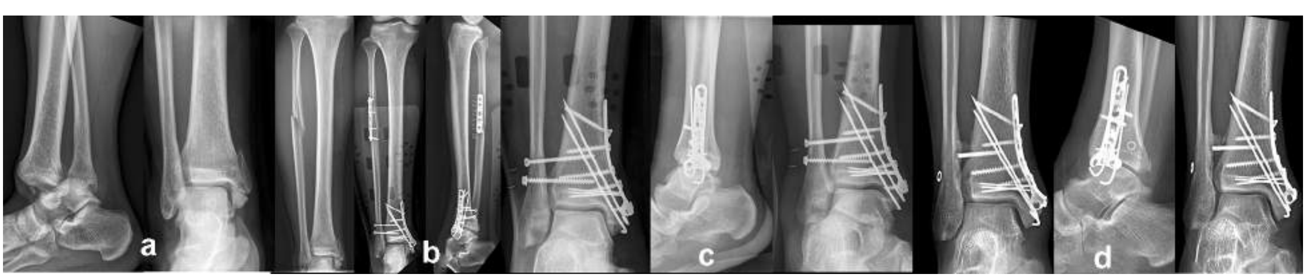

Fig. 5 **A** A 36-year-old man sustained an ankle dislocation. **B** After fixing the medial malleolus and fibular shaft fracture, the proximal end of the incisura fibularis was localized and syndesmotic screw was inserted in the expected site based on the tibial tubercle view. **C** The postoperative radiographs of the ankle showed good reduction adequacy. **D** The postoperative radiographs of 12 months showed the maintenance of reduction after the removal of syndesmotic screws

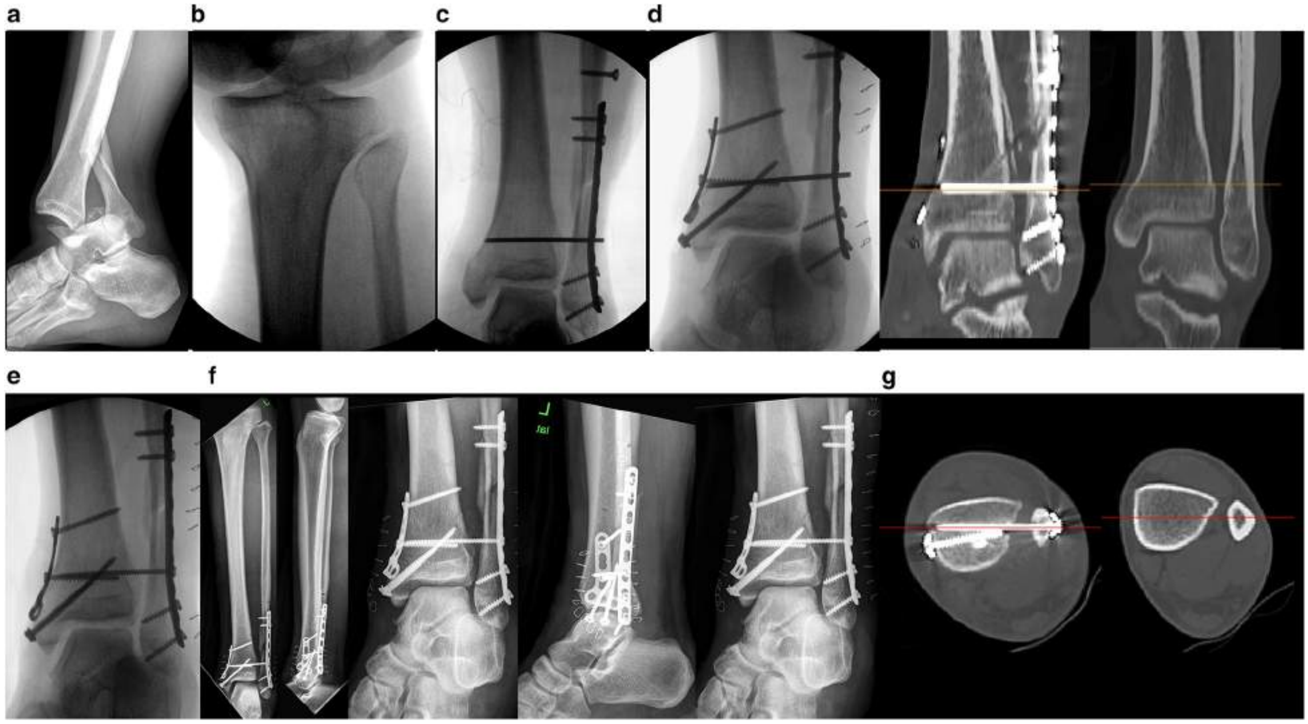

Fig. 6 **A** A 53-year-old man sustained an ankle dislocation. **B** After fixing the fibular fracture, the syndesmotic anteroposterior projection was made and (**C**, **D**) a K-wire of 2.4 mm was placed as a provisional syndesmotic fixation. **E** After the soft tissue around the ankle settled down, the provisional K-wire was replaced with 3.5 cortical screws. **F** The postoperative radiographs showed good reduction adequacy. **G** The computed tomography images show that the screw trajectory was the bisecting line of the fibula and incisura

an area of known variability, there could be some errors in our results. In the practical application of our overlapping method, there might be more radiation exposure of fluoroscopy compared with conventional or arthroscopic techniques. If the tibia had deformity due to a disease or a previous fracture and combined fracture, there may be a limitation. In the case of high fibular fracture (maisonneuve fracture), anatomical reduction and fixation should be given priority. In addition, proximal fibular overlapping may be difficult to identify in patients with multiple fractures due to position problems. Despite these limitations, our findings are valuable for understanding the anatomy of syndesmotic joints and the optimal trajectory of screws and will be helpful for assessing the reduction adequacy in intra- and postoperative images. The authors believe that the quantitative parameters of the morphological measurements were significant because they were based on scientific and reliable software analyzes. Regarding the report that up to 80% of malreduction is present after syndesmotic fixation[17], a comparative clinical study through postoperative CT in the clinical practice would be required in the future.

Conclusion

Based on the computational analysis, the syndesmotic cylinder in the proximal end of the incisura fibularis could be consistently placed parallel to the ground by internally rotating the tibia until there was a nonlinear or linear overlap between the proximal fibula and the tibia regardless of joint morphology.

Author contributions Jun-Young LEE conceived the study and participated in its design and coordination and helped to draft the manuscript. Gu-Hee Jung participated in the design of the study and wrote the manuscript, participated in the sequence alignment, and drafted the manuscript. Jae-Hwan Lim performed the statistical analysis. Jun-Young LEE, Gu-Hee Jung, and Jae-Hwan Lim fine-tuned and verified virtually placed syndesmotic cylinder along the provisional line. Hyeon-Joon Lee and June-Yeon Lee measured and collected data such as TTA, syndesmosis joint side difference, joint type, and height of fibular insisura.

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Declarations

Conflict of interest All authors listed above certify that they have no affliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

Ethics approval and consent to participate This study was based on nationally recognized data and was exempted from IRB.

Informed consent For this type of study informed consent is not required.

Consent for publication Not applicable.

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CORRECTION

Correction to: Implications of the Overlapping Degree Between Proximal Fibula and Tibia for Placing the Optimal Syndesmotic Screw: A Virtual Cadaveric Study

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The original version of this article, published on June 15, 2021, contained a mistake. The funding note was missing. The correct information is given below. The original article has been corrected.

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ORIGINAL ARTICLE

Normative Reference Values for Trunk Range of Motion and Isometric Muscle Strength in Asymptomatic Young Indian Adults

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Abstract

Purpose To determine normative reference values for trunk range of motion (ROM) and isometric strength (TIS) in asymptomatic young, Indian adults.

Methods Age, gender, body mass index, lifestyle, and dynamometer-based device measurements of trunk ROM and TIS in extension (EXT), flexion (FLX), and rotation (ROT) were recorded and analysed in 80 asymptomatic subjects between 20 and 40 years of age. Correlation analysis was performed to determine factors influencing EXT and FLX ROM and TIS.

Results The normative reference values for mean trunk EXT, FLX, right ROT, and left ROT ROM were 23° (95th percentile 31.9°), 40.2°(95th percentile 51.5°), 36.8°(95th percentile 57.7°), and 35.4° (95th percentile 55.7°), respectively; and for mean EXT, FLX, right ROT, and left ROT TIS were 118.1 Nm (95th percentile 278.8 Nm), 63.8 Nm (95th percentile 159.4 Nm), 39.9 Nm (95th percentile 113.6 Nm), and 42.8 Nm (95th percentile 108.9 Nm), respectively. The mean EXT ($p = 0.0002$), right ($p = 0.02$), and left ROT ROM ($p = 0.01$), and the mean EXT, FLX, and ROT TIS ($p < 0.0001$) were significantly greater in males compared to females. The FLX, EXT, and ROT TIS showed significant strong correlation with EXT and FLX TIS. Mean TIS values in Indian subjects were lower when compared to subjects from other countries.

Conclusion This study established normative reference values for trunk ROM and TIS in asymptomatic young Indian adults. These reference values can be helpful to diagnose trunk ROM and TIS deficits, identify subjects at risk for LBP and disability, and individualise rehabilitation treatment in them.

Keywords Trunk muscle strength · Range of motion · Isometric contraction · Spine · Low back pain

Introduction

Reduced trunk muscle strength and trunk range of motion (ROM) are important causes of functional limitations and disability in subjects with low back pain (LBP) [1–4]. Trunk muscle weakness increases the risk of onset and recurrence of LBP [2, 3, 5]. Identifying weakness and lack of flexibility in key trunk muscles and treating them has been reported to prevent pain and improve outcomes following spine surgery [3]. Hence, restoring trunk muscle strength and trunk range of motion (ROM) using active trunk or lumbar strengthening and stabilisation exercises can reduce pain and disability, improve function, and prevent recurrence in patients with LBP treated with rehabilitation or spine surgery [6–8]. Furthermore, improvement in the trunk or lumbar ROM and strength is a useful parameter to measure the effectiveness of rehabilitation treatment in patients with LBP [9–11]. Hence, measuring trunk range of motion (ROM) and trunk isometric strength (TIS) in a patient with LBP undergoing rehabilitation treatment or preoperatively in patients undergoing spine surgery will help quantify deficits in trunk ROM and strength, individualise rehabilitation treatment based on these deficits, and record improvement with treatment.

Objective quantification of trunk muscle strength is typically performed using isometric measurement devices. However, baseline paraspinal muscle strength and trunk mobility may vary based on the subject characteristics such as gender, age, duration of symptoms, pain intensity and disability on presentation [5, 11–14]. Previous studies on trunk ROM and

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trunk isometric strength (TIS) were primarily performed in Caucasian subjects and specifically evaluated lumbar or trunk extensor or flexor muscle strength rather than global trunk ROM and strength [5, 11–14]. Furthermore, the reference values of trunk ROM and TIS reported in Caucasian subjects or subjects or other ethnic backgrounds may not apply to Indian subjects.

Similar to global trends, the burden of LBP is high in India and it is among the top ten causes of years lived with disability (YLDs) in the Indian population [15]. However, to the best of our knowledge, no studies in the literature have investigated trunk ROM and TIS in asymptomatic Indian subjects and reported reference values for these parameters in asymptomatic Indians in the vulnerable 20–40 years' age group. We believe that establishing normative reference values for trunk ROM and TIS parameters in asymptomatic Indian subjects will help design patient-specific rehabilitation treatment protocols based on these deficits either as part of conservative management of LBP or in patients who require perioperative rehabilitation. Hence, we aimed to measure trunk ROM and TIS in asymptomatic Indian subjects and determine factors that influence trunk ROM and TIS.

Materials and Methods

Study Design

This observational cohort study was conducted at a chain of outpatient clinics specialising in spine rehabilitation (QI Spine Clinic, India) from April 2019 to March 2020 in asymptomatic (without LBP) volunteers within the 20–40 years' age group. The study protocol was approved by an institutional review board and ethics committee. All participants signed informed consent for participation in this study and the use of their anonymized data.

Patient Population

Subjects were recruited from among the asymptomatic relatives of patients with LBP who visited a chain of spine rehabilitation clinics for evaluation and treatment of their spine pain, and among physical therapists working at any of our 8 spine rehabilitation clinics in 3 cities. The inclusion criterion was subjects without LBP or absence of any musculoskeletal symptoms within the last 1 year at the time of evaluation who consented for trunk ROM and TIS testing. The exclusion criteria were subjects < 20 years or > 40 years of age on presentation, subjects with a history of spinal disorders such as spine trauma, spine tuberculosis, and kyphotic/scoliotic deformities, and subjects with previous spine surgery.

Clinical Evaluation

All subjects underwent clinical evaluation which included proper history regarding any musculoskeletal symptoms and past illnesses, and a thorough clinical examination before recruitment. All subjects were clinically examined for posture, lumbar range of movement, straight leg raising (SLR) test, and motor and sensory function (myotomal and dermatomal loss and deep tendon reflexes) to determine the absence of LBP or any other musculoskeletal symptoms and signs. All subjects underwent a device-based trunk ROM and TIS testing following their clinical examination.

Trunk Range of Motion and Isometric Strength Testing Protocol

Trunk ROM and TIS were tested in all subjects using a dynamometer-based device (David® Spine Concept System, David® Health Solutions, Helsinki, Finland) using a protocol previously described [16]. The David Spine Concept System (David® Health Solutions, Helsinki, Finland) is a dynamometer-based device which measures highest peak-torque value as maximum isometric contraction force (in Nm) using specialised load cells and measures trunk ROM using motion sensors [16]. Measurement of TIS and ROM in a seated position with hip and lower limb restraints help to isolate and test the trunk in extension (EXT), flexion (FLX), and rotation (ROT) in a safe and controlled manner. Each measuring device has a monitor which provides a real-time display of the force curve. The device terminal software (eValuated Exercise or EVE software, David® Health Solutions, Helsinki, Finland) collects and processes the force data and presents it on the screen [16]. Good to excellent reliability and reproducibility of TIS testing using this device has been reported previously [16]. The testing setup consisted of 3 separate testing devices (for EXT, FLX, and ROT) for testing in a specific plane of motion. The participants were tested in the seated position on all the 3 devices, fastened in position with a knee-lock system and a thigh restraining belt to immobilise both hips and thighs and allow movements only at the lesser back and trunk. To test for EXT TIS, the trunk was initially locked in 30º flexion from the upright sitting position and a maximal isometric contraction in trunk extension was performed by the subject (Fig. 1a). To test for FLX TIS, the trunk was initially placed in a neutral upright position and a maximal isometric contraction in trunk flexion was performed by the subject (Fig. 1b). Finally, to test for right or left ROT TIS, the lower body was laterally rotated at 30º in the transverse plane and a

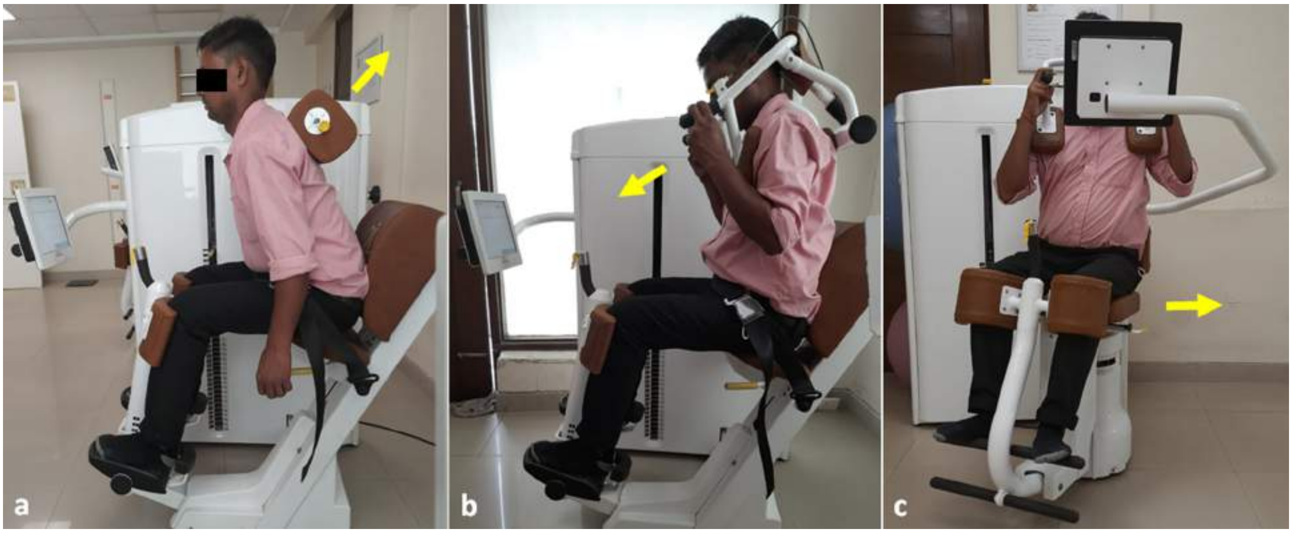

Fig. 1 Images of the test device showing initial patient position and direction of isometric contraction or force applied by the patient (arrow) during extension (**a**), flexion (**b**), and rotation (**c**) trunk isometric strength testing

maximal isometric contraction in trunk rotation was performed by the subject (Fig. 1c). All initial positions of the trunk, before isometric contraction, were confirmed visually on the screen of the device.

All participants were tested in a standard sequence with trunk EXT performed first followed by FLX, and right and left ROT. As an initial warm-up, all participants performed a maximum of 3 slow, sub-maximum dynamic motion at low loads throughout the full range of trunk motion and performed a maximum of 3 isometric test contractions at sub-maximum loads. After the warm-up, all participants generated their maximum isometric contraction by gradually increasing their torque moment up to their maximum within the first 2–3 s of each contraction. The best value obtained out of 3 attempts was stored. If these 3 tests varied by more than 10%, or if the peak moment was achieved later than 3 s after the onset of the contraction, then further trials were permitted until a consistent maximum was achieved. Intervals between maximum test repetitions or attempts were a minimum of 15 s. The 3 different maximum isometric tests (EXT, FLX, and ROT) were separated by 5 min. The entire strength evaluation was performed under the supervision of a spine physiotherapist trained and experienced in the use of the equipment. Maximum EXT, FLX, right and left ROT ROMs were measured on all 3 devices sequentially after unlocking the device after the specific isometric trunk strength tests. All equipment had a monitor placed in front of the participant which provided a real-time display of the motion value and force curve. Both strength (torque) and motion values were captured by an inbuilt software and stored in its server which were later retrieved for each patient.

Study Outcome Measures

Demographic data including gender, age, body mass index (BMI), and lifestyle (sedentary, semi-active, or active) were collected in all subjects. Lifestyle was categorised based on American College of Sports Medicine (ACSM) recommendations as sedentary for prolonged sitting at work or during leisure and lack of physical activity during most part of the day, as active if performing daily moderate-to-vigorous physical activities, and as semi-active lifestyle if the lifestyle more active than sedentary but did not involve daily moderate-to-vigorous physical activities [17]. For trunk ROM, maximum EXT, FLX, right ROT, and left ROT were recorded in degrees. For TIS, maximum torque for trunk EXT, EXT, right ROT, and left ROT were recorded in Newton-metre (Nm). To compare the mean EXT, FLX, and ROT TIS of the subjects in the current study with other ethnic population, we performed a literature review of similar studies published in the last 20 years (2000–2020) that had evaluated TIS in a similar group of asymptomatic subjects using similar devices and measured isometric strength in Nm. For comparisons among countries, we used mean TIS values (in Nm) according to gender.

Statistical Analysis

Using the mean FLX TIS reported in a previous study conducted in a similar asymptomatic study population [16], alpha error of 0.05, power of 80%, and the anticipated mean FLX TIS for the current study based on an initial pilot test, a sample size of minimum 73 subjects was calculated for the study using an online sample size calculator (ClinCalc

Online Calculator, ClinCalc LLC, USA). After adjusting for possible dropouts and the minimum sample size recommended in the literature to generate stable means and standard deviations for normative test data [18], a minimum sample size of 80 subjects was finalised. Categorical data were compared using the Chi-square test and continuous data were compared using one-way analysis of variance (ANOVA). The 10th–95th percentiles for trunk ROM and TIS were defined for all subjects, males, and females. Mean EXT, FLX, and ROT ROM and mean EXT, FLX, and ROT TIS were compared between males and females. Correlation analysis was performed to determine correlation between age, gender, BMI, lifestyle, EXT, FLX, and ROT ROM and the EXT and FLX ROM. Similarly, correlation analysis was performed to determine correlation between age, gender, BMI, lifestyle, EXT, FLX, and ROT TIS and the EXT and FLX TIS. A Pearson's correlation analysis was used to determine correlation between 2 continuous variables and the point-biserial correlation analysis was used to determine correlation between a categorical (gender and lifestyle) and a continuous variable. A p value of < 0.05 was considered significant. Statistical analysis was performed using the GraphPad QuickCalcs online statistical analysis tool (GraphPad Software, San Diego USA).

Table 1 Demographic parameters in the study population

Parameters	All subjects	Males	Females
n	80	24	56
Age (years)	27.9 ± 3.6 (27.0–28.7)	28.1 ± 3.2 (26.7–29.4)	27.8 ± 3.8 (26.7–28.8)
BMI (kg/m^2)	25.3 ± 4.5 (24.2–26.3)	26.2 ± 5.0 (24.0–28.3)	25 ± 4.3 (23.8–26.1)
Gender			
Males	24 (34%)	24 (100%)	–
Females	56 (66%)	–	56 (100%)
Lifestyle			
Active	20 (25%)	7 (35%)	13 (65%)
Semi-active/sedentary	60 (75%)	17 (28.5%)	43 (71.5%)

All values presented as mean ± standard deviation (95% confidence interval) or number (percentage)

n number of subjects, *BMI* body mass index

Results

Based on the inclusion and exclusion criteria, data from 80 subjects were analysed for this study. The demographic details of the study group are summarised in Table 1. There was no significant difference in mean age ($p = 0.73$), mean BMI ($p = 0.27$), and lifestyle ($p = 0.58$) when male and female subjects were compared (Table 1).

Trunk ROM and TIS in the Study Population

Mean trunk ROM and TIS values in the study population are summarised in Table 2. The distribution of ROM and TIS from 10 to 95th percentiles in all subjects and according to gender are shown in Fig. 2. The normative reference value for mean EXT ROM, FLX ROM, right ROT ROM, and left ROT ROM in the study population were 23° (95th percentile 31.9°), 40.2° (95th percentile 51.5°), 36.8° (95th percentile 57.7°), and 35.4° (95th percentile 55.7°), respectively (Table 2, Fig. 2a–c). The normative reference values for mean EXT TIS, FLX TIS, right ROT TIS, and left ROT TIS were 118.1 Nm (95th percentile 278.8 Nm), 63.8 Nm (95th percentile 159.4 Nm), 39.9 Nm (95th percentile 113.6 Nm), and 42.8 Nm (95th percentile 108.9 Nm), respectively (Table 2, Fig. 2d–f). The mean EXT ROM was significantly lesser when compared

Table 2 Trunk range of motion (ROM) and isometric strength (TIS) in study population and comparison between male and female subgroups

Parameters	All subjects	Males	Females	Males vs females	
				MD	*p* value
n	80	24	56	–	–
EXT ROM (°)	23.0 ± 6.6 (21.5–24.4)	27.0 ± 7.1 (24.0–29.9)	21.1 ± 5.6 (19.6–22.6)	5.9	**0.0002**
FLX ROM (°)	40.2 ± 8.1 (38.3–42.0)	39.3 ± 9.3 (35.3–43.2)	40.6 ± 7.5 (38.5–42.6)	1.3	0.51
Right ROT ROM (°)	36.8 ± 10.0 (34.5–39.0)	40.7 ± 9.3 (36.7–44.6)	35.2 ± 10.0 (32.5–37.8)	5.5	**0.02**
Left ROT ROM (°)	35.4 ± 10.2 (33.1–37.6)	39.6 ± 10.5 (35.1–44.0)	33.5 ± 9.7 (30.9–36.0)	6.1	**0.01**
EXT TIS (Nm)	118.1 ± 73.0 (101.8–134.3)	197.8 ± 74.8 (166.2–229.3)	83.9 ± 36.8 (74.0–93.7)	113.9	**< 0.0001**
FLX TIS (Nm)	63.8 ± 37.6 (55.4–72.1)	101.8 ± 42.9 (83.6–119.9)	47.5 ± 19.1 (42.3–52.6)	54.3	**< 0.0001**
Right ROT TIS (Nm)	39.9 ± 30.1 (33.2–46.5)	69.0 ± 37.9 (52.9–85.0)	27.4 ± 13.2 (23.8–30.9)	41.6	**< 0.0001**
Left ROT TIS (Nm)	42.8 ± 31.2 (35.8–49.7)	75.5 ± 36.4 (60.1–90.8)	28.9 ± 13.6 (25.2–32.5)	46.6	**< 0.0001**

All values presented as mean ± standard deviation (95% confidence interval)

$p < 0.05$ is considered statistically significant (bold)

n number of subjects, *BMI* body mass index, *Nm* Newton-metre, *EXT* extension, *FLX* flexion, *ROT* rotation, *MD* mean difference

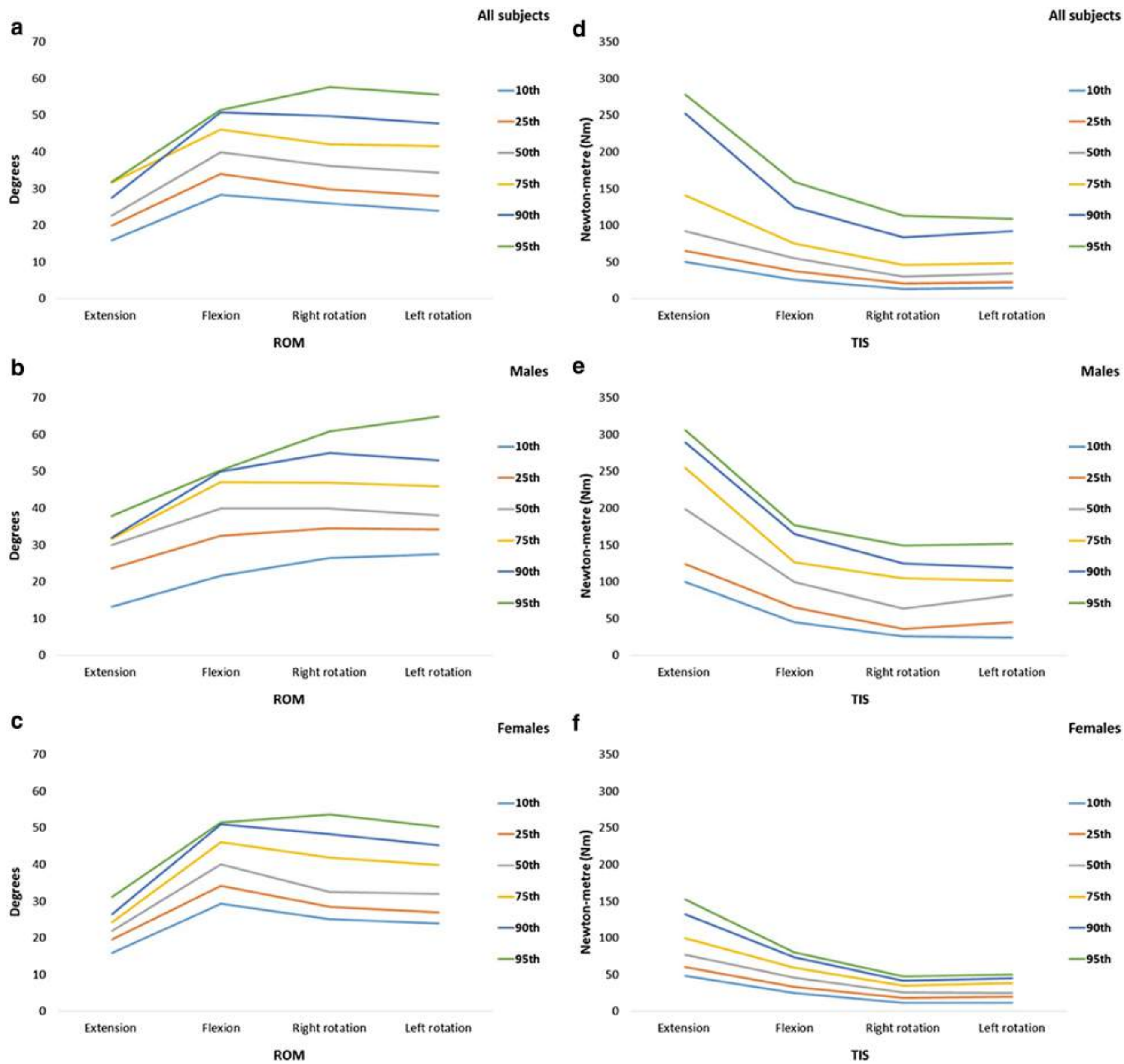

Fig. 2 Percentile values for mean trunk range of motion (ROM) (**a**–**c**) and isometric strength (TIS) (**d**–**f**) in all, male, and female subjects

to FLX ROM ($p < 0.0001$) and ROT ROM ($p < 0.0001$) (Table 2). The mean EXT TIS was significantly greater when compared to mean FLX TIS ($p < 0.0001$) and ROT TIS ($p < 0.0001$) (Table 2).

Based on gender, the mean EXT and ROT ROM were significantly greater in male subjects when compared to female subjects whereas the mean FLX ROM was not significantly different between males and females (Table 2). Similarly, the mean EXT, FLX, and ROT TIS were significantly greater in male subjects when compared to female subjects (Table 2).

Correlation Between Subject Characteristics and EXT and FLX ROM and TIS

The EXT ROM showed significant positive but weak correlation with male gender, and FLX and ROT ROM whereas FLX ROM showed significant positive but weak correlation with EXT and ROT ROM (Table 3). The EXT TIS showed significant positive but weak correlation with higher BMI, significant positive and moderate correlation with male gender, and significant positive and strong correlation with FLX and ROT TIS (Table 3). The FLX TIS showed significant

Table 3 Correlation between extension (EXT) and flexion (FLX) range of motion (ROM) and isometric strength (TIS) and various parameters in the study population

Parameters	EXT		FLX	
	r	*p* value	*r*	*p* value
For ROM				
Gender	0.40	**0.0002**	− 0.07	0.53
Age	0.01	0.92	− 0.14	0.21
Lifestyle	− 0.02	0.86	0.02	0.86
BMI	− 0.18	0.11	− 0.18	0.11
EXT ROM	–	**–**	0.25	**0.02**
FLX ROM	0.25	**0.02**	–	–
Right ROT ROM	0.41	**0.0001**	0.31	**0.005**
Left ROT ROM	0.37	**0.0007**	0.39	**0.0003**
For TIS				
Gender	0.71	**< 0.00001**	0.66	**< 0.00001**
Age	0.15	0.18	0.12	0.28
Lifestyle	0.01	0.92	0.01	0.92
BMI	0.31	**0.005**	0.21	0.06
EXT TIS	–	**–**	0.81	**< 0.00001**
FLX TIS	0.81	**< 0.00001**	–	**–**
Right ROT TIS	0.79	**< 0.00001**	0.87	**< 0.00001**
Left ROT TIS	0.78	**< 0.00001**	0.88	**< 0.00001**

$p < 0.05$ is considered statistically significant (bold)

BMI body mass index, *r* correlation coefficient, *EXT* extension, *FLX* flexion, *ROT* rotation

positive and moderate correlation with male gender, and significant positive and strong correlation with EXT and ROT TIS (Table 3).

Comparison of Indian Population with Other Ethnicities

Based on a literature review of similar studies performed in other ethnic populations to measure isometric trunk strength in asymptomatic subjects, the mean EXT, FLX and ROT TIS in Indian subjects were significantly lower when compared to subjects from Israel, Denmark, South Korea, Austria, and Australia and this difference was greater among female subjects when compared to male subjects (Table 4, Fig. 3).

Discussion

The current study established normative reference values for mean trunk EXT, FLX, and ROT ROM, and TIS in asymptomatic Indian subjects between 20 and 40 years of age. The trunk ROM pattern in the current study, where FLX and ROT ROM were greater than EXT ROM, was similar to previous studies that analysed trunk ROM [19, 20]. Kachingwe and Phillips [19], in a study of 91 asymptomatic adults (21–57 years of age), reported significant difference between EXT, FLT, and ROT ROM measured using a goniometer and inclinometer based back range of motion (BROM) instrument. Trunk ROM using smart-phone based inclinometers have shown similar patterns of EXT-FLX ROM in asymptomatic subjects where FLX ROM was significantly greater than EXT ROM [20]. Although the female gender has been reported to have greater ROM for most joints [21], our findings indicate that this may not be true for trunk ROM where EXT and ROT ROM were significantly greater in males when compared to females. It is possible that bodyweight distribution and genetic variations may be associated with this gender-based difference in trunk ROM [22].

Kienbacher et al. [16], in an analysis of 81 asymptomatic subjects (39 subjects < 50 years of age, 42 subjects ≥ 50 years of age), reported a significantly higher EXT TIS when compared to FLX and ROT TIS, and a significantly higher EXT, FLX, and ROT TIS values in male subjects when compared to females. Similarly, Nissan et al. [23], in a study of 38 asymptomatic subjects, reported a significantly higher EXT TIS compared to FLX and ROT TIS and significantly higher EXT, FLX, and ROT TIS values in male subjects when compared to females. Hence, the variations in EXT versus FLX TIS and gender-based variations in TIS found in the current study were confirmed by similar studies involving other ethnic populations [16, 23, 24].

In terms of factors affecting EXT or FLX TIS, Danneskiold-Samsøe et al. [24], in an analysis of isometric trunk strength in 174 asymptomatic subjects (20–80 years of age), reported age as a significant factor that determined trunk TIS in both males and females. This is contrary to the findings of the current study, where no significant correlation was found between age and TIS, which was probably due to the difference in the age range of the study populations. Furthermore, we found that lower EXT TIS was associated with lower FLX and ROT TIS in subjects, and decreased TIS in an individual was global and affected all 3 groups of muscles. The mean EXT, FLX, and ROT TIS in the Indian population were significantly lower when compared to study populations from other countries (Fig. 2). These ethnic and geographic variations in skeletal muscle strength could be explained by variations in muscle mass [25], muscle composition [26], and physical functional capacity [27].

To the best of our knowledge, this was the first study in the literature that aimed to determine the normative reference values for trunk ROM and TIS in asymptomatic, young Indian adults. However, the current study has a few limitations. First, subjects in this study were recruited using convenience sampling, which may have introduced a selection bias. Second, we analysed trunk ROM and TIS in a population within the 20–40 years age group. This was done to avoid increasing age, possible co-morbidities, and past

Table 4 Comparison of extension, flexion and rotation trunk isometric strength in the current study with similar studies previously published in the literature

Study	Country	n	Mean age (years)	Study population	Device used for measurement	Mean EXT TIS (Nm)		Mean FLX TIS (Nm)		Mean ROT TIS (Nm)	
						Males	Females	Males	Females	Males	Females
Nissan et al. [23] 2000	Israel	38	31.5	Community	IsoStation B-200 (Isotechnologies Co., USA)	222 + 71	155 + 40	172 + 55	77 + 15	113 + 34	69 + 12
Danneskiold-Samsøe et al. [24] 2009	Denmark	174	50 (20–80)	Community	Lido Active (Lido Multi Joint II; Loredan Biomedical, USA)	236 ± 39.7 to 336 ± 48.8	154 ± 40.4 to 232 ± 67.6	108 ± 30.2 to 147 ± 20.0	69.7 ± 11.6 to 96.5 ± 19.2	NR	NR
Cho et al. [5] 2014	South Korea	19	45.6 (22–72)	Hospital visitors	Biodex® System 4 (Biodex Medical Systems, New York, USA)	275.0 ± 68.1*	–	158.2 ± 53.4*	–	NR	NR
Kienbacher et al. [16] 2017	Austria	39	33 (18–49)	Hospital staff, personal contacts, Community	DAVID F110 extension (DAVID® Health Solutions Ltd, Helsinki, Finland)	297.2 ± 74.6	186.7 ± 40.4	159.5 ± 33.5	81.8 ± 22.8	138.5 ± 41.2	60.0 ± 23.4
Kienbacher et al. [16] 2017	Austria	42	67 (50–90)	Hospital staff, personal contacts, Community	DAVID F110 extension (DAVID® Health Solutions Ltd, Helsinki, Finland)	277.7 ± 69.9	172.3 ± 35.1	142.7 ± 35.7	80.8 ± 19.6	122.1 ± 45.0	50.2 ± 19.2
Pranata et al. [14] 2017	Australia	20	34.8 (25–60)	Community	MedX Lumbar Extension Machine (MedX®, Ocala, FL, USA)	182.0 ± 16.4*	–	NR	NR	NR	NR
Current study 2020	India	80	27.9 (20–40)	Physiotherapist, Patient contacts	DAVID system (DAVID® Health Solutions Ltd, Helsinki, Finland)	197.8 ± 74.8	83.9 ± 36.8	101.8 ± 42.9	47.5 ± 19.1	72.2 ± 37.1	28.1 ± 13.4

All values presented as mean ± standard deviation or mean (range)

n number of subjects, *NR* not reported, *TIS* trunk isometric strength, *EXT* extension, *FLX* flexion, *ROT* rotation

*Values reported as mean for entire study population

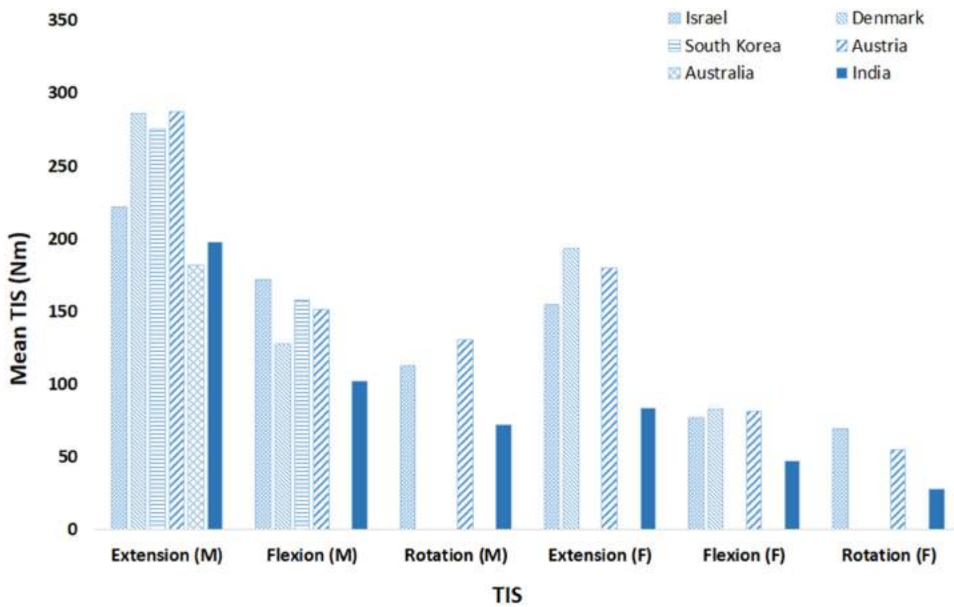

Fig. 3 Comparison of mean extension, flexion, and rotation trunk isometric strength (TIS) in males (M) and females (F) between Indian subjects and subjects from other countries

episodes of LBP from affecting the ROM and TIS values. The 20–40 years' age group is the typical age of onset of LBP in most populations [28]. Hence, it is important to determine ROM and TIS normative reference values in this age group so that their change over time with increasing age and repeated episodes of LBP can be objectively quantified. Finally, a majority of the study population had a semi-active or sedentary lifestyle which may affect the normative reference values. However, a large percentage of people in India have been reported to have an inactive or sedentary lifestyle, with fewer than 10% engaging in regular or daily recreational physical activity [29], which indicates that our study sample was representative of the general Indian population in terms of lifestyle. Hence, the findings of the current study need to be replicated in a larger group of subjects of varying age and lifestyle derived from the general population.

Conclusions

The current study established normative reference values for trunk ROM and TIS in asymptomatic young Indian adults. The mean and 95th percentile values for EXT and ROT ROM, and EXT, FLX, and ROT TIS were significantly greater in male subjects when compared to female subjects. Male gender was associated with greater EXT and FLX TIS, and FLX, EXT, and ROT TIS had a significant and strong correlation with EXT and FLX TIS. The mean EXT, FLX, and ROT TIS were significantly lower in Indian subjects when compared to subjects from other countries. These reference values can be helpful to diagnose trunk ROM and TIS deficits, identify subjects at risk for LBP and disability, and individualise rehabilitation treatment in them.

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Declarations

Conflict of Interest On behalf of all the authors, the corresponding author states that there is no conflict of interest.

Ethics and Institutional Review Board (IRB) Approval This study has been approved by an Institutional Ethics Committee and has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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ORIGINAL ARTICLE

Hip Surveillance for Children with Cerebral Palsy: A Survey of Orthopaedic Surgeons in India

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Abstract

Background The purpose of this study was to assess Indian orthopaedic surgeons' current practices and beliefs regarding hip surveillance for children with cerebral palsy (CP), to determine potential support for developing hip surveillance guidelines, and to identify knowledge gaps and key obstacles to guideline implementation in India.

Methods An anonymous, cross-sectional online survey was sent to approximately 350 Paediatric Orthopaedic Society of India (POSI) members who were queried on their practices and beliefs about hip surveillance for children with CP, as well as perceived challenges and requirements for the successful implementation of hip surveillance guidelines in the Indian context.

Results Out of 107 responses obtained from POSI members, almost all (96.2%) agreed that hip displacement requires standardized monitoring, using surveillance and surgery to prevent hip dislocation. Approximately half (51.5%) of respondents reported using existing hip surveillance guidelines, with most (41.2%) using the Australian guidelines. Almost all (97%) surgeons indicated that hip surveillance guidelines in India are needed, with 100% expressing interest in following guidelines specific to India. Respondents most frequently indicated late referrals to orthopaedics (81.2%), loss of patients to follow-up (78.2%), and lack of resources (43.6%) as challenges to successful hip surveillance in India. Perceived requirements for implementation included developing Indian-specific guidelines (83.2%) as well as educating surgeons (56.4%), physiotherapists/pediatricians (90.1%), and families (82.2%).

Conclusion Orthopaedic surgeons practicing in India understand the importance of preventing hip dislocations in children with CP through hip surveillance and timely surgical intervention. The results demonstrated strong support for the development of hip surveillance guidelines designed specifically for the Indian healthcare system.

Keywords Cerebral palsy · Hip surveillance · Hip displacement · Survey

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Introduction

Cerebral palsy (CP) describes a group of conditions, affecting the development of movement and posture, that are attributed to non-progressive disturbances in the fetal or infant brain [1]. In children with CP, hip displacement is the second most common musculoskeletal deformity, with an estimated incidence of approximately 35% [2, 3]. For most children with CP, the hip joint is normal at birth; however, the musculoskeletal pathology leads to progressive hip displacement [4–6]. Hip displacement often remains asymptomatic until the hip is dislocated, which can subsequently cause pain, impaired ability to stand, sit, or walk, and may negatively impact a child's quality of life [3, 7–9]. The timing at which hip displacement is identified can impact the treatment options available. Preventive and reconstructive surgeries are recommended to treat progressive hip displacement prior to dislocation [4, 10–12]. Left undetected and untreated, salvage surgeries such as a femoral head resection with valgus osteotomy may be necessary if the severity of femoral head damage is too great to allow for reconstruction [11, 13, 14]. Salvage procedures are associated with inconsistent pain relief, high rates of revisions, and greater risk of complications, and are thus reserved as a last option for painful, dislocated hips [15, 16].

Hip surveillance is defined as the process of identifying and monitoring early indicators of hip displacement through systematic screening [17]. The goal of hip surveillance is to identify hip displacement early and ensure a child is seen by an orthopaedic surgeon when all treatment options are available [18]. To date, national and regional surveillance programs have been developed and adopted in parts of Australia, Canada, and Europe, with evidence supporting the use of surveillance to prevent dislocations and avoid the need for salvage surgery [17, 19–22]. Although there is growing evidence to support the need for hip surveillance for children with CP, there are currently no standardized guidelines in India, the world's second-most populous country with an estimated population of 1.37 billion people in 2019 [23]. Existing surveillance programs are designed to meet the needs of the local populations and healthcare systems and may not be transferrable to developing countries such as India. Creating a national standard for hip surveillance in India would require the support of pediatric orthopaedic surgeons providing care to children with CP, as hip surveillance is successful only when combined with timely orthopaedic intervention. The purpose of this study was to investigate the variation in beliefs, practices, and attitudes related to hip surveillance in children with CP among pediatric orthopaedic surgeons in India. A secondary objective was to investigate surgeons' perceived obstacles to implementing hip surveillance in India and possible strategies for success.

Materials and Methods

A 31-item survey was developed, based on current literature and consensus opinions, and reviewed by all authors (Appendix 1). The study was approved by the institutional Research Ethics Board and the Paediatric Orthopaedic Society of India (POSI) Research and Grants Committee. The anonymous survey was electronically distributed by email and the messaging platform WhatsApp to approximately 350 orthopaedic surgeons who were members of POSI.

The survey included questions related to surgeon demographics, practice, and beliefs about hip surveillance. Respondents were asked to estimate compliance for getting X-rays and surgery among their patients with CP and were also asked to report their confidence in completing different components of hip surveillance. To understand attitudes and beliefs towards hip surveillance, respondents were given a series of five statements regarding hip surveillance and were asked to select their agreement on a 5-point Likert scale. Questions then explored whether surgeons believed there was a need for hip surveillance, when a child should be referred to an orthopaedic surgeon, as well as critical elements and perceived obstacles to implementing hip surveillance for children with CP in India. Finally, respondents were asked to identify if they currently follow surveillance guidelines. These respondents were further asked to indicate the type of guidelines, perceived effectiveness of the guideline, and frequency with which the guideline was followed. Survey responses were collected and managed using the Research Electronic Data Capture (REDCap), a secure web application designed for building and managing online surveys and databases, hosted at our research institution. Data were analyzed using descriptive statistics.

Results

Demographic Data

A total of 107 responses were collected from orthopaedic surgeons who were members of POSI (30.6% response rate). It was not mandatory for the respondents to answer every question of the survey. If > 90% of the survey questions were answered, the responses were included in the final analysis. The entire questionnaire was completed by 99/107 (92.5%) respondents and the remaining 8 completed > 90% of the survey questions. The respondents' demographics and practice characteristics are summarized in Table 1. The mean years in practice was 12 years

Table 1 Summary of respondent demographics and practice characteristics

Years in practice ($n = 107$)	
0–5 years	31 (29.0%)
6–10 years	30 (28.0%)
11–15 years	16 (15.0%)
16–20 years	11(10.3%)
21 + years	19 (17.8%)
Orthopaedic sub-specialty fellowship training ($n = 93$)	
Pediatric orthopaedics	84 (90.3%)
Other	9 (9.7%)
Urban vs. Rural ($n = 107$)	
Urban	92 (86.0%)
Rural	10 (9.3%)
Semi-urban	5 (4.7%)
Practice setting ($n = 106$)	
Private clinic or nursing home	26 (24.5%)
Corporate hospitals	16 (15.1%)
University or teaching hospital	23 (21.7%)
Combined private and teaching hospital	40 (37.7%)
Other	1 (0.9%)
Pediatric caseload ($n = 107$)	
0–20%	10 (9.3%)
21–40%	11 (10.3%)
41–60%	10 (9.3%)
61–80%	21 (19.6%)
81–100%	55 (51.4%)
CP Caseload ($n = 102$)	
0–20%	52 (51.0%)
21–40%	36 (35.3%)
41–60%	10 (9.8%)
61–80%	3 (2.9%)
81–100%	1 (1.0%)
Follow-up frequency ($n = 106$)	
As needed	19 (17.9%)
Once per year	8 (7.5%)
Twice per year	32 (30.2%)
More than twice per year	47 (44.3%)
Age of referral to orthopaedic surgeon ($n = 107$)	
< 2 years old	13 (12.1%)
2–5 years old	70 (65.4%)
6–10 years old	24 (22.4%)
> 10 years old	0 (0%)

(ranging from 1 to 48 years). Most respondents indicated having received fellowship training in an orthopaedic sub-specialty, with 90.3% of those with sub-specialty training selecting Pediatric Orthopaedics (Table 1).

Surgeon caseloads were, on average, 74.9% pediatric, with an average 26.4% of pediatric caseloads being children with CP. Surgeons reported seeing an average of seven (range 0 to 50) patients with CP who had a Reimer's migration percentage of 100% in the past 12 months. Referral and follow-up frequency practices among respondents are shown in Table 1.

Table 2 Reasons for lack of X-ray and surgery compliance among respondents' patients with CP

X-ray noncompliance reasons ($n = 107$)	
Cost	26 (24.3%)
Worry about radiation from repeated X-rays	14 (13.1%)
Not understanding the importance of hip surveillance	73 (68.2%)
Difficulty accessing X-ray	6 (5.6%)
Another healthcare provider advises against X-ray	9 (8.4%)
Physiotherapist	6 (66.7%)
Neurologist	3 (33.3%)
General practitioner or family doctor	9 (100%)
Pediatrician	4 (44.4%)
Other healthcare provider	2 (22.2%)
Other	9 (8.4%)
Surgery noncompliance reasons ($n = 107$)	
Lack of proper counselling	7 (6.5%)
Cost/Lack of resources	68 (63.6%)
Fear of surgery	67 (62.6%)
Poor health and nutrition	31 (29.0%)
Another healthcare provider advises against surgery	23 (21.5%)
Physiotherapist	19 (82.6%)
Neurologist	10 (43.5%)
General practitioner or family doctor	17 (73.9%)
Pediatrician	10 (43.5%)
Other healthcare provider	5 (21.7%)
Other	12 (11.2%)

Compliance with X-rays and Surgery

On average, respondents reported that 65.1% of patients follow their advice for getting repeated/regular X-rays and less than half of parents/families (48.5%) comply with surgeon recommendations to undergo surgery for hip displacement. Table 2 shows the probable reasons why patients may not comply with either X-ray or surgery. While cost (selected by 24.3% of respondents) may be a factor, more than two-thirds of respondents felt that lack of awareness of the importance of hip surveillance may prevent parents from complying with their surgeon's recommendations for regular X-rays. Lack of finances and fear of surgery were selected by > 60% of respondents and over one-fifth (21.5%) of respondents felt that other healthcare providers involved in the care of these children, including physiotherapists, neurologists, and primary care physicians, occasionally advise against timely hip surgery.

Beliefs about Hip Displacement and Surveillance in CP

Responses related to beliefs about hip displacement and surveillance are shown in Table 3. More than 80% of respondents strongly felt that hip displacement in children with CP is a problem that requires standardized monitoring and is preventable with regular surveillance and timely surgical intervention. Levels of confidence in completing different aspects of hip surveillance are summarized in Table 4. When queried specifically about hip surveillance in India, almost all surgeons (97.0%, 96/99) expressed a need for an Indian hip surveillance guideline, with 100% (99/99) expressing interest in following a guideline. Table 5 shows when respondents thought a child should be seen by an orthopaedic surgeon for concerns about hip displacement and perceived challenges to successful surveillance in India. Approximately two-thirds of respondents (65.3%) selected that the child should be referred to the orthopaedic surgeon once the migration percentage exceeds 30%.

Table 5 also shows the orthopaedic surgeons' requirements for successful surveillance in India. When queried further on which healthcare providers would be critical to successful guidelines in India, the most frequently selected healthcare providers were orthopaedic surgeons (88.0%, 88/100), followed by physiotherapists (86.0%, 86/100), neurologists (65.0%, 65/100), and occupational therapists (45.0%, 45/100). Respondents also identified pediatricians, general practitioners, non-governmental organizations, special education facilities, accredited social health activist (ASHA) workers, and government rural healthcare workers as being important to the success of hip surveillance in India.

Use of Existing Hip Surveillance Guidelines

Utilization of guidelines, their perceived effectiveness, and adherence to guidelines are shown in Table 6. Approximately half (51.5%, 51/99) of surgeons reported using a hip surveillance guideline in their own practice, with most using the Australian Standards of Care (41.2%). Of those respondents who did not follow a guideline, 43.2% (19/44) indicated that they were aware of guidelines for CP hip surveillance, most notably the Australian guidelines and the American Academy for Cerebral Palsy and Developmental Medicine (AACPDM) Care Pathway.

Discussion

Pediatric orthopaedic surgeons in India support the prevention of hip dislocations in children with CP through regular hip surveillance and timely surgical intervention, despite some variation in practice with regards to hip surveillance.

Table 3 Respondents' agreement with statements about beliefs and practice related to hip surveillance in children with CP

Level of agreement	1 Not at all (%)	2 (%)	3 (%)	4 (%)	5 Very much so (%)
A dislocated hip will become painful in a child with CP ($n=104$)	0	2.9	10.6	26.9	59.6
Hip displacement in children with CP is a problem that requires standardized monitoring ($n=104$)	0	1.0	2.9	14.4	81.7
Hip dislocation should be prevented by hip surveillance and surgical treatment ($n=104$)	0	1.0	2.9	13.5	82.7
Hip displacement should be assessed by measuring Reimer's migration percentage on an AP pelvis radiograph ($n=102$)	0	2.0	2.9	17.6	77.5
I identify Gross Motor Function Classification System (GMFCS) levels for all my patients with CP. ($n=104$)	1.0	1.9	2.9	10.6	83.7

Table 4 Respondents' confidence in completing components of hip surveillance

Level of confidence	1 Not at all (%)	2 (%)	3 (%)	4 (%)	5 very much so (%)
Determining a child's GMFCS level ($n=99$)	1.0	0.0	2.0	21.2	73.7
Determining that a child has Group IV hemiplegic gait pattern ($n=99$)	2.0	3.0	6.1	35.4	53.5
Determining how frequently a child with CP should have a hip X-ray for hip surveillance ($n=100$)	1.0	2.0	12.0	31.0	54.0
Knowing which position the child should be placed in when having a hip X-ray ($n=99$)	1.0	2.0	12.1	19.2	65.7

Table 5 Respondents' beliefs about the timing of referral, challenges, and requirements for successful hip surveillance in India

Timing of referral to an orthopaedic surgeon ($n=101$)	
Once migration percentage is greater than 30%	66 (65.3%)
Once migration percentage is greater than 40%	19 (18.8%)
Once migration percentage is greater than 50%	11 (10.9%)
Function has decreased, related to the hip	51 (50.5%)
Hip abduction, with hips and knees in 90° of flexion, is < 30°	45 (44.6%)
Hip abduction, with hips and knees in 0° of flexion, is < 30°	48 (47.5%)
There is asymmetrical hip abduction	66 (65.3%)
The child has increased pain, related to the hip	64 (63.4%)
I don't know/I prefer not to answer	1 (1.0%)
Other	5 (5.0%)
Surveillance challenges ($n=101$)	
Lack of buy-in from other healthcare professionals	40 (39.6%)
Late referrals to the orthopaedic surgeon	82 (81.2%)
Lack of resources	44 (43.6%)
Loss to follow-up	79 (78.2%)
Lack of standardized X-rays	32 (31.7%)
Families worry about too many X-rays	13 (12.9%)
Other	7 (6.9%)
Surveillance requirements ($n=101$)	
Designing a guideline considering the Indian factors in mind	84 (83.2%)
Better training to pediatric orthopaedic surgeons	57 (56.4%)
Making physiotherapists/pediatricians more aware about its importance	91 (90.1%)
Making family members more aware about its importance	83 (82.2%)
Other	7 (6.9%)

Table 6 Characteristics of respondents who reported following a hip surveillance guideline

Guideline type ($n=51$)	
Australian Standards of Care	21 (41.2%)
Sweden's CPUP	0 (0%)
British Columbia, Canada's Hip Surveillance Consensus	4 (7.8%)
AACPDM Hip Surveillance Care Pathway	12 (23.5%)
Alfred I. duPont Institute (Freeman Miller) recommendations	10 (19.6%)
Other	4 (7.8%)
Guideline effectiveness ($n=51$)	
Effective	50 (98.0%)
Not effective	1 (2.0%)
Frequency of guideline adherence ($n=51$)	
< 25%	0 (0%)
25–50%	3 (5.9%)
50–75%	17 (33.3%)
> 75%	31 (60.8%)

There is also strong support among orthopaedic surgeons for the development of Indian-specific hip surveillance guidelines for children with CP, with almost all respondents indicating both a need for and interest in implementing national guidelines. Despite agreement on the importance of hip surveillance in children with CP, just 51.5% of respondents reported using existing guidelines in their own practice, and even of those that do, only 39.2% follow those guidelines 75% of the time or less. These findings draw similarities to the findings of a survey of POSNA membership, which found that 18% of their respondents followed a specific CP hip surveillance protocol, with 21% following the guidelines 75% of the time or less [24]. Inconsistent use of guidelines contributes to the variation in screening, diagnosis and management of hip displacement, thereby increasing costs and impacting the quality of care that is provided [24]. The inconsistent use of hip surveillance but high guideline awareness among respondents may also suggest that the current hip surveillance protocols are not entirely applicable to the Indian context, emphasizing the need to develop and implement a tailored hip surveillance guideline in India.

While developing CP hip surveillance guidelines, education of orthopaedic surgeons on the clinical and radiographic components of hip surveillance will be necessary. Encouragingly, 83.7% of respondents indicated that they identify the Gross Motor Function Classification System (GMFCS) level for all of their patients with CP; however, only 73.7% indicated that they were very confident in determining the GMFCS level. The ability to confidently identify the GMFCS level is critical, as existing hip surveillance guidelines use GMFCS levels to guide the frequency of hip surveillance [17, 19, 20, 25]. Future studies are needed to evaluate the knowledge and use of GMFCS among general orthopaedic surgeons in India. Migration percentage (MP) is the most widely accepted and most frequently used radiological measure to monitor and identify risk of hip displacement [26]. The standardized positioning of the pelvis with neutral adduction/abduction, flattened lordosis, neutral pelvic obliquity, and patella facing upwards is of critical importance to correctly measure MP—this also ensures the reliability of measurements taken between subsequent radiographs [17, 19, 25, 27]. While almost all respondents (95.1%) agreed that hip displacement should be assessed by measuring Reimer's MP on an AP pelvis radiograph, 15.1% of surgeons indicated that they were not at all or only somewhat confident with knowing in which position a child should be placed for a hip X-ray.

Surgeons reported that only two-thirds of their patients follow their recommendation for regular/repeated X-rays, with the most common reasons for not following recommendations being the patient/family's lack of understanding about the importance of X-rays, followed by cost and radiation concerns. A study by Toovey et al. examining the experiences of parents of children with CP when engaging with hip surveillance in Australia, similarly identified a lack of knowledge among parents as a barrier to engagement [28]. These findings emphasize the need to educate parents and families on the value of hip surveillance and the importance of following the schedule of clinical and radiographic examinations. Parents and families who are educated about the subject may be more likely to play an active role in their child's hip surveillance [28]. Education may also aid in decreasing the number of patients lost to follow-up, which was one of the most frequently identified challenges to implementing guidelines in India. Recommendations for surgery were reported to be followed less often than recommendations for imaging at just 48.5%. Fear of surgery, lack of finances, and poor health and nutrition were the most frequent reasons surgeons reported for their patients refusing surgery. Further exploration of why patients may not be undergoing surgery will be important, as hip surveillance is only advantageous if the child undergoes surgery when recommended. Taken together, these results highlight a need to increase awareness of the value of hip surveillance and treatment of hip displacement among families of children with CP in India. Ensuring that the perspectives of Indian parents and families are included and understood will be important for future guideline development. In British Columbia, Canada, the Child Health BC Hip Surveillance Program involved parents of children with CP in the consensus-building and program implementation process, emphasizing the need to consider the child and family when establishing and implementing a surveillance guideline [29].

Although it is evident that orthopaedic surgeons in India are willing to adopt national guidelines, there must be a collaborative effort among all critical members of a child's healthcare team for hip surveillance to be successful. The results of the survey showed that 21.5% of respondents had other healthcare providers occasionally advise against surgery. This corresponds to the opinion of many respondents who felt that a lack of buy-in from other healthcare professionals and late referrals may be a significant barrier to guideline implementation. Important healthcare providers that were identified in this survey include neurologists, pediatricians, and physiotherapists. It will be important to work collaboratively with these groups to examine these potential challenges in more depth. Involving and educating other healthcare providers will be especially important, as orthopaedic surgeons may not see patients with CP at an early enough age for hip surveillance to be effective. Lack of resources was identified as a challenge to surgery compliance (63.6%) and guideline implementation (43.6%) and will also need to be considered when developing feasible guidelines for the Indian healthcare system.

There was a substantial variation among respondents as to what MP warrants a referral to an orthopaedic surgeon. While over 60% of respondents selected MP > 30%, 18.8% selected MP > 40% and 10.9% selected MP > 50%. Existing guidelines most commonly use MP > 30% as an indication for a child to be referred to an orthopaedic surgeon as this is the threshold for an "at risk" hip [3, 17, 19, 25, 26]. In contrast, surgical intervention is often considered once MP exceeds 40% or 50% [27, 30]. While developed countries with universal healthcare may have the capacity to support the referral of children at a lower MP, the Indian healthcare system may not be able to support this practice. Surgeons in India may wish to see children when they are more likely to require surgical intervention. Alternatively, since an overwhelming majority (81.2%) felt that late referrals posed a challenge to hip surveillance in India, healthcare providers may elect to set the threshold lower to account for the time delay that often occurs between examination and referral, particularly in rural or underserved areas.

These survey results offer important insights into developing hip surveillance guidelines in a developing country and will be used to inform future discussions regarding guideline development in India. Current hip surveillance guidelines have been developed and applied in first world countries with universal healthcare and may not be relevant to the Indian context. While the development of a nation-wide program may be challenging, given India's large population size and diversity of practice settings, it is important for healthcare providers in India to adopt a standardized guideline for hip surveillance in children with

CP that works within their own setting. With a population of approximately 1.37 billion people [23], the development of national guidelines has the potential to benefit many children with CP and their families.

This study has several limitations. Most respondents reported practicing in urban areas, thus the results here may not apply to orthopaedic surgeons who practice in a rural setting. The use of a survey to collect information is also an inherent limitation. The responses collected may only reflect a particular viewpoint, and non-respondents may have very different beliefs and attitudes about hip surveillance which we were unable to collect. Additionally, although the survey aimed to capture all aspects of practice, beliefs, and attitudes towards hip surveillance, it could not capture a complete understanding of the respondents' feelings, opinions, or experiences with regards to surveillance. Despite these limitations, this study provides valuable information in understanding current practice and informing next steps toward guideline development in India.

Conclusion

There is strong support among pediatric orthopaedic surgeons in India for the prevention of hip dislocations in children with CP through hip surveillance and surgical intervention. In order for successful implementation to occur, it will be necessary to resolve context-specific barriers to surveillance that were identified in this survey. Solutions include educating families and members of the child's healthcare team on the importance of hip surveillance and more training to orthopaedic surgeons and allied professionals on the components of surveillance.

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Declarations

Conflict of Interest Kishore Mulpuri has received research support from Allergan, Pega Medical and Depuy Synthes (Johnson and Johnson). None are directly relevant to the research in this paper. For the remaining authors none were declared.

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ORIGINAL ARTICLE

Piezoelectric Bone Surgery. Overview in Applications and Proof of Feasibility in Hand and Plastic Surgery

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Abstract

Purpose Piezoelectric bone surgery was already extensively used in a number of surgical procedures ranging from dental to maxillofacial surgery. The authors aimed to determine whether piezosurgery was suitable and advantageous for performing osteotomies in Hand and Plastic reconstructive surgery.

Methods The authors overviewed a variety of applications for Piezosurgery® Device, from Mectron, in bone reconstructive surgery with over the last 8 years. An overall number of 156 bone cutting procedures in adults and children was described at the phalanges, metacarpal bones and distal radius level, as well as in bone graft harvesting and bone remodeling following carpal scaphoid nonunion, scapho-lunate bone-ligament-bone reconstruction and fibula free flap in maxillofacial defects.

Results The consolidation rate was 87.5% in scaphoid nonunion grafting and fixation. Bone healing was achieved in all other cases. No intra-operative complications were recorded.

Conclusion Piezosurgery® allowed high precision in bone cutting as well as custom-made graft and surface roughness were obtained, while preserving nerves, vessels and tendons integrity. The instrument may be handling moved into the surgical space in absence of vibrations, with a clear view onto the bone. The mechanical and biological characteristics of the piezoelectrical effect perfected this technique as an effective and useful instrument in Hand and Plastic surgery. The selective bone cutting properties avoided injuries to the surrounding soft tissues and thermal damage of the bony cells. Best advantages were described in feasibility and flexibility for intra-articular osteotomies, custom-made grafts and reconstructive microsurgical techniques.

Keywords Piezoelectric · Bone surgery · Osteotomy · Bone graft · Hand surgery · Plastic surgery

Introduction

The traditional procedure such as sawing, drilling, grinding and milling were associated with several drawbacks facing with bone cutting or remodeling [1–4]. In Hand and Plastic surgery, major challenges arose by the small bones and the proximity of fine anatomical structures.

Bone healing in osteotomy was minimized reducing the thermal damages. A wide variety of parameters were involved in heat generation such as instrument thickness, the force and the speed applied by the rotatory tools, or the utilization of coolant to minimize the temperature rising [2, 5, 6]. Greater force and higher speed resulted in less thermal damage to the bone, as well as multiple drill-hole osteotomy, instead of sawing [7, 8]. Chisels and scalpels may avoid thermal injuries but significantly increased the risks of breakage and inaccurate cutting. When milling was requested in accurate machining of bone surfaces, the thermal damage was greater than cutting, reaching since to 2 mm in depth. According to the bone thickness and properties, the applied cutting forces increased according to the bone density, and temperature increased 10% with a 12% increase in bone density [9].

On the other hand, nerve and tendon lesions were feared complications recurring to oscillating saws and rotational instruments or chisels.

Osteotomies required accurate execution, high precision, strict control, limiting also the damage to surrounding either

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neurovascular or tendon structures. Piezosurgery® was an advanced device which used the ultrasonic microvibrations to fulfill accurate and selective cut on the bone, in harmony with the surrounding soft tissues and with the thermal bone biology [2, 6]. The piezoelectric effect applied electric tension across the devise producing ultrasonic vibrations and waves. The mechanical contact and the cutting-hammering movement of the tip of the instrument onto the bone induced linear disorganization and fragmentation. Only mineralized tissue was selectively cut at the frequency range of 25–30 kHz, because of soft tissue would only be cut by above 50 kHz [3, 6]. The bone temperature was maintained by the cavitation effect which also washed away debris and cleared the surgical field, enhancing the visibility and ease of operation [4].

The escalating role of piezoelectric bone surgery was improved in surgical techniques requiring fine and high defined cut and remodeling, ranging from implantology and reconstructive maxillo-facial surgery to hand and plastic surgery.

Materials and Methods

Piezosurgery® Device from Mectron (Carasco GE, Italy) was used in 156 bone osteotomies and bone grafts, instead of the usual oscillating saw or chisels/scalpels in adults (102 patients), or multiple drill-hole technique in children (54 patients). Over the last 8 years, the authors used the piezoelectric effect in 83 osteotomies at the phalanges, metacarpal bone and distal radius, as well as in 73 bone grafts following carpal scaphoid nonunion and scapho-lunate bone-ligament-bone reconstructions, of free fibula flaps. Bone union rate was the outcome of interest in all cases.

Congenital Deformities

Piezosurgery® was employed in 49 corrective osteotomies in children. Sixteen children with Madelung deformity underwent to Vickers ligament release and volar palate fixation of the dome osteotomy (Fig. 1) with or without reversing bone wedge grafting [10]. In two children with acquired Pseudo-Madelung, following post-traumatic radius malunion, the Piezosurgery® was employed for both radius osteotomy and trapezoidal bone graft from the iliac crest with plate fixation in one child. In the other, the severe deformity was fixed by external fixator allowing gradual lengthening and correction of the radius (2 cm per month until useful correction and consolidation at 6 months). In all children the stable fixation of the osteotomy allowed early rehabilitation program and no plaster cast immobilization. In thirty-one children with clino-camptodactyly, the opening wedge osteotomy performed to correct angular deformity was fixed with K-wires from 5 to 6 weeks, once healing was radiographically confirmed. The digit was immobilized in a gutter orthosis until consolidation.

Distal Radius Malunion

Seventeen corrective osteotomies were performed in adult following dorsally displaced extra-articular distal radius malunion or intra-articular ones. Piezosurgery® allowed osteotomy following volar plate fixation at the epiphyseal fragment without removal of the hardware due to the small-size and handling of the device. On the same base, the technique was performed in the intra-articular corrective osteotomies of the fragments by dorsal surgical approach, because of the high level of roughness of adjacent surfaces and favorable angle and direction of the procedure.

Fig. 1 Intra-operative features of the Piezoelectric dome osteotomy in Madelung deformity correction. Radiographic follow-up of volar plate fixation

Osteotomies and Arthrodesis at the Hand

Piezosurgery® was used in eight metacarpal bones, allowing the bone fixation with dedicated plate for rotational correction before the osteotomy. At the phalangeal level, the technique was used in three multiplanar condylar osteotomies according to Teoh technique [11], and in five inter-phalangeal joints arthrodesis with endomedullary screw fixation. In the last one patient, the phalangeal osteotomy was performed in a scarred and amputated donor digit to harvest a remodeled bone graft for another survival digit reconstruction (Figs. 2 and 3).

Bone Graft

Forty-five bone grafts from iliac crest or distal radius were harvested and accurately remodeled without milling or grinding. Because of the relevant bias in retrospective analysis of scaphoid nonunion, the inclusion criteria enrolled only 35 waist fracture nonunion in presence of proximal and distal poles large enough to support the screw fixation.

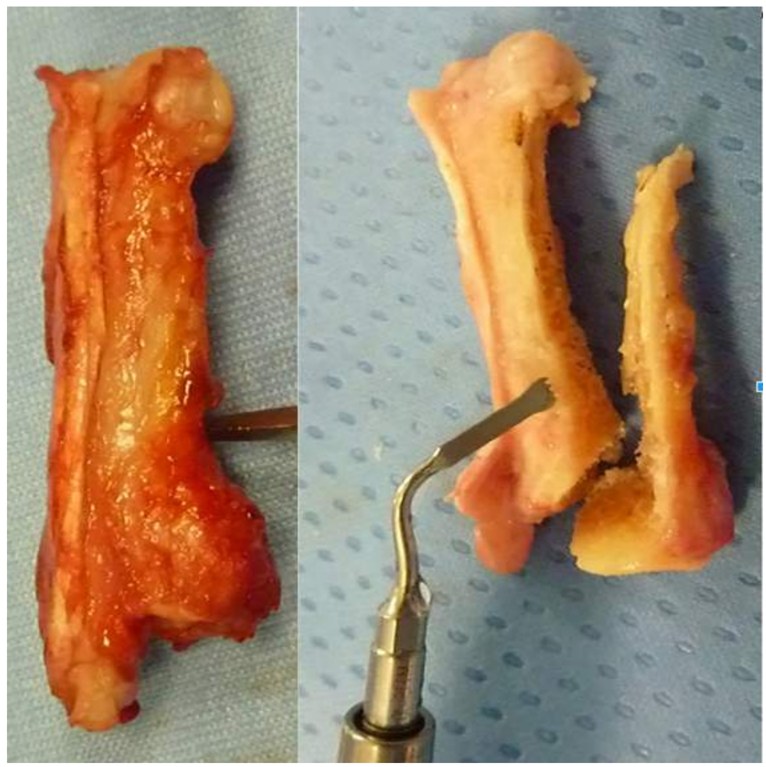

Fig. 2 Particular of the piezoelectric bone graft harvesting from donor amputated digit, remodeled according to the bone loss of the survival digit

Fig. 3 Operative features of the implantation and reconstruction of the phalangeal and articular bone loss. Radiographs showed the bone union and osteointegration at the follow-up

Cortico-cancellous or wedge bone graft from iliac or radius occurred within 12 months of acute fracture. Vascular or non-vascular bone graft were both recorded because did not appear to influence the union rate in the selected typology of patients [12].

In other five patients, the scaphoid nonunion followed failure of primary screw fixation of fracture. All cases were fixed by scaphoid plate and augmented with double bone graft [13]. The bone grafts were harvested from iliac crest by Piezosurgery®. The axial bone graft was accurately and anatomically remodeled to perfect fill the cavitation of the screw removal, and the transverse one was remodeled to correct the humpback deformity and scalloped to envelope the axial graft (Fig. 4).

Five chronic scapho-lunate (S-L) injuries underwent to reconstruction with bone-ligament-bone, the Piezosurgery® was used to harvest and remodel the complex from the donor site, allowing ligament sparing and a precise and well-structured bone stock, as well as a roughness inset of the complex into the scaphoid and lunate.

Reconstructive Microsurgery

Fibula flap has become fundamental in maxillary and mandibular defects. 28 fibula free flaps were harvested with Piezosurgery® and modeled either in the donor site (thanks to previous Computer-aided Design and Manufacturing) or in the new location, with safely vascular sparing in both cases [14].

All osteotomies with stable fixation had a post-operatively early rehabilitation program started at the hand and wrist with no immobilization, except for the children with K-wire fixation in phalanges or metacarpal bones.

All patients were assessed to value union-rate with radiographic post-operative examinations. Scaphoid CT was assessed in case of uncertain union by X-ray at the follow-up.

All surgical procedures were conducted with the Piezosurgery® *Plus* Unit and the osteotomy-standard medical handpieces (connected to the medical insert in channel 1 of the Unit). The MT1S-10 standard medical handpiece was used in grafts, phalanges and metacarpal bone osteotomies (length: 10 mm; saw width: 3 mm; saw thickness: 0.35 mm). The dome osteotomy in children was performed recurring to the quite larger MT1-10 standard medical handpiece (length: 10 mm; saw width: 4 mm; saw thickness: 0.55 mm). Only for the distal radius osteotomy in adult or the fibula, the authors used the MT1-10 or the MT4-10/20 plus handpiece (length: 10/20 mm; saw width: 4 mm; saw thickness: 0.55 mm), connected to the plus insert in channel 2 allowing more power, in presence of highly mineralized bone.

The ultrasonic tips of various handpieces vibrate at a controlled speed of 60–200 mm/s, with a linear vibration from 60 to 200 μm horizontally and from 20 to 60 μm vertically. The Piezosurgery® Unit allows seven levels of power, since to 50 W for the plus habdpieces (channel 2 connected) in higher mineralized and larger bones. The irrigation presents five levels of quantity, in linear growing relationship with the degree of power, allowing since to 60 ml/min jet in the *standard* insert and to 81 ml/min in the more powerful *plus* insert.

The osteotomy at the hand and wrist were all performed from 4 to 6 range of power (from 25 to 40 W) and at four level of irrigation. However, the Unit has an automatic feedback in power and irrigation regulation adjusting the selected level to the bone resistance.

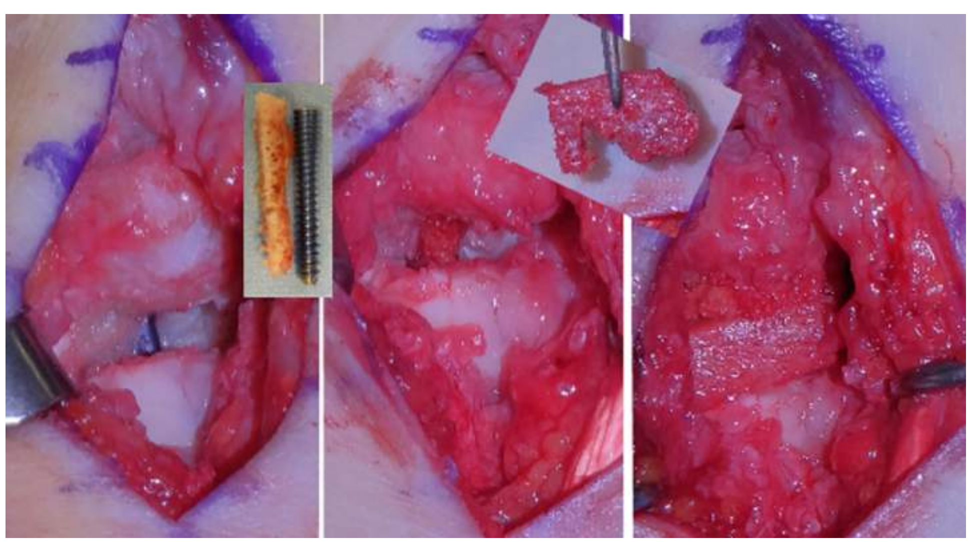

Fig. 4 Intra-operative features of the double bone grafts harvested by piezosurgery. Axial bone graft to fill the cavitation following screw removal. Transverse wedge cortical bone graft to correct and fill the bone loss of the nonunion, and particular of the bone scalloping to envelope the other graft

Results

Corrective osteotomies at the metacarpal bone and phalangeal level healed in all cases, both in stable fixations in adults or K-wire fixations in children. The mean consolidation time was 31 days in children and 42 days in adults.

All radius dome osteotomies or corrective osteotomies healed with a mean consolidation time of 58 days in children and 85 days in adults (no bone grafting was used in plate fixation).

In the scaphoid nonunion, following acute fracture or prior synthesis failure, the mean consolidation time was 83 days and 87.5% of union rate was recorded (5 failure and 35 unions). In bone-ligament-bone of S-L reconstructions, the mean consolidation time was 39 days.

All fibula flaps consolidated in a mean time of 51 days.

At no point in all cohorts there were any neurovascular or tendon disturbances or adverse surgical events.

Despite the thin instruments no breakage of the handpieces were recorded respecting the correct technique.

Discussion

Piezoelectric bone surgery was introduced almost 20 years ago in dental surgery to improve outcomes and bone-implant integration [1]. According to the operative environment, the instruments were designed handy, thin and small. These characteristics, added to the relevant soft tissue sparing property, outweighed piezoelectric surgery over traditional tools and explained its escalating role in wider and wider number of surgical procedures [2–6]. Hand surgery and microsurgery have great potential and are high suitable to piezoelectric surgery [6, 8].

The authors presented an overview of the applications in corrective osteotomies in Hand and Plastic reconstructive surgery. The casuistry highlighted and analyzed the results, the certain or possible advantages and pitfalls.

During the osteotomy, precautionary measures should be taken into account to minimize the extent of temperature rise during sawing. Some author introduced the multiple drill-hole technique to reduce thermal damage, but did not avoid the bone heat [7, 8, 15]. Moreover, the final cutting with scalpel did not fulfill precise cutting or undesired breakage. The piezoelectric effect avoided any alteration in temperature and injury to bony cells, and leaded to safe incision without damaging underlying vital structures like nerve, tendons and vessels [16–21]. A simultaneous decrease of some pro inflammatory cytokines in the bone was described, allowing neo-osteogenesis [2]. Limitation in retraction and stretching of soft tissues was significantly, such as in stripping of the periosteum and in bony exposure [22].

The instrument was handled and moved into the surgical space comparable to a pen and the cut was highly precise. The absence of vibrations, the fine tip and the clear view onto the bone enabled variable courses and angles, and accurately curved cutting (in *Madelung dome osteotomy*) as well as custom-made graft or surface remodeling and roughness (in *scaphoid and S-L reconstruction*). The high precision and thin cutting was very useful in closer and meticulous osteotomies (in *Teoh technique, intra-articular malunion, fibula flap, pediatric patients*). The handling and downsizing of the Piezosurgery® devices allowed bone cutting without removal of the previously fixed dedicated plates (in *dorsally displaced distal radius malunion, de-rotative osteotomy at the hand)*. Fixation of the bone before cutting reduced surgical duration, and facilitated the intra-operative maneuvers.

The issues of roughness of the bony surface and of accurate and modeled cut were relevant not only in effective and more physiological healing, but also in bone graft harvesting [15]. This was useful in scaphoid nonunion and S-L reconstruction techniques, needing small, wedge or custom-made grafts, such as axial cavity filling or saddle shaping. The accuracy of bone surfaces contact affected the stability and the course of treatment. In absence of sufficient mechanical forces between containing components of the osteotomy the healing occurred under unfavorable angle and direction [23, 24]. Stable fixation and optimal interface of the bone and graft were effective in union rate and time of healing [25, 26].

The sparing soft tissue effect such as the lack of thermal increase and vibration played a relevant role in harvesting microvascular free or pedicled bone grafts for scaphoid reconstruction or fibula free flaps. Piezosurgery® has proved to be more suitable compared to either traditional or more recent J-plasma devise [14] cutting methods, because of the safety of the procedures, giving also minimal periosteal elevation. In the vascularized bone grafts, the vessels were easily respected, with a clear view of the operative field and no local bleeding, positively affecting the microsurgical dissection and environment both in the donor and receiving sites.

Depending on the density, thickness and size of the bone, the time needed for the osteotomy was overall slightly longer than the time needed while using the usual saw, but quite similar to the multiple drill-hall technique. Contraindications have been reported in patient or operator with electrical pacemakers [2] and substantial amount of initial investment was required with the application of piezosurgery. In contrast to conventional micro saws or drilling osteotomy, the piezoelectric surgery required minimal pressure. Contact load of 150 g's allowed the better depth cut and avoided the breakage of the thin devices. The learning curve is not demanding but it is very important a correct technique in cutting to avoid breakage of the blades and thermal damage of the bone. The handpieces should be moved continuously backward and forward with minimun pressure. Despite these limitations and disadvantages, surgical time [27, 28] and efforts were largely enhanced by the technical advantages in feasibility and flexibility of the technique as well as the pre-fixed plate opportunity.

Despite many histomorphological studies showed no signs of lesions to the mineralized tissues or suffering of the osteocytes, with increasing in neo-osteogenesis, there was a lack of evidence in better rate and earlier bone union. No studies described homogeneous cohorts, without relevant bias, comparing instruments in osteotomies. Even this study did not prove significance in bone healing outcomes, but showed a consolidated proof of feasibility for piezosurgery, ideally sized for hand and reconstructive surgery and microsurgery.

Conclusion

Piezoelectric surgery was a safe and efficient technique, providing selective micrometric bone cuts for minimally invasive procedures requiring high precision. The technical and biological characteristics of the piezoelectric effect perfected this technique as an effective and useful instrument in Hand surgery. The handy and fine device provided an opportunity for a variety of dedicated and clever osteotomies related to the biological and biomechanical aspects of the different pathologies. Soft tissue sparing was high effective in microsurgical reconstructive procedures.

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Availability of Data and Material All retrospective reviewed data and material are available into the software and archives of the Institute.

Code Availability Not applicable.

Declarations

Conflict of Interest All the authors declare they have no financial interests, no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement, etc.) that might pose a conflict of interest in connection with the submitted article.

Ethical Approval The article does not contain any trial with human participants or animals performed by any of the authors. The retrospective analysis of the human data was in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No studies regarding human and/or animal rights were conducted in the study.

Informed Consent Informed consent was obtained from all patients before surgery as well as for the collected data at the follow-up.

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ORIGINAL ARTICLE

Quality and Content Analysis of Carpal Tunnel Videos on YouTube

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Abstract

Introduction Carpal tunnel syndrome is a disease that reduces the quality of life, and it is characterized by numbness, tingling in the fingers, and weakness in the hand, which we frequently encounter in our daily clinical practice. In this study, we aimed to evaluate the videos in terms of quality and reliability by watching the first 50 YouTube videos most relevant to the carpal tunnel in the YouTube video channel, which is often the first reference point as a source of information.

Method Among the videos that appear after typing "carpal tunnel" in the search tab of the YouTube, we eliminated those with advertisements and those that are not in English and evaluated the top 50 most relevant videos about the carpal tunnel. A specific YouTube channel was not selected during the search; however, the most relevant videos on carpal tunnel syndrome were determined. The duration, the number of views, the number of likes, dislike numbers, upload times, and upload sources of the videos were recorded and evaluated. The content, quality, and reliability of the videos were evaluated according to the GQS, JAMA, and DISCERN scales.

Results The average length of the 50 videos included in the study was 315.18, the average number of views was 150,977.4, and the average number of likes was 1410.86. The average number of days when the videos were uploaded to the internet was calculated as 1259.62 days. The GQS average of 50 videos included in the study was calculated as 2.7, the JAMA score average as 2.14 and the DISCERN score average as 33.62, and the video quality, content, and reliability were low. There was no statistically significant relationship between uploading sources of videos to the internet and video content, quality, and reliability ($p > 0.05$). The number of views, the number of days uploaded to the internet, the number of views, the number of likes and dislikes, like rates, and the video power index of the videos showed no statistically significant relationship with JAMA, DISCERN, and GQS.

Conclusion Social media is one of the easiest methods to access information today. The high number of contents, quality, and reliability of social media videos are crucial for patients to obtain accurate information, gain awareness about diseases, and receive guidance on treatment. This study found out that the quality, content, and reliability of the existing videos on the carpal tunnel were at a low level. We propose that the videos' content and quality should be improved and become more beneficial for patients.

Keywords Carpal tunnel · Social media · YouTube · Video quality

Introduction

Given the fact that technology has a very important place in our daily life, internet usage is becoming more and more common accordingly. With the widespread use of technological devices such as smartphones, computers, and tablets, the first source of reference for information has become the internet and social media. Especially in recent times when people are in quarantine due to the pandemic, the internet is used more frequently as a source of information.

With over 1 million users, YouTube ranks first as a source of information [1]. Internet ranks first as a source of information especially in the field of health [2]. A survey study revealed that half of the internet access in the last 1 month was for the sake of obtaining information in the field of health [3]. People frequently search for diagnoses, especially by physicians, treatment methods, and general information

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about diseases via the internet [4, 5]. Various studies have shown that informative videos on social media platforms such as the internet and especially YouTube, which is the first source of reference, are insufficient [6, 7]. Remarkably, a study of bone tumors revealed that the videos were insufficient, misleading patients in this regard [8].

Carpal tunnel syndrome is characterized by numbness, tingling, feeling of burning, and weakness in the fingers that occur when the median nerve is compressed under the transverse ligament. It is a disease that we encounter frequently in our daily clinical practice. While it is seen with a frequency of 3–3.4% in women, it is between 0.6 and 2.7% in men [9]. Delaying the diagnosis and treatment process of carpal tunnel syndrome may lead to irreversible results. These irreversible results may be seen in patients even after the treatment such as muscular atrophy, paralysis, and weakness in the hands due to delayed diagnosis and treatment. As it is a common disease and has irreversible consequences resulting from delaying the diagnosis and treatment, it is necessary for patients to be informed correctly, to receive a rapid diagnosis, and to be guided accurately in this sense. The quality, content, and adequacy of the YouTube videos as a source of information on this disease, in which delaying the diagnosis and treatment may lead to irreversible results in addition to being a common disease, have not been evaluated from this perspective before. Besides, the literature review revealed that the video quality and content are generally at a low level. A study examining the contents of videos aimed at patient education about carpometacarpal arthritis, where conservative treatment and exercise therapy are generally preferred, determined that the content and quality of the videos were insufficient [10]. This study aimed to demonstrate the adequacy of the videos on the carpal tunnel in the YouTube social media platform, which has been evaluated for some other diseases.

Materials and Methods

We have included the first 50 videos that are most relevant to the carpal tunnel by typing "carpal tunnel" in the YouTube search engine as of December 20, 2020, provided that the language of the video is English. The top 50 most relevant videos were selected without any filtering while searching the videos. Considering that the videos reflect the general characteristics and the users' tendency to watch, the top 50 videos were considered sufficient for the purposes of the research. We excluded the ones with advertisements, sponsored videos, advertising content and those whose language is not English. The videos included in the study were watched and evaluated by two different orthopedists.

The length of the videos included in the study, their upload dates, the number of likes, dislikes, sources of uploading to social media, the number of views, content, and whether the preparation method included animation were recorded. The sources of uploading the video to social media were categorized as academic content sites, medical content sites, animation sites, physicians, and physiotherapists. Video contents were categorized as surgical techniques and approaches, disease-specific information, exercise training, commercial product training, patient experience, and diagnostic test videos. DISCERN Score, Global Quality Score, Journal of American Medical Association (JAMA) Score were used in the conformity and quality evaluations of the videos. Video power index was used to evaluate the popularity of videos. The video power index was calculated with the formula where the like rate multiplied by the view rate as a percentage.

The JAMA Score, which is used to evaluate the reliability and accuracy of basic medical information on websites, basically consists of four parts. It is evaluated between 0 and 4 points by giving 1 point for each of the criteria for authorship, bibliography, copyright, and up-to-dateness (Table 1).

The Global Quality Scoring system, which includes the criteria of the adequacy of the information in the video content, general information flow, accessibility to information, and the level of usefulness to patients, is categorized between 1 and 5. The lowest quality videos are scored 1 and the highest quality videos 5 (Table 2).

The DISCERN scoring system, which consists of 15 questions in total, evaluates the reliability of the video, the conformity, and the quality of treatment options. The first 8 questions evaluate the reliability of the video, the next 6 questions the details of the treatment options, and the 15th

Table 1 JAMA scoring system

JAMA scoring system rating sections	No	Yes
Authorship authors and contributors,their affiliations, and relevant credentials should be provided	0	1
Attribution references and sources for all content should be listed clearly,and all relevant copyright information should be noted	0	1
Disclosure website ''ownership'' should be prominently and fully disclosed,as should any sponsorship	0	1
Advertising, underwriting, commercial funding arrangements or support,or potential conflicts of Interest	0	1
Currency dates when content was posted and updated should be indicated	0	1

Table 2 Global Quality Score

Score	Global score description
1	Poor quality, poor flow of the site, most information missing, not at all useful for patients
2	Generally poor quality and poor flow, some information listed but many important topics missing of very limited use to patients
3	Moderate quality, suboptimal flow, some important information is adequately discussed but others poorly discussed, somewhat useful for patients
4	Good quality and generally good flow, most of the relevant information is listed, but some topics not covered, useful for patients
5	Excellent quality and excellent flow, very useful for patients

question evaluates the overall quality of the video. Each question is scored between 1 and 5. 63–75 points are considered excellent, 51–62 points good, 39–50 medium, 27–38 insufficient, and 16–26 very insufficient (Table 3).

We evaluated whether there was a statistically significant relationship between the number of views of the videos, the number of days uploaded to the internet, the number of views, the number of likes and dislikes, the like rates, and the video power index, whether they had animated content, the content type, the source of uploading to the internet, and JAMA, DISCERN, and GQS.

Since this study was not performed on humans or animals, it was not authorized by the ethics committee.

Statistical Analysis

Descriptive statistics of the data obtained from the study are given with mean and standard deviation for numerical variables, and by frequency and percentage analysis for categorical variables. Normal distribution test of GQS, JAMA and DISCERN scores was performed with Kolmogorov–Smirnov and Shapiro–Wilk tests. The data were not compatible with a normal distribution ($p < 0.05$). Spearman correlation analysis was used to examine the relationship between numerical variables. In addition, the Mann–Whitney *U* test was used for categorical variables with two groups, and the Kruskal–Wallis test for categorical variables containing three or more groups in the analysis of GQS, JAMA and DISCERN scores according to categorical variables. The analyses were carried out with SPSS 22.0 software. A significance level of $p < 0.05$ was chosen.

Results

The average length of 50 videos included in the study was calculated to be 315.18 (57–850) s. When the number of views of the videos was evaluated, the least-watched video had 2575 views, while the most-watched video had 1,223,368 and the average number of views was 150,977.4. When the videos were evaluated in terms of the number of likes, the average number of likes was found to be 1410.86 (12–15,000). When the number of dislikes was examined, the average number of dislikes was 50.46 (1–371). The average number of days when the videos were uploaded to the internet was calculated as 1259.62 (22–3973) days. The like rate of the videos was evaluated as 95.38 (99.70–86.35).

Table 3 DISCERN scoring

Section 1—Is the publication reliable?	Section 2—How good is the quality of information?
1.Are the aims clear?	9. Does it describe how each treatment works?
2.Does it achieve its aims?	10. Does it describe the benefits of each treatment?
3. Is it relevant?	11. Does it describe the risks of each treatment?
4. Is it clear what sources of information were used to compile the publication?	12. Does it describe what would happen if no treatment is used?
5. Is it clear what sources of informaiton used in the publication?	13. Does it describe how the treatment choices affect overall quality of life?
6. Is it balanced and unbiased?	14. Is it clear that there may be more than one possible treatment choice? 15. Does it provide support for shared decision-making?
7. Does it provide details of additional sources of support and information?	Section 3—Overall rating of the publication?
8. Does it refer to areas of uncertainty?	15. Based on the answers to all of the above questions, rate the overall quality of the publication as a source of information about treatment choices

Table 4 General features of videos

	Minimum	Maximum	Mean
Length (s)	57.00	850.00	315.18
Number of views	2575.00	1,223,368.00	150,977.40
Number of likes	12.00	15,000.00	1410.86
Dislikes	1.00	371.00	50.46
Number of days of uploading	22.00	3973.00	1259.62
Like rate	86.34	99.70	95.38
View rate	3.51	1162.36	148.83
Video Power Index	3.24	1113.26	142.77

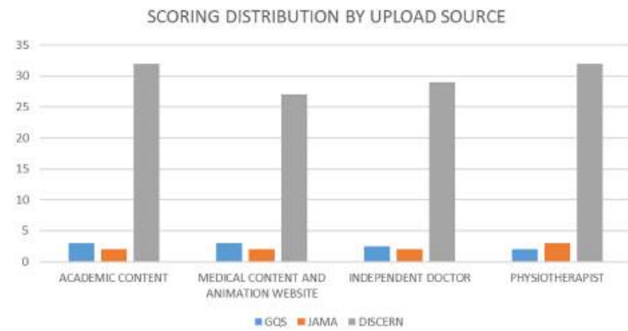

Fig. 1 Scoring distribution by upload source

When the videos were evaluated with calculations in terms of video power index, the video power index was calculated as 1,113.26 the highest, 3.24 the lowest, and 142.77 on average. When the videos were analyzed in terms of view rate, the average view rate was 148.83 (3.51–1162.36) (Table 4).

When the videos were evaluated to determine whether they had animated content, 15 (30%) videos were animated, whereas 35 (70%) videos were not animated.

When the source of uploading the videos to the internet is analyzed, 22 (44%) of them are uploaded by the medical content and animation website, 17 (34%) of them by academic sources, 8 (16%) of them by an independent physician, and 3 (6%) of them by a physiotherapist. When the content of the videos included in the evaluation is analyzed, 22 (44%) were disease-specific clinical evaluation videos, 14 (28%) were exercise training videos, 7 (14%) were surgical technique and approach videos, 4 were (8%) patient experience videos, 2 (4%) were commercial product training videos, and 1 (2%) was diagnostic test technique video.

Among the parameters used for the quality and conformity analysis of the videos, the mean GQS was 2.7, the JAMA average score was 2.14 and the DISCERN average score was 33.62. Only 3 videos were rated excellent with 5 points in the GQS assessment. While 2 videos were scored as excellent, scoring 63 or above in the Discern scoring, 4 videos received full points according to the JAMA scoring system.

No statistically significant relationship was determined between the number of views of the videos, the number of days uploaded to the internet, the number of views, the number of likes and dislikes, like rates and video power index and JAMA, DISCERN, GQS ($p > 0.05$). A statistically significant, positive relationship and low level of correlation was found between JAMA, DISCERN, GQS, and video duration ($p < 0.05$).

No statistically significant difference was found between whether the videos had animated content, content type, upload source, and JAMA, DISCERN, and GQS scores ($p > 0.05$) (Fig. 1).

A statistically significant, positive relationship and high level of correlation was found between GQS and JAMA ($p < 0.05$). A statistically significant, positive relationship and very high level of correlation was found between GQS and DISCERN ($p < 0.05$). A statistically significant, positive relationship and high level of correlation was found between JAMA and DISCERN ($p < 0.05$).

Discussion

This study aimed to analyze the 50 videos most relevant to the carpal tunnel in the YouTube social media channel, which is often the first point of reference, and evaluate them in terms of competence, quality, and conformity. As there was no study of carpal tunnel videos before and it was needed to increase the quality of internet videos, the first source of information for patients, we are led to conduct such a study.

With the spreading use of the internet day by day, the number of social media users and the number of video views on these channels are increasing day by day. YouTube is the most popular channel among social media channels and has the highest number of users. The first source of reference for health-related issues was the internet and especially YouTube, which attracted the attention of the researchers, and the first study on this subject was conducted in 2007 [11]. After this study, many studies with video quality analysis on different subjects have been carried out [12].

Among the videos included in this study, 22 (44%) of them are uploaded by the medical content and animation website, 17 (34%) of them by academic sources, 8 (16%) of them by an independent physician, and 3 (6%) of them by a physiotherapist. In compliance with previous studies, the present study found that there were more uploads not managed by healthcare professionals, such as sites that produce medical content and animation as upload sources [13].

When the literature was reviewed, the past studies found a relationship between uploading sources of videos to the internet and video quality [14, 15]. However, this study found no significant relationship between the source of uploading the videos analyzed and evaluated and the JAMA, GQS, and DISCERN scores. When all videos were evaluated from a statistical point of view, although no significant relationship was found, three videos with the highest GQS value were uploaded to the Internet by health professionals. This study, in which the first 50 videos about the carpal tunnel were analyzed, evaluated the sources of uploading, may have produced such a result due to the majority of them not being health professionals.

In the present study, the average length of videos was calculated as 315.18 (57–850) s, while the average video length was found to be between 377 and 635 s, according to the literature data in previous studies on various subjects [12].

DISCERN, JAMA, and GQS parameters, which were used to evaluate videos in different aspects such as content, suitability for treatment, quality, accuracy, and reliability, were calculated as 33.6, 2.14, and 2.7, respectively, and revealed that overall video quality and adequacy were low in comparison with the literature [16, 17]. In a similar study analyzing YouTube videos on bone tumors, the mean GQS, JAMA, and DISCERN scores were found to be 2.22 (1–4), 2.12 (1–3), and 33.48 (17–66), respectively [8]. In another study conducted with a quality analysis of videos on scoliosis, JAMA scoring was examined and the average of JAMA scoring was determined to be 1.32 [16]. When these studies are compared with the present study, similar results were generally found. This study discovered that all 3 videos that got the highest point from the GQS scoring were uploaded to the Internet by health professionals, suggesting that the low quality and content of the videos were mostly related to the source of uploading.

Previous studies have shown that there is no correlation between video views and like rates and video quality [18]. Similarly, this study did not determine a statistically significant relationship between JAMA, DISCERN, GQS, and the average number of views, the number of likes, like rates, and video power index of all videos. Besides, the average views, number of likes, like rates, and video power index values of the first three videos were below the average according to GQS, JAMA, DISCERN scores. A previous study conducted with hand surgeons has shown that physicians had little interest in social media [19]. The low level of interest with regards to social media among physicians may be the reason why high-scoring videos in their content and quality are less in number and shadowed by other videos. These data are meaningful in terms of showing that useful and quality videos are in the background in terms of the number of views and likes and that videos with low quality and quality are viewed more.

As a result, this study, where we analyzed the most relevant 50 videos related to the carpal tunnel that we encountered on YouTube, showed that the video uploading sources were mostly external sources rather than health professionals, and the video quality and content were generally insufficient. Considering that the internet and especially YouTube are the first source of reference for people in terms of health, as in all other subjects, increasing the content and quality of YouTube videos is significant in terms of contributing to achieving more accurate information, earlier diagnosis, and early treatment process. We believe that this study conducted on the carpal tunnel will help the carpal tunnel patients to get more accurate information, become aware of their diseases by helping to increase the video quality on the YouTube social media channel, and reduce the unwanted consequences that may arise due to delayed treatment.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest

Ethical standard statement Study does not contain any human or animal resources.

Informed consent For this type of study informed consent is not required.

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ORIGINAL ARTICLE

Clinical Outcomes of Patients with Stage II and IIIA Kienböck's Disease After Undergoing Conservative Management

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Abstract

Purpose The current study aimed to demonstrate the outcomes of patients with Lichtman stage II and IIIA Kienböck's disease with mild pain and good range of motion (ROM) after conservative management. We hypothesized that we can conservatively manage patients with early-stage Kienböck's disease including those with stage IIIA.

Patients and Methods This study is a retrospective case series. Between January 2012 and December 2017, 38 patients were enrolled in this study. The mean follow-up period of conservatively managed group was 49.1 months. The flexion–extension (FE) arc, grip strength, Pain Visual Analog Scale (pVAS), Modified Mayo Wrist Score (MMWS), and disabilities of the arm, shoulder, and hand (DASH) score were determined for functional evaluation. The radiographic parameters were assessed using the Stahl's index and carpal height ratio. The morphological changes in the lunate were also evaluated with plain radiographs.

Results A total of 31 of 38 patients (81.6%) showed favorable outcomes after conservative treatment. The mean pVAS score, MMWS, and DASH score showed statistically significant improvement, as well as the morphology of lunates on the plain radiograph. The mean FE arc was slightly decreased without statistical significance. The grip strength showed improvement with statistical significance. One patient showed the same radiographic morphology, but did not manifest any pain. A total of five (13.2%) patients who experienced aggravated pain and decreased ROM underwent surgical treatment. The other patient required surgical intervention but was provided conservative treatment due to her circumstances.

Conclusion Favorable outcomes can be expected in patients with Lichtman stages II and IIIA avascular necrosis of the lunate (Kienböck's disease) with mild pain and good ROM who undergo conservative management.

Level of Evidence IV.

Keywords Kienböck's disease · Avascular necrosis of lunate · Conservative treatment · Lichtman's stage IIIA

Introduction

The etiology and the natural course of avascular necrosis of lunate (Kienböck's disease) remain unknown [1, 2]. Despite various treatment options, no definite treatment protocols have been established. Several studies had reported the natural course of Kienböck's disease and showed favorable outcomes of conservative management compared with surgical interventions in a series of long-term follow-ups [3–5].

Recently, several studies have reported that surgical treatment has superior outcomes over conservative treatment. Lichtmann et al. published a treatment algorithm in which patients with early-stage Kienböck's disease (stage 0, I, and II) are provided with conservative treatment for 3 months; however, surgical interventions are necessary in advanced stages including stage IIIA [6]. Only fewer arguments have

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been made regarding the need for conservative treatment in patients with Lichtman stage I Kienböck's disease. Otherwise, treatment strategies for stages II and IIIA are still under debate.

We experienced various spontaneously healed lunates even in stage IIIA patients, particularly with mild symptoms after a long-term follow-up (Fig. 1). Based on our experiences, the current study aimed to demonstrate the outcomes of patients with Lichtman stage II and IIIA Kienböck's disease with mild pain and good range of motion (ROM) after conservative management. We hypothesized that we can conservatively manage patients with early-stage Kienböck's disease including those with stage IIIA.

Methods

The current study was performed with the approval of our institutional review board (SMC 2020-01-046-003). Between January 2012 and December 2017, 105 patents with Kienböck's disease visited the outpatient clinic and were treated by a single orthopedic surgeon. Among them, 73 patients had Lichtman stages II and IIIA [7]. We determined conservative management in 42 patients who had 1) a Pain Visual Analog Scale (pVAS) score of ≤ 3, and 2) showed a flexion–extension (FE) arc in the affected wrist of $\geq 85\%$ of the normal wrist. After excluding 4 (9.5%) patients who were followed up less than 2 years, 38 patients were finally enrolled in this study.

We only included stages II and IIIA as these stages are borderline, and it remains unclear whether these stages require surgical treatment or conservative management. The patients visited our clinic once a month; if their symptoms and morphology of the lunate on plain radiograph improved, the follow-up period was extended and the patients were required to visit our clinic every 3–6 months. The plain radiographs of the wrist were acquired at the posterior-anterior (PA) and lateral view at every visit. The patients were closely observed and were informed that they might undergo surgical treatment anytime if their symptoms did not improve. Medications such as acetaminophen were used upon patients' request. An orthosis or cast was not applied, but the patients were informed to refrain from lifting heavy objects and performing vigorous activities using the affected wrist. They were allowed to perform their daily activities. Although immobilization elicits better outcomes when maintained for a longer period, it could also cause other complications such as joint stiffness, muscle atrophy due to disuse, contact skin irritation, and limitation of daily activities.

Due to the aggravation of pain or deterioration of the lunate as observed on serial plain radiographs, surgical treatment was performed. The criteria for converting to surgery were as follows: (1) pVAS increase of more than two steps from baseline without evidence of morphological improvement on the plain wrist radiographs, and (2) fragmentation or subchondral fracture progression as seen on a series of plain wrist radiographs. Patients who continued conservative management without conversion to surgical treatment were categorized as the CM group. The other patients who

Fig. 1 A 52 year-old male patient who had Lichtman stage IIIA Kienböck's disease with mild pain and good range of (ROM) at the first visit. The initial Pain Visual Analog Scale (pVAS), disabilities of the arm, shoulder, and hand (DASH) score, and Modified Mayo Wrist Score (MMWS) were 3, 25, and 75, respectively. The flexion–extension arc of the affected wrist was 115°, which was 92% of the flexion–extension arc of the normal wrist (**A**). At the last visit after 86.9 months, the patient manifested occasional pain only after performing vigorous activities (pVAS 1, DASH 4.5, MMWS 95). Sclerosis of the lunate was improved, and there was no evidence of collapse on the plain radiograph (**B**)

converted to surgical treatment were categorized as the SC group.

Functional Evaluation

The FE arc, grip strength, pVAS, Modified Mayo Wrist Score (MMWS), and disabilities of the arm, shoulder, and hand (DASH) score were obtained at every visit. FE arc was measured using a hand-held goniometer and recorded at every visit, and the MMWS was obtained using this parameter. Grip strength was measured with a hand-held dynamometer (Jamar® Hydraulic Hand Dynamometer, Sammons Preston Inc., Bolingbrook, Illinois, USA) by a single research assistant at every visit. The pVAS score, MMWS, and DASH score were also collected at every follow-up by the same research assistant.

Radiographic Evaluation

Radiographic parameters were assessed using Stahl's index (STI), while carpal height ratio (CHR) was obtained on plain radiographs at the first and last visit. STI is calculated by dividing the height of the lunate with the largest width of the lunate on the lateral plain radiograph; a decrease in STI indicates progression of lunate collapse [8]. CHR is calculated by dividing the carpal height (height of lunate and capitate) with the length of the third metacarpal bone, which determines the "expression of the extent of carpal collapse" [9]. A morphological change in the lunate on the plain radiograph indicates a change in the pathognomonic features of Kienböck's disease and denotes the problems occurring in the lunate such as sclerosis, fragmentation, cyst formation, and subchondral fracture. Revascularization of the lunate was defined as restoration of the normal opacity of the bone in the area with previous sclerosis, which implies avascular change in the bone in plain wrist PA and lateral view. The healing of fragmentation or subchondral fracture was indicated by the restoration of the normal opacity of the bone or a diminished fracture line. Radiographic evaluation including determining the Lichtman's classification and other radiographic parameters was performed by a senior surgeon (MJP) with 20 years of experience and his fellow surgeon (JHL) who were blinded to the patients' information. After the two surgeons double checked and cross-matched the radiographs, the conclusive values were determined.

Data Analysis

The outcomes of the treatment were determined by analyzing the pVAS, MMWS, and DASH score and by evaluating the morphological changes in the lunate. We categorized the outcomes as "successful," "maintained," and "failure." As a minimal correlation was observed between radiologic staging and subjective symptoms including pain and discomfort when using the wrist in performing daily activities, the radiographic parameters were not included in the analysis of the treatment outcomes [10].

"Successful" included the patients who satisfied the following criteria: a 1-point increase in pVAS compared with the initial pVAS and whose lunate showed evidence of revascularization on plain radiograph. "Maintained" was defined as the state wherein the patients' symptom was tolerable or satisfactory, but the morphology of the lunate on the latest plain radiographs remained the same. "Failure" was defined based on the following criteria: (1) aggravation of pain (elevation of pVAS) with deterioration of the lunate (collapsed or fragmented) as observed on plain radiograph, thus requiring surgical treatment, and (2) continuous conservative treatment despite the progression of the disease due to old age or refusal to undergo surgical treatment.

Statistical Analysis

The collected data were analyzed using a paired t-test and the Wilcoxon signed rank test to compare the pVAS, FE arc, grip strength, MMWS, and DASH scores at initial follow-up with those at the last follow-up; significance was set at $p < 0.05$. All analyses were performed using the SPSS statistics software version 25 (SPSS Inc., Chicago, IL, USA).

Results

Five (SC group, 13.2%) of the 38 patients, who were determined to undergo conservative treatment at baseline, were converted to surgery due to pain aggravation and deterioration of their radiological morphology; these patients were categorized as "failure" in the data analysis. The mean duration from the first visit until the performance of surgery was 11.7 months (Fig. 2). Detailed information is described in "Data Analysis."

A total of 33 patients (CM group) who continued conservative management were evaluated by comparing their subjective symptoms with the overall function at the first and last visit. The mean follow-up duration of the CM group was 49.1 months. In this group, Lichtman stages II and IIIA were observed in 10 and 23 lunates, respectively. A comparison of the characteristics of the CM group and the surgically treated group is presented in Table 1.

The mean values for subjective symptoms including pVAS, MMWS, and DASH score improved significantly. The mean grip strength decreased significantly. The mean FE arc at the last visit deceased slightly by 0.5°; however, it did not reach statistical significance (Table 2).

The mean STI and CHR of the CM group at the last follow-up exiguously worsened compared with those at

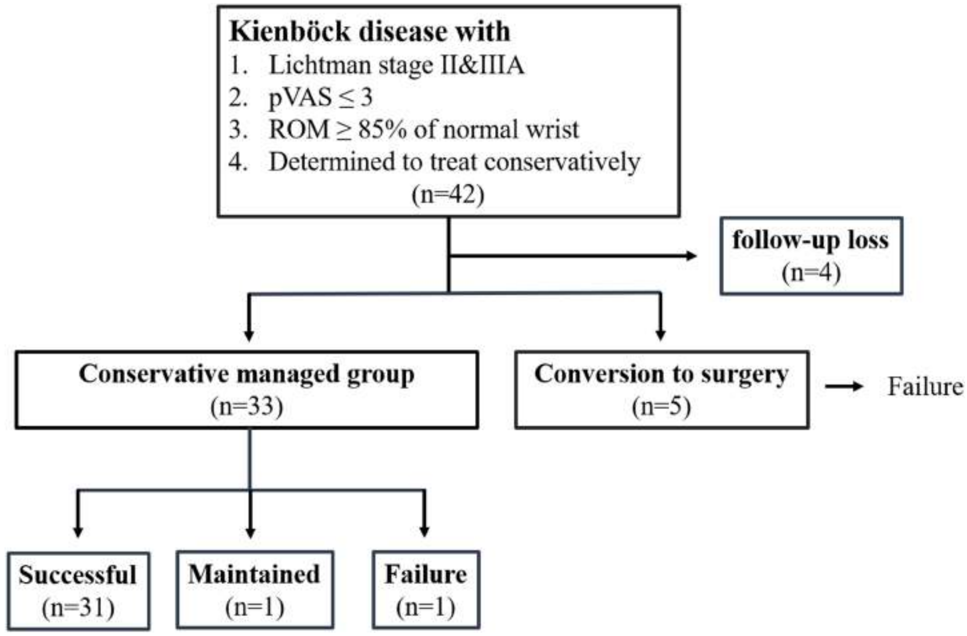

Fig. 2 Flowchart of the patients' inclusion and treatment process

Table 1 Patients' demographic data

	Conservatively managed group ($n=33$)	Surgically converted group ($n=5$)
Gender, male/female	16/17	3/2
Mean age (range, SD)	51.6 (16–81, 16.5)	32.8 (20–56, 15.7)
Follow-up duration (range, SD)	49.1 (21.1–92.1, 24)	11.7 (5.4–24.2, 7.6)
Dominant arm involvement, *n* (%)	14 (43.8%)	0 (0%)
Lichtman stage (II/IIIA)	10/23	0/5
Manual labor (non-mild/moderate/heavy)	17/12/4	2/2/1

SD standard deviation

Follow-up duration' of the 'surgically converted group' refers to the duration between the first visit to the surgery

Table 2 Functional outcomes of the conservatively managed group

	First visit	Last visit	*p* value
pVAS (SD)	2.1 (0.7)	0.7 (0.9)	< 0.001*
DASH (SD)	16.8 (7.0)	5.5 (4.5)	< 0.001*
MMWS (SD)	85.8 (4.9)	91.4 (5.0)	< 0.001*
Grip strength, kgf (SD) (affected/normal side)	81.9 (16.2) / 86.5 (14.6)	80 (15.3)	0.003*
FE arc (SD)	130.0 (6.5)	129.5 (6.7)	0.488

SD standard deviation, *pVAS* Pain Visual Analog Scale, *DASH* disabilities of the arm, shoulder, and hand, *MMWS* Modified Mayo Wrist score, *FE arc* flexion–extension arc

*Statistical significance

Table 3 Radiographic outcomes of the conservatively managed group

	First visit	Last visit	*p* value
Stahl's index (SD)	0.43 (0.07)	0.42 (0.07)	0.133
Carpal height ratio (SD)	0.51 (0.03)	0.51 (0.03)	0.909
Ulnar variance (SD)	0.24 (1.73)		

SD standard deviation

baseline. The mean ulnar variance (UV) at baseline was 0.24 mm. In the CM group, 6 wrists had negative, 19 had neutral, and 8 had positive variance (Table 3). In the SC group, 4 wrists had negative UV, and the remaining 1 wrist had positive UV.

Data Analysis

Of 38 patients, 31 (81.6%) showed successful outcomes after conservative treatment. Their pain and function improved as well as the morphology of lunates on plain radiographs. In this group, the affected lunates showed changes in subchondral bone fracture, and fragmentations in the lunates eventually healed. Moreover, the sclerotic change in the avascular portion of the lunates significantly improved (Fig. 3).

One patient was categorized as "maintained" after 62 months of follow-up for subchondral bone fracture, and plain radiograph showed progression to lunate collapse; nevertheless, the patient's pain lessened and he had minimal functional limitations in daily activities (MMWS 85; DASH 5.83; grip strength 98 kgf; FE arc 129.2°) (Fig. 4).

The remaining six patients (15.8%) were categorized as "failure." Pain and function worsened in four patients. They also showed progression of fragmentation concomitant with the collapse of the lunate in the PA and lateral view, thus

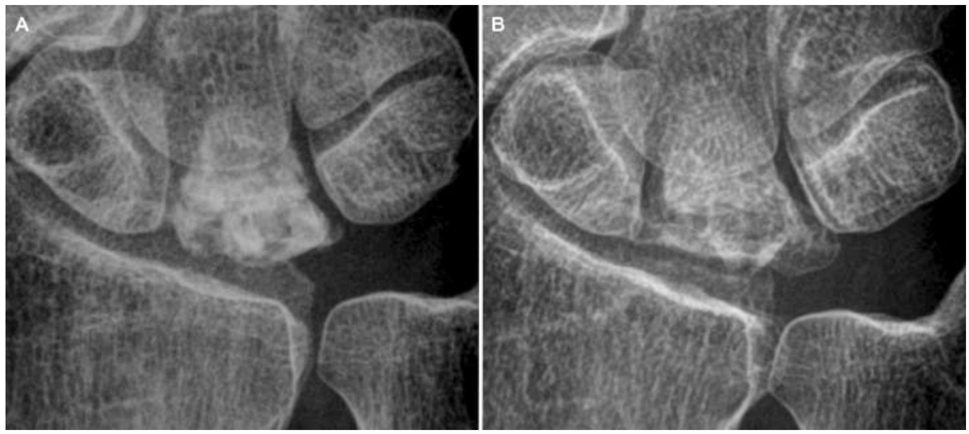

Fig. 3 A 62 year-old female patient with a Pain Visual Analog Scale (pVAS) score of 3 and range of motion (ROM) score of 92.3% in the normal side (**A**). After a follow-up of 69.3 months, her pain (pVAS: 0) and ROM (96.5%) on the opposite side improved. The sclerosis and erosion of the lunate had recovered (**B**)

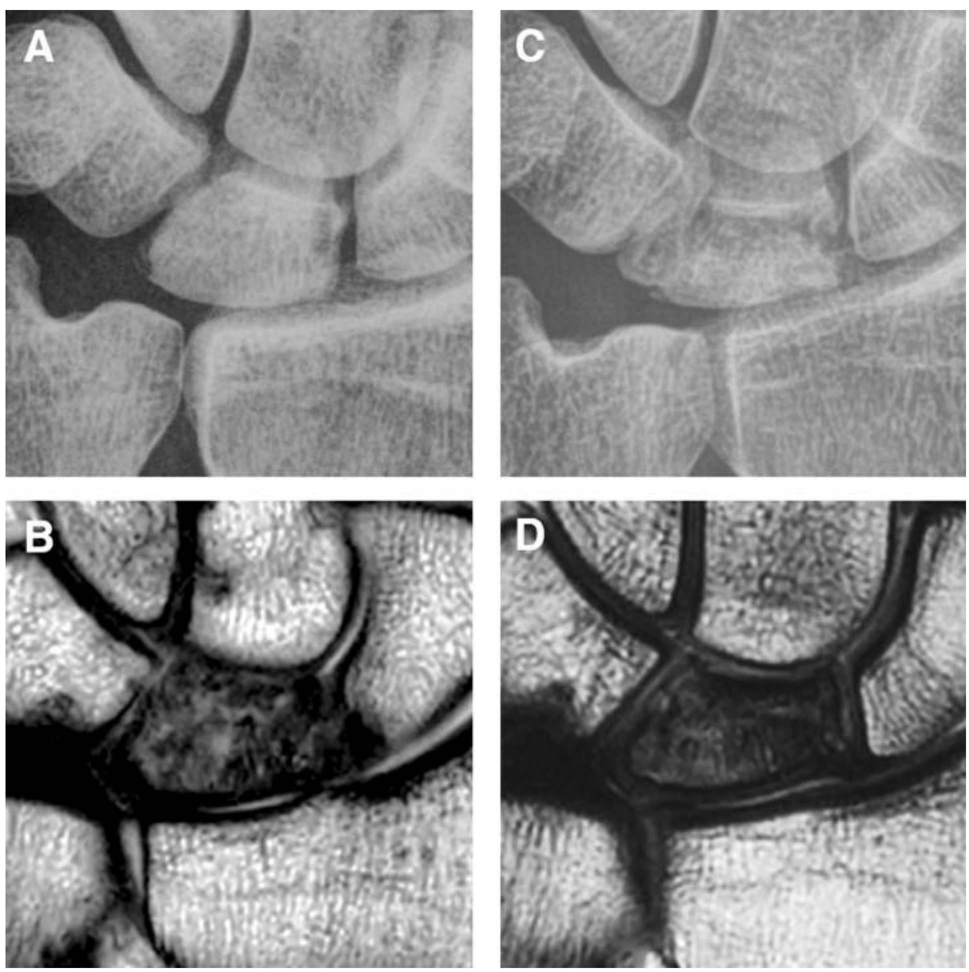

Fig. 4 A 72 year-old male patient. We chose to observe the patient conservatively as he had early-stage Kienböck's disease with mild symptoms and good function (**A** plain radiograph wrist PA view; **B** MRI T2-weighted image; pVAS: 1, DASH: 8.5, MMWS: 90, ROM: 90.4% of the normal wrist). After 50 months, the patient's disease remained stable; however, he still had minimal pain and good function. Thus, we opted to observe the patient closely (**C** plain radiograph wrist PA view; **D** MRI T2-weighted image)

requiring surgical treatment. One patient showed no progression on the plain wrist radiograph; nevertheless, the pain was aggravated. The remaining patient manifested poor pVAS and reduction in FE arc, as well as decrease in functional scores; hence, the patient was scheduled for surgical intervention. However, the patient refused to undergo surgical treatment due to her circumstances.

Discussion

The current case series showed that patients with Lichtman stage II or IIIA Kienbock's disease, and mild pain and well-preserved functions of the affected wrist could obtain satisfactory outcome if they only received conservative treatment. Of the 38 patients, 32 (84.2%) had no limitations in daily activities and experienced minimal pain with good ROM. Only six patients (15.8%) required surgical intervention due to aggravated pain and functional limitations in daily activities during observation.

In 31 patients categorized as "successful," three lunates showed mild progression to collapse, but finally healed as shown on plain radiographs. Their subjective symptoms and functional outcomes also improved. The radiographic morphology of the lunate does not closely correlate with the clinical course as reported in other studies [10, 11]. In a systemic review comparing treatment options including nonsurgical treatments, Innes and Struach noted that 83% of patients reported improvements in pain after core decompression; 86%, after undergoing vascularized bone graft; and 90%, after osteotomy was performed in the early stages of Kienböck's disease (stages I, II, and IIIA) [4]. Similarly, Matsumoto et al. stated that 14 out of 16 patients (87.5%) with Lichtman stage IIIA reported improvements in pain, while 12 (75%) showed improvements in MMWS after undergoing vascularized bone graft and temporary scaphocapitate fixation [12]. These studies showed comparable outcomes with the current study. With regard to the morbidity after surgery, such as surgical site pain, infection, and stiffness due to immobilization, conservative management is recommended over surgical treatments especially when the pain is mild and the function is good.

There have been many reports claiming the superiority of their own surgical options; nevertheless, the conclusive treatment is still under debate. In a systematic review comparing the long-term outcomes of radial osteotomy and non-operative treatment, Shin et al. argued that radial osteotomy was not superior to non-operative treatment in terms of disease progression [13]. Lichtman and his colleagues suggested conservative treatment in patients with early-stage Kienböck's disease (Lichtman stage 0, I, and II); however, they simultaneously proposed surgical interventions for the same stage lunate after only 3 months of observation [6]. Furthermore, every researcher has asserted the positive effects and outcomes of diverse surgical techniques such as vascularized bone graft, keyhole revascularization, radius core decompression, and fixation of lunate bone itself, supporting their own hypothesis [12, 14–18]. Several authors published long-term outcomes comparing the outcomes of surgical treatment and conservative treatment in patients with Kienböck's disease, which underpinned our result. Martin and Squeire found that there was no difference in DASH scores between surgically treated patients and nonsurgically treated patients [5]. Innes and Strauch also indicated in their systematic review that no active treatment is superior in the treatment of Kienböck's disease. Moreover, there is insufficient evidence to show that the outcomes of any intervention are superior to placebo or the natural course of the disease [4]. These studies did not evaluate the subjective symptoms and functional status of patients with Lichtman stage IIIA, which was highlighted in the current study.

FE Arc and Radiographic Parameters

There were slight changes in the patients' mean STI and CHR at the last follow-up (STI 0.43–0.42 [$p=0.133$]; CHR 0.51–0.51 [$p=0.909$]). However, no statistically significant difference was observed. Leeuwen and his colleagues evaluated 48 patients who had either radial shortening osteotomy or nonsurgical treatment, who showed a slight progression of Kienböck's disease within 1 year or more regardless of the treatment [19].

The mean FE arc decreased by 0.5 degrees at the last visit without statistical significance. The patients reported that they did not have any difficulties in performing daily activities using the affected wrist. The limitations in the ROM were attributed to the occurrence of synovitis and fragmentation of lunate, as well as to joint stiffness due to pain. As subjective data such as pVAS, MMWS, and DASH score improved, we presumed that the synovitis subsided and the fracture eventually healed; therefore, the FE arc was preserved. With regard to the FE arc of the wrist in patients with Kienböck's disease, conflicting results have been reported; however, most of the studies reported a slight decrease in the motion arc with statistical significance [4, 20].

Unlike the reports of other studies [6, 15, 21, 22], according to our results, especially in Lichtman stage IIIA, assessment of the natural course of the disease can only be performed in patients with minimal pain and well-preserved function. Then, how could we insist on the provision of conservative management, instead of surgical treatments, as stated by several authors? This can be associated with the recent popularization of magnetic resonance imaging (MRI). It is feasible to perform MRI at a local clinic even when the patient only manifests mild pain; MRI provides a high diagnostic rate when carried out during the early stages.

Therefore, it is possible to observe patients with very early stage or asymptomatic late stage Kienböck's disease who are in the healing process.

We conservatively managed patients with stages II and IIIA Kienböck's disease. A conservative management refers to observing the patient closely and performing an extremely short-term follow-up. However, it does not mean that nothing was done; in conservative management, the patients were followed up closely every month. Patients were monitored for changes in symptoms and deterioration of lunate morphology on plain wrist x-ray scans. If there was aggravation of their symptoms or changes in the morphology of the lunate, these changes were considered as indications of progression to lunate collapse and synovitis due to subchondral bone fracture; hence, the patients were converted to surgical treatment.

Limitations

The current study has several limitations. First, it is a retrospective case series. Initially, the treatment strategy was prospectively designed; however, the data analysis was performed retrospectively. To demonstrate the advantage of conservative management of stage II and IIIA Kienböck's disease over surgical options, further prospective comparative studies are warranted. Second, MRI was not performed in patients with mild symptoms and healed lunates at the last follow-up. On the contrary, we considered the plain wrist radiographs as a tool for analyzing the disease course. We thought MRI was not needed to the patients without suspicious symptom. Third, we could not collect the symptom duration before the first visit. A careful data recruitment is needed in a further prospective study. Lastly, four patients who underwent conservative management were lost to follow-up. We were able to obtain data from two patients with intermittent minimal pain and good ROM. However, we excluded these patients due to lack of final wrist x-ray scans. We could not contact the other two patients as their contact numbers were lost. We assumed that the patients did not need to visit our clinic because of the satisfactory outcomes; however, it could not be affirmed.

Favorable outcomes can be expected in patients with Lichtman stages II and IIIA avascular necrosis of the lunate (Kienböck's disease) with mild pain and good ROM who undergo conservative management.

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Declarations

Conflict of Interest All authors approved the manuscript and all authors declare that are no conflicts of interest regarding the publication.

Ethical Standard Statement The current study was performed with the approval of our institutional review board (SMC 2020-01-046-003).

Informed Consent The current study did not required the informed consent, for this study was performed retrospectively with medical records and also did not violated any rights of the participants.

Ethical Review Committee Statement The current study was performed with the approval of our institutional review board (SMC 2020-01-046-003).

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ORIGINAL ARTICLE

Bone Marrow Aspirate Concentrate as a Reliable Adjunct in Tibiotalocalcanal Fusion: A Radiographic Modified RUST Score Analysis

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Abstract

Background Tibiotalar and subtalar arthritis requiring tibiotalocalcaneal (TTC) fusion can be technically challenging and is dependent on reliable fusion for a good clinical outcome. Initial data regarding bone marrow aspirate concentrate (BMAC) has shown promise in use as an aide in both fracture and fusion healing. The purpose of this study is to determine the outcomes in TTC fusion when utilizing BMAC as an adjunct.

Methods Twenty consecutive patients who underwent TTC fusion with BMAC adjunct between March 2013 and November 2017 were retrospectively screened for inclusion. Patients were included regardless of comorbidities or risk factors for non-union, and only excluded if they did not have a minimum of 12 months of clinical and/or radiographic chart data. Follow-up was obtained at regular intervals of 6 weeks, 3 months, 6 months and 1 year. Modified RUST scores were applied to grade bony union in a blinded fashion by two orthopedic trauma fellowship-trained surgeons and agreement was assessed via intraclass correlation coefficient (ICC).

Results Twenty patients were screened and 12 met inclusion criteria for analysis. Majority were male (66.6%) at a mean age of 55.4 years and they were all treated via TTC fusion for a diagnosis of tibiotalar and subtalar arthritis. There were no postoperative complications and no reoperations in this cohort; no donor site morbidity was associated with BMAC. By the 3-month follow-up timepoint, all but one patient received a minimum modified RUST score of 10 indicating bony union (ICC 0.91); by the 6-month time point (ICC 0.94), all 12 patients were deemed united.

Conclusion BMAC as an adjunct in the setting of TTC fusion is a safe treatment option that can promote reliable, consistent bony fusion with minimal complications.

Keywords Ankle arthritis · BMAC · Hindfoot fusion · Subtalar arthritis · Subtalar fusion · Tibiotalar arthritis · TTC fusion

Introduction

Hindfoot and ankle arthritis is a debilitating disease affecting 9–15% of patients in the general adult population [9, 17]. Up to 70–80% of cases result from severe trauma to the ankle and hindfoot which can cause osteochondral damage and incongruity of the joint leading to arthritis. Other predisposing factors leading to the development of post-traumatic osteoarthritis (PTOA) include obesity, age greater than 30 at time of injury, time to surgery, and quality of surgical

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reduction [2, 5, 23, 26, 36, 38]. Lübbeke demonstrated that up to 60–70% of patients developed PTOA when having three or more of the aforementioned risk factors [25]. Other causes of arthritis involving the ankle and subtalar joint include infection, chronic instability, avascular necrosis of the talus, and inflammatory arthritis. Not only does arthrodesis continue to be the gold standard in treatment of PTOA, but also long-term functional outcomes are similar to alternative procedures such as total ankle arthroplasty (TAA), making it a cost-effective method in alleviating these patients' discomfort [15]. Furthermore, TAA does not prevent advancements or address concomitant subtalar arthritis in these patients [6].

Reliable clinical outcomes of arthrodesis procedures are dependent on obtaining an adequate fusion mass and this continues to be an area of concern for TTC fusions [11, 16]. Bone marrow aspirate concentrate (BMAC) can help facilitate bone healing and growing evidence has shown promising results when it is utilized in non-unions, fracture healing, bone defects, spinal fusions, and distraction osteogenesis [21]. In a cohort of 20 tibial non-unions following various treatment options, Connolly et al. demonstrated the efficacy of percutaneous bone marrow applied to the non-union site and observed a 90% union rate at an average of 6 months [4]. Similar results were demonstrated by Braly et al., who evaluated 11 distal meta-diaphyseal tibial non-unions status post plate and screw fixation. All patient achieved bony union at an average of 8 months following treatment with bone marrow aspirate [1].

With the benefits of BMAC well established, there are limited studies evaluating its potential use in procedures involving hindfoot fusions. The purpose of this study was to retrospectively evaluate radiographic union rates with the use of BMAC as an adjunct in TTC fusion.

Materials and Methods

All research was conducted in accordance with the Declaration of Helsinki and Western Institutional Review Board approval was obtained prior to start of the study. Our institutional orthopedic trauma registry was screened for patients undergoing TTC fusion between March 2013 and November 2017. All surgical procedures were performed by a single attending orthopedic surgeon. Twenty patients were screened for inclusion diagnosis of contaminant subtalar and tibiotalar arthritis requiring operative intervention after having failed conservative measures. Patients were only excluded if they did not have a minimum of 1-year follow-up. Demographic data collected were age, gender, and comorbidities including smoking status. Postoperative and follow-up plain radiographs were obtained for each patient to evaluate for non-union rates, callus formation, and bony union via the modified RUST score [24, 39].

Radiographic Modified RUST Score Analysis

The modified RUST score was described by Litrenta et al. to determine union at the fracture site and has shown to have a higher intraclass correlation coefficient than that of the RUST Score. The scoring system involves looking at the AP and lateral radiographs and scoring each cortex indvidually. Scoring system was as followed: 1 = no callus formation, 2 = callus present, 3 = bridging callus present and 4 = remodeling and fracture site not visible. This differs from the RUST scoring system in that callus presence and bridging callus were scored the same making the max score for each cortex out of three points instead of four. A minimum union definition required a summative mRUST score of 10, while a score of 13 yielded fracture/fusion mass that had healed/remodeled [24, 39]. Modified RUST scores were given in a blinded, randomized fashion to minimize bias by two orthopedic trauma fellowship-trained surgeons at each follow-up interval at 6 weeks, 3 months, 6 months and 1 year.

Statistical Analysis

Consistency between the two observers' mRUST scores were analyzed using intraclass correlation coefficient analysis. The reliability analysis assumed a consistency model with intent to report average measures of the two raters, also known as ICC(2,2). Shapiro–Wilk testing was used to confirm deviation from normality in observer-averaged mRUST scores, as is expected for interval scoring data. Testing for differences in observer-averaged mRUST scores over time was performed using nonparametric tests, as is generally appropriate for ordinal and non-normally distributed interval data. Repeated-measures (related samples) Friedman's two-way analysis of variance by ranks tests were carried out to determine the effect of time on mRUST score. All statistical analysis was performed in SPSS Statistics 25 (IBM Corp., Armonk, N.Y., USA).

Surgical Procedure

All TTC fusions were performed with patients placed supine on a standard operating room table. Patient was prepped and draped in normal sterile fashion isolating the involved extremity. The tip of the lateral malleolus and the fourth and the fifth metatarsal bases were marked out. An incision was made starting on the posterior border of the fibula, approximately five fingerbreadths proximal to the tip, curving around the posterior aspect of the lateral malleolus anteriorly towards the base of the fourth metatarsal and incised through the subcutaneous tissue. Extensor digitorum brevis

(EDB) was visualized distally on the anterior border of peroneus brevis insertion. Dissection was carried proximally around the posterior border of the fibula. The peroneus longus and brevis were identified. The EDB was elevated subperiosteally. An osteotomy was made 2–3 fingerbreadths proximal to tip of lateral malleolus. The direction of the osteotomy was from superolateral to inferomedial, approximately 2–3 mm from the joint line. The osteotomy was completed with an osteotome providing exposure to the ankle joint. From this anterolateral approach, both the tibiotalar and subtalar joints were decorticated. Drill holes were then placed throughout the articular surfaces. The tibiotalar joint was then confirmed to be well reduced under fluoroscopy. A stab incision was made in the plantar aspect of the foot and a retrograde wire was placed through the calcaneus to the talus and finally to the tibia. Placement of the wire was confirmed on fluoroscopy on both AP and lateral images. An opening reamer was then used, followed by placement of a long ball-tip guidewire. Reaming was then continued to the end point marked on the tibia corresponding to the proximal end of the nail. The nail was then inserted and with assistance from the jig, a dynamic screw was placed medial to lateral through a predrilled bicortical opening in the tibia. Prior to compression, percutaneous BMAC was obtained from the ipsilateral iliac crest approximately 5 min prior to compression. Incision is made three fingerbreadths lateral and one fingerbreadth inferior to ASIS. Under fluoroscopic guidance, a trocar is inserted into the iliac crest utilizing the obturator oblique inlet view to ensure the trocar is within the inner table. The trocar is advanced the entire length and 1 cc of heparin is injected followed by aspiration of the bone marrow. Once confirmed the aspiration is of bone marrow, the trocar is then withdrawn 1 cm at a time and at each interval 2–3 cc are aspirated through a 10 cc syringe until it is filled. The BMAC was then mixed with the decorticated bony tissue remnants and placed in both the subtalar and tibiotalar joints to maintain fusion position. Next, the calcaneal dynamic screw fixation was applied followed by a compression device to reduce the joint. Then, using standard free and fluoroscopic techniques, two additional proximal tibia screws were applied through stab incisions from medial to lateral distally. The surgical incision was closed with subcutaneous sutures and nylon for skin closure.

Results

A total of 20 patient charts were reviewed and 12 patients met inclusion criteria of a minimum 12-months follow-up (see Fig. 1). The cohort consisted of 4 females, 8 males, with an average age of 55.4 ± 11.1. The average BMI of the patient population was 30.2 ± 7.1. Of note, three patients were smokers, three had diabetes, one had cardiovascular disease, one had renal disease and one had liver disease. There were no postoperative complications and no reoperations in this cohort; additionally, no donor site morbidity was associated with BMAC harvesting. Of these 12 patients, one patient had native arthritis of the hindfoot and subtalar joint, 11 patients developed arthritis after trauma to the region, 4 of the 11 patients that sustained trauma also had infections from their initial fixation and underwent-stage procedure which involved initial antibiotic spacer placement followed by TTC fusion.

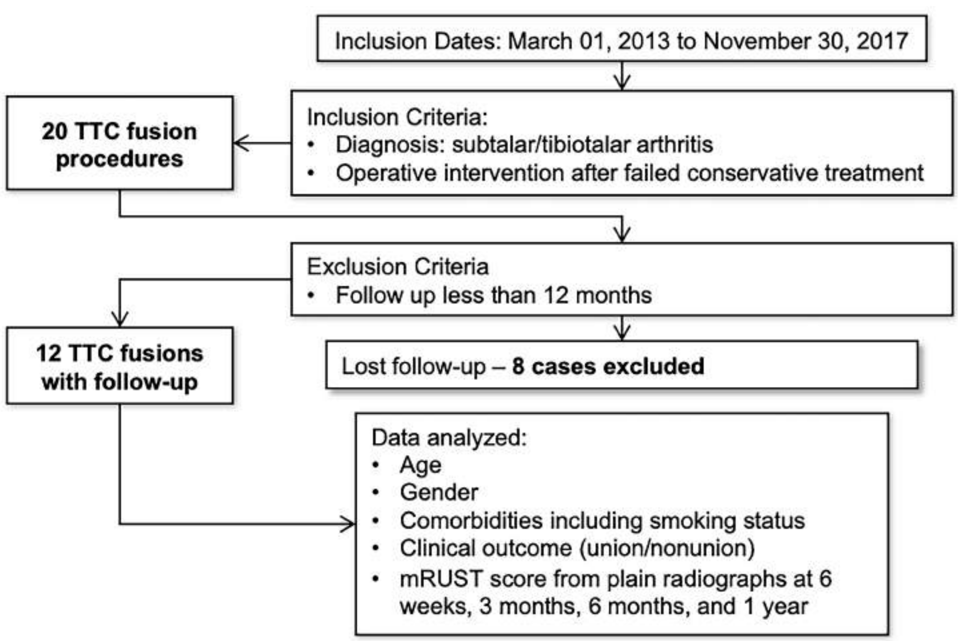

Fig. 1 Inclusion/exclusion flowchart of cohort

Radiographic scoring was completed for all 12 patients, at all four timepoints, by both observers (48 scores per observer). The intraclass correlation coefficient with two-way random effects and average measures from two observers was ICC(2,2) = 0.931 (95% confidence interval [CI]: 0.876–0.961, $p < 0.001$). This indicates "excellent" internal reliability based on average measurement reporting [37].

As expected, radiographic scores tended to increase with time (see Fig. 2). The rounded average of the observers' mRUST scores for all patients and timepoints was non-normally distributed at 6 months and 12 months ($p < 0.001$) with notable ceiling and floor effects, and the distribution was borderline non-normal at 6 weeks and 3 months ($p = 0.051$ and 0.056, respectively). Accordingly, nonparametric statistics were used for all subsequent statistical tests. Friedman's repeated-measures test showed that the variation in mRUST scores was statistically significantly different across timepoints, $\chi^2(3) = 34.4$, $p < 0.001$. Pairwise comparisons were performed between timepoints with a Bonferroni correction for multiple comparisons. The mRUST scores at 6 weeks were significantly different from the scores at 6 and 12 months ($p < 0.001$) and the mRUST score at 3 months was significantly different from the 12-month score ($p = 0.005$). No other pairwise comparisons were significant (all $p \geq 0.239$).

At 6-weeks follow-up, 2/12 (16.7%) of cases were assigned a modified RUST score of 10 or higher by both raters, indicating consensus on radiographic union. By the 3-months follow-up interval, 11/12 cases (91.7%) were assigned an mRUST score of 10 or higher by both reviewers, indicating consensus on radiographic union. At 6 months and 1 year, 100% of patients were deemed radiographically united (mRUST > = 10) by both reviewers, while 11/12 (91.7%) were considered healed/remodeled by both reviewers (Table 1).

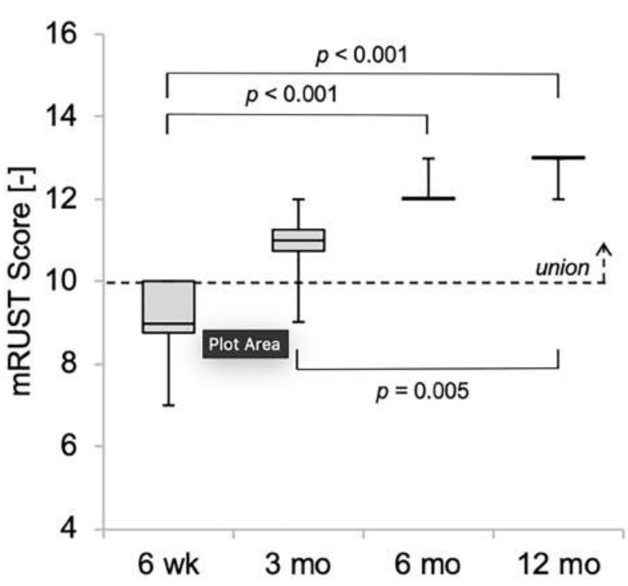

Fig. 2 Box plot of observer-averaged mRUST at 6 week, 3 months, 6 months, and 12 months. Pairwise comparisons were performed between timepoints with a Bonferroni correction for multiple comparisons between various time points

Discussion

Even with patients who have well-documented risk factors for failure of hindfoot fusion procedures, our study showed 16.7% of the cohort had consensus signs of union at the 6-weeks follow-up, 91.7% by 3 months, and 100% of patients at 1 year follow-up were deemed healed/remodeled (Fig. 3). These results were not affected by underlying comorbidities including obesity, smoking, diabetes, cardiovascular, renal, or liver disease, although the sample size was small so statistical analysis by comorbidity subgroups was not possible. Comparing our time to union to other studies that did not use BMAC, Pelton et al. found that 29/33 patients attained fusion during their study at an average time to union of 3.7 months [31]. Niinimaki evaluated 34 patients who underwent TTC fusion procedure with the use of a compressive retrograde nail and only 76% had radiographic union at 16 weeks after the operation [30]. This allows us to infer that BMAC could be a reliable adjuvant to aid in bony union, but further prospective studies are necessary to support this hypothesis.

Hindfoot fusion allows for early ambulation and affords patients pain relief, but risk factors such as smoking, non-compliance, and diabetes may pose an increased risk of failure. A case–control study by Cobb et al. demonstrated that patients who are active smokers had an increased relative risk of non-union about the ankle of up to 14-fold compared

Table 1 Modified RUST scores at follow-up intervals

Case number	6 weeks	3 months	6 months	1 year
Case 1	8/9	11/13	13/13	13/13
Case 2	9/10	11/11	13/12	13/13
Case 3	10/10	12/12	12/13	12/13
Case 4	10/10	13/12	13/13	13/13
Case 5	9/10	11/11	13/12	13/13
Case 6	9/11	10/12	12/13	13/13
Case 7	8/9	11/12	12/13	13/13
Case 8	9/9	11/10	12/12	13/13
Case 9	7/8	9/10	12/12	13/13
Case 10	9/11	11/12	12/13	13/13
Case 11	9/10	11/11	12/12	13/13
Case 12	9/9	10/12	12/13	13/13

Legend: (Observer 1/Observer 2); Combined intraclass correlation coefficient (ICC) calculated to be 0.931

Fig. 3 **A** Initial fixation of a pilon fracture with multiple plates and screws. **B**. Immediate postoperative radiographs showing placement of TTC with BMAC present. **C** 6 weeks postoperative radiographs showing patient has already obtained a mRUST > 10 indicating bony union

to former smokers and nonsmokers [3]. When evaluating the bone marrow of heavy smokers, there was a significant amount of adipose tissue seen that had infiltrated the marrow and therefore a decreased number of progenitor cells [34]. Thus, non-union in tobacco users may be a result of compromised bone marrow, decreasing the healing potential of the patient. This supports our theory that some patients may benefit from osteogenic adjuvants such as BMAC to increase union rates.

In addition, non-weightbearing compliance during the initial months following fusion procedures is critical in obtaining bony union. When patients start ambulating on the operated extremity prior to union, there is an increase in micromotion at the articulating sites that are intended for fusion, this increase in motion causes non-union as a result [10]. The effect of diabetes on fracture healing is well documented in the literature and has been shown to decrease bony union capacity leading to increased healing times [12, 13, 22, 27]. Perlman et al. also demonstrated higher rates of non-union in patients who underwent arthrodesis/fusion for PTOA when compared to patients without prior traumatic injury [32]. Overall, the reported union rate for TTC fusion without adjuvant BMAC has varied widely in the literature, ranging from 12 to 96% [8, 14, 28, 30]. Our results showed that regardless of comorbid factors that may prevent the patient from healing, with the adjuvant properties of BMAC, all patients obtained bony union.

Our findings are consistent with previous literature that demonstrated the benefits of using BMAC in the treatment of bony non-unions in other parts of the body [1, 4]. Hernigou et al. evaluated the use of BMAC on ankle non-unions in diabetic patients in comparison to bone iliac crest autograft. Their study reported that BMAC promoted healing of the non-unions more often than autograft (82% vs 62%) with fewer associated complications [18]. Similarly, McAlister et al. demonstrated 97% radiographic union with the use of BMAC in various procedures involving the foot and ankle including fusions, arthrodesis, and fractures. Our study concurs with these results, as we found rapid fusion and zero cases of non-union in our TTC patients when utilizing this technique.

When considering whether to use this technique for an individual patient, it is critical to remember that BMAC's potential to aide in bony union depends on the concentration of mesenchymal stem cells, which is influenced by the location of the aspiration, the aspiration technique, and the patient's age [7, 19, 29, 33, 35]. All these factors can lead to a decrease in the concentration of MSCs and research has demonstrated that concentrations less than 1000 MSCs/mL or less than 30,000 total MSCs fail to treat non-unions [20]. Our method of harvesting BMAC from the anterior iliac crest follows the guidelines that these studies have set. This ensures adequate amount of MSCs are present to aide in TTC fusion, which includes harvesting from the iliac wing and utilizing a 10 cc syringe.

Our study is not without limitations. The main limitation is the small number of cases included in the study, which prevented us from statistically assessing the efficacy of BMAC for TTC fusion in the presence of comorbidities. This study is also a retrospective design of a single cohort and lacks a control group. No comparative group further hinders obtaining statistical data and elevating the level of evidence present. Weightbearing compliance was also not measured, so this study is limited by an intent-to-treat interpretation with actual patient behavior that may have been different from surgeon instructions. Further research is needed to evaluate the time to ambulation and full weight bearing status with a correlation drawn to radiographic signs of bony union.

Conclusion

Treatment of post-traumatic osteoarthritis of the ankle and subtalar joint remains challenging with ankle arthrodesis and TTC being the standard of care. Improved functional outcomes, improved performance of activities of daily living, and decreased pain have been shown to be a result of TTC fusion in previous studies. Bony union at the ankle can be hindered by comorbidities including diabetes, smoking, and post-traumatic arthritis. Our results suggest that the use of BMAC as an adjunct in TTC fusion is a safe treatment option that can promote bony fusion, excellent healing rates, and decrease need for revision surgery.

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Declarations

Conflict of Interest On behalf of all authors, the corresponding author states that there are no conflicts of interest to disclose.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed Consent For this type of study, informed consent is not required.

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ORIGINAL ARTICLE

Short Term Clinico-Radiological Outcome of Extra Osseous Talo-Tarsal Stabilization (EOTTS) in Flat Foot: An Indian Perspective

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Abstract
Introduction Flexible flat foot is one of the most common foot conditions found amongst any age group across the world. One very important reason for this condition is the incongruency or partial dislocation of one or more joints within the talo-tarsal mechanism. This flexible talo-tarsal malalignment is termed as recurrent talo-tarsal joint dislocation (RTTJD).
Materials and Methods Between 2016 and 2018, 32 patients were advised Extra osseous talo-tarsal stabilization (EOTTS) as a standalone procedure for RTTJD following detailed clinical examination including foot posture index (FPI) scoring and weight-bearing radiographic evaluation. Subjective assessment was done through Maryland Foot Score (MFS) questionnaire. Radiological parameters like talar declination angle, talar second metatarsal angle and tibio-calcaneal valgus angle were assessed for preoperative and postoperative comparison. 15 patients (20 feet) underwent surgery and rest 17 patients (25 feet) became our control group. A retrospective record analysis of longitudinal data was done over a period of 4 years. The purpose of this study is to depict the short-term results of EOTTS procedure in terms of functional and radiological improvement and compare it with the non-surgical group.
Result Significant improvement was seen in MFS from 67.31 ± 16.04 to 95.47 ± 4.36 over a mean follow-up period of 30.66 ± 7.09 months. Total FPI improved by $96.83 \pm 4.80\%$ at final follow-up of EOTTS group. Radiologically, maximum correction achieved was in coronal plane ($93.07 \pm 30.05\%$).
Conclusion EOTTS, as a standalone procedure improved the foot radiological angles and restored the normal foot biomechanics significantly in presence of competent spring ligament and posterior tibial tendon. This procedure resulted in excellent patient satisfaction score as assessed by MFS questionnaire.
Level of Evidence III.

Keywords Extra osseous talo-tarsal joint stabilization (EOTTS) · Flat foot · Recurrent talotarsal joint dislocation (RTTJD) · Arthroereisis · Minimally invasive surgery

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Introduction

Flat foot is one of the most common foot conditions found amongst any age group across the world. In India, the medical fraternity, especially the orthopedic surgeons have travelled a long way in understanding the ever-evolving foot and ankle concepts. The indications for which the treatment is sought for a flat foot are also different as compared to the west. It could be for a cosmetic reason, especially for a girl's marriage, pain in foot or for recruitment in armed forces. Sports is still on the last priority for which treatment is sought. People don't seek treatment for a deformed foot if it does not give any trouble. Also, any pain in proximal musculoskeletal chain is least thought to be because of a hyper-pronated foot.

Majority of rural Indians wear slippers (*Chappal*) and their compliance with orthotics is very poor. Surgery for flat foot is despised by majority of patients. Cost of surgery has to be borne by the patients in majority of cases. Postoperative surgical rehabilitation puts them out of their work place. Many physicians advise against surgical intervention as they feel that flat foot cannot be stitched back.

While introducing Extra Osseous Talo-tarsal Stabilization (EOTTS) in India, the author faced loads of resistance which drove him to do this study. Unacceptability by patients to a new technique, strong belief of physicians in conservative means without any strong evidence and inadequate knowledge about flat foot prevailing in society were some of them.

One important reason for flexible flat foot is the incongruency or partial dislocation of one or more joints within the talo-tarsal mechanism. The talo-tarsal mechanism is composed of talonavicular and middle, anterior, and posterior talocalcaneal joint (Fig. 1). This dislocation or subluxation may exist as recurrent/dynamic/reducible or rigid/static/non-reducible condition. The flexible talo-tarsal malalignment is termed as Recurrent talo-tarsal joint dislocation (RTTJD) [1].

RTTJD leads to anteromedial displacement of talus on calcaneus with extensive force acting anteromedially rather than postero-laterally (Fig. 2A). The gold standard for the diagnosis of RTTJD is weight bearing radiographic evaluation.

The factor that differentiates normal from abnormal talo-tarsal alignment is overlap of the articular facets. This flexible entity of malalignment has a greater potential to contribute to secondary abnormalities than a rigid deformity [2].

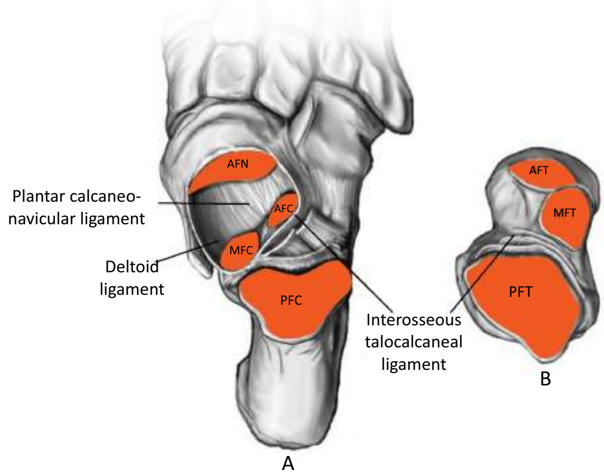


Fig. 1 Talo-tarsal mechanism of foot. (**A**) Dorsal view of hindfoot (after removing talus) with plantar calcaneonavicular ligament, deltoid ligament & Interosseous talocalcaneal ligament and (**B**) Inferior view of Talus. *AFN* Articular facet of navicular, *MFC* Medial facet of calcaneum, *AFC* Anterior facet of calcaneum, *PFC* Posterior facet of calcaneum, *AFT* Anterior facet of talus, *MFT* Medial facet of talus, *PFT* Posterior facet of talus

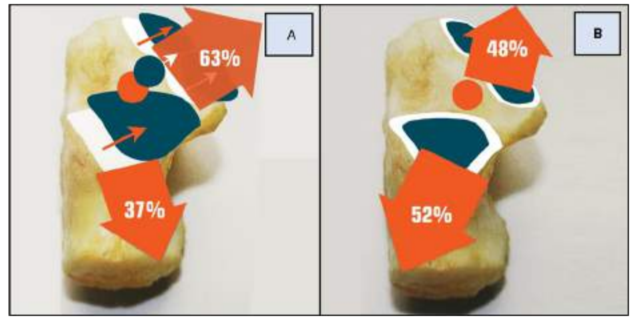


Fig. 2 (**A**) Anteromedial displacement of talus on calcaneus, (**B**) EOTTS shifts force from anteromedial to posterolateral by 24%

The incongruent talo-tarsal deformity leads to a pathologic chain reaction in the entire foot structure distally, and also proximally, up the musculoskeletal chain and therefore a patient with RTTJD can present with a spectrum of picture ranging from low back ache, knee pain, shin splint, arch pain, bunion, plantar fasciitis, tarsal tunnel syndrome, gait abnormalities and can eventually complicate to medial column overloading stress injuries and hindfoot and midfoot arthritis [3].

Interestingly, not all patients with RTTJD will have a fallen arch. Some may have excessive heel valgus while others may have gross forefoot abduction. The root of the problem is a hypermobile talus and not a fallen arch.

Whatever be the pathology for a misaligned foot, the least invasive intervention must be chosen to decrease pain and improve function. The procedure should have least effect on other joints of foot [4].

The technique of subtalar intervention has taken more than half a century to reach the present stage in treating flat foot. Grice did an extra articular subtalar arthrodesis using cortical strut graft for pediatric pes planus [5]. Haraldsson inserted allograft cortical bone wedges in the sinus tarsi to restrict subtalar eversion without arthrodesis [6]. First subtalar arthroereisis with a free floating implant was described by Subotnick [7]. Sinus tarsi implants are now made of silicone, polyethylene, titanium, stainless steel, or bioresorbable polymers.

In the present times, there are many sinus tarsi devices in the market. Understanding their types gives us a broader outlook of their functioning mechanism, their advantages and drawbacks. Sinus tarsi devices can be classified into 2 major types, type I and type II (Fig. 3) [8].

Type I devices are further subclassified into type IA (cylindrical) and type IB (conical) (Fig. 3).

1. Type I device functions by impingement of lateral process of talus to block the talar motion (Talar door stop)

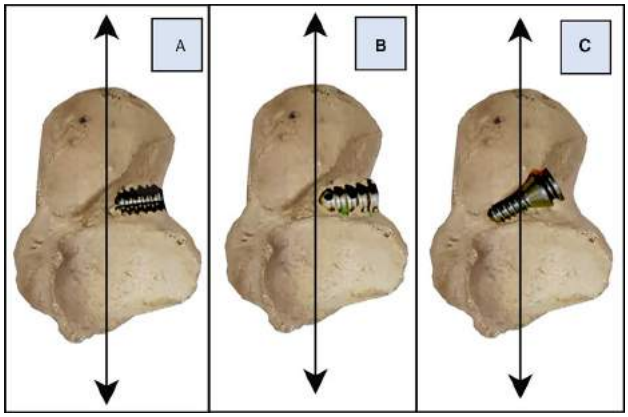


Fig. 3 (**A**) Type IA device, (**B**) Type IB device, (**C**) Type II device

having a reported removal rate as high as 40%. The mechanism by which type I device functions is called arthroereisis [9, 10].

2. Type II device is known as HyProCure (Macomb, MI, USA) and is made of titanium. It is designed to have a lateral-conical and medial- cylindrical geometry, is inserted into the tarsal sinus in a posterior-medial-superior direction. The device is stabilized medially by anchorage from soft tissues within the canalis portion of the tarsal sinus, and laterally by tapered portion of the device that abuts against the entrance to prevent over insertion.

The anterior leading edge of this device goes medially beyond the longitudinal talar bisection line, stabilizes the talus and restore the normal axis point of subatalar joint. It functions by allowing the normal helicoidal motion of the talus within the tarsal mechanism. Reported removal rate is 4–6% [8]. The mechanism by which type II device works is called extra osseous talo-tarsal stabilization (EOTTS).

The type II device is designed to provide the closest anatomical fit with the sinus and canalis portions of the tarsal sinus, thus provides greater distribution of forces and gives better results [11]. Type II device is superior in design and function as compared to type I device. It remarkably stabilizes the complicated tri-planar talo-tarsal motion at the “cruciate pivot point”. Cruciate pivot point is located at the entrance of the canalis portion of the tarsal sinus along the longitudinal talar bisection line. It is the origin of a rectangular coordinate system along the axes of which (Fig. 4) the helicoidal motion of the talus during pronation and supination occurs and is the ideal location where the excessive anterior-medial-plantar displacement of the talus within the tarsal mechanism should be eliminated or minimized. The threaded cylindrical portion offers no resistance to talar motion. It doesn’t bear any weight because it obtains an interference grip in the anteroposterior direction and not in the supero-inferior line of axial body weight [12]. The oblique alignment of type II device further contributes to its long-term survivability. Unlike the type I laterally anchored devices that function as a talar door stop, the type II device functions like a stent placed within an artery to keep it open.

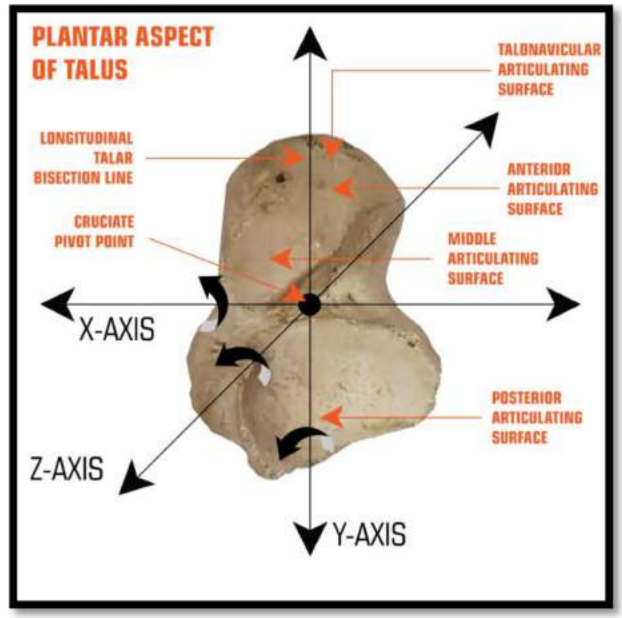


Fig. 4 Cruciate pivot point

EOTTS prevents shifting of posterior facet force to anterior and medial facet by approximately 24% (Fig. 2B) and thus patients with medial column pain benefit significantly [1]. Literature has enough evidence that EOTTS has positive effect on plantar faciopathy [13], tarsal tunnel syndrome [14], abnormal plantar pressures [15], stretched spring ligament [16], forefoot deformities [17] and on knee [18, 19] and lower back pain [20, 21] arising from hyper-pronated foot.

In the present study, EOTTS was done as a standalone procedure using type II device on 15 patients (20 feet) suffering with RTTJD. The purpose of this study is to depict the short- term result of EOTTS procedure in terms of functional and radiological improvement and compare it with the functional outcome of those who did not undergo any surgical intervention. Also, to formulate a road map so that the surgery is done on a patient only when appropriately indicated and not otherwise.

Patients and Methods

Between 2016 and 2018, 181 flat foot patients were seen in the Outpatient department of our tertiary care center for foot and ankle. All these patients presented with one or more of the following symptoms: foot pain, easy fatigability while walking and running, early eccentric wearing of shoes, obvious looking deformed foot and shin pain.

All the patients underwent a detailed clinical and radiological evaluation by a single foot and ankle orthopedic surgeon. 58 patients were diagnosed with RTTJD. 26 patients were advised EOTTS along with other bony or soft tissue procedures and 32 patients were advised EOTTS as a standalone procedure. Out of these 32 patients, 15 patients (20 feet) underwent surgery and rest 17 patients (25 feet) didn't opt for any surgical intervention. These 17 patients became our control group. Demographic comparison of both the groups is given in Table1.

Clinical assessment included detailed foot and ankle examination and Foot posture index (FPI) scoring [22]. Standardized anteroposterior (AP), lateral and long axial [23] radiographs of foot and AP radiograph of ankle were taken preoperatively and postoperatively in bilateral resting stance position (Fig. 6). Parameters like talar declination angle (sagittal plane), talar second metatarsal angle (axial plane) and tibio-calcaneal valgus angle (coronal plane) were considered for preoperative and postoperative comparison. Normal values of the above angle measurements is given in Table 2 [24–26]

Postoperative assessment was done at 3 months and at final follow-up. The patients were also asked to complete the MFS Questionnaire. Initial (before the start of treatment) and final MFS scores were assessed and compared for both groups (Tables 3 and 4). The final MFS scoring for non- operative group was done through telephone and text messages.

A written informed consent was taken from the patients willing for surgery and from both the groups using their clinico-radiological data for the study. Ethical committee approval was taken for the study.

Table 1 Comparison of Sociodemographic parameters between Non operative (control) and EOTTS group

Parameters	Categories	Non operative	EOTTS	*P* value
Age (years)	Mean (SD)	25.52 (10.26)	24.26 (5.96)	0.63
Gender	Male (%)	56	63.16	0.63
	Female (%)	44	36.84	
Occupation	Athlete (%)	0	10.53	0.23
	Businessman (%)	12	0	
	Clerk (%)	8	0	
	House wife (%)	12	21.05	
	IT professional (%)	20	15.79	
	Job (%)	4	0	
	Lawyer (%)	0	5.26	
	Shop owner (%)	0	5.26	
	Student (%)	44	42.11	
Side	Left (%)	48	42.11	0.70
	Right (%)	52	57.89	
Follow up (months)	Mean (SD)	35.23(7.32)	31.10 (6.85)	0.09

SD Standard deviation, *IT* Information Technology

Table 2 Comparison of Clinico-radiological parameters in EOTTS group

Paired *t* test	Normal range	Before (mean)	SD	After (mean)	SD	*P* value
MFS	#	67.32	16.05	95.47	4.36	< 0.001
FPI Rearfoot	*	4.53	0.70	0.16	0.37	< 0.001
FPI forefoot	*	4.58	0.77	0.16	0.37	< 0.001
FPI total	0–5	9.12	1.1	0.32	0.48	< 0.001
TDA	21	28.21	4.00	18.11	2.10	< 0.001
T2MA	16.2 ± 7.3	28.89	4.91	13.32	4.81	< 0.001
TCVA	0–5	10.95	3.92	1.42	2.32	< 0.001

#A normal range for MFS score cannot be ascertained. However, increased score indicate decreased abnormality

*A normal range for forefoot and rearfoot FPI cannot be ascertained individually in pronation. However. increased score indicate increased abnormality

MFS Maryland foot score, *FPI* Foot Posture Index, *TDA* Talar declination Angle, *T2MA* Angle between axis of talus and axis of 2nd metatarsal on Axial plane, *TCVA* Tibio calcaneal valgus angle

Table 3 Comparison of MFS Parameters in EOTTS group

MFS parameters	Before (mean)	SD	After (mean)	SD	*P* value
Pain	30.79	10.31	43.42	2.39	< 0.001
Distance walked	6.37	2.56	9.47	0.90	< 0.001
Stability	3.26	0.93	3.79	0.42	0.004
Support	3.63	0.50	4.00	0.50	0.005
Limp	3.11	0.81	4.00	0.81	< 0.001
Shoes	4.84	1.46	8.95	1.13	< 0.001
Stairs	2.58	1.17	3.58	0.84	< 0.001
Terrain	2.84	1.01	4.00	1.01	< 0.001
Looks	5.53	2.70	9.37	0.96	< 0.001
Motion	4.37	0.96	4.89	0.32	0.014
Total	67.32	16.05	95.47	4.36	< 0.001

MFS Maryland foot score, *SD* Standard deviation

Table 4 Comparison of MFS Parameters in Non operative (control) group

MFS parameters	Before (mean)	SD	After (mean)	SD	*P* value
Pain	34.6	4.31	32.6	3.85	0.005
Distance walked	6.8	2.12	4.84	3.17	< 0.001
Stability	3.08	0.70	2.48	1.33	0.005
Support	3.96	0.2	3.4	1.12	0.013
Limp	3.84	0.37	3.6	0.65	0.011
Shoes	7.64	2.89	6.12	3.38	0.015
Stairs	3.44	0.51	3.2	0.58	0.011
Terrain	2.32	0.75	2.16	0.55	0.327
Looks	6.8	1	6.48	0.87	0.043
Motion	3.68	1.46	3.48	1.39	0.364
Total	76.16	9.66	68.36	9.65	< 0.001

MFS Maryland Foot Score, *SD* Standard deviation

In the surgical group, only those patients were involved in whom EOTTS was done as an isolated procedure. In case of patients with bilateral foot involvement, second foot was operated at least 21 days after the 1st surgery.

Clinical inclusion criteria for surgery were:

1. Age > 10 years.
2. At least one visible deformity: arch collapse, heel valgus and forefoot abduction.
3. Flexible flat feet (Patient was able to recreate the arch)
4. Absence of equinus deformity. (At least 10 degrees of ankle dorsiflexion could be achieved)
5. Absence of posterior tibial tendon insufficiency.
6. No instability along the 1st ray

Radiological inclusion criteria were:

1. Talar-2nd metatarsal angle on DP view: 16–35 degrees
2. Talar declination angle < 36 degrees.

Clinical exclusion criteria were:

1. Active infection overlying sinus tarsi of the involved foot.
2. Body mass index > 35
3. Any neuromuscular imbalance in lower limb.
4. Previous surgery done on foot for pes planus
5. Incompetent spring ligament as per neutral lateral heel push test [27].

Radiological exclusion criteria were:

1. Tarsal coalition
2. Degenerative changes of ankle and foot joints.
3. Talar-2nd metatarsal angle on DP view > 35 degrees
4. Metatarsus adductus
5. Talar declination angle > 35 degrees
6. Distal tibial epiphyseal abnormality in pediatric patients.

Intervention

The patient was placed supine on the operating table. For pediatric patients, general anesthesia was used and for adult patients ankle block worked fine. An approximately 1.5 cm linear skin incision was made perpendicular to the axis of foot over the soft spot of sinus tarsi. Using curved tenotomy scissors, the soft tissues (Talocalcaneal interosseous ligament) within the sinus and canalis portions of the sinus tarsi were transected to create pathway for guide wire and trial sizers insertion. This step was the most vital for proper placement of the actual implant. The guide wire was directed lateral to medial, anterior to posterior (towards medial malleolus) and inferior to superior into the sinus tarsi. Trial sizing was performed to determine the appropriate stent (implant for EOTTS) size to achieve the best correction. First trial sizer to be inserted was no. 5 which could be subsequently increased to no. 6 and so on to maximum no. 10 size till satisfactory correction was achieved. The goal was to restore the talo-tarsal motion to 3–5 degree of pronation. Once the proper size was determined, the corresponding stent was inserted. Guide wire was removed and incision was closed with absorbable subcuticular suture followed by application of a sterile and dry compression dressing.

Postoperative Course

The patients were instructed non-weight bearing for 2–3 days post-surgery. Cryotherapy was given for 3–4 times a day till inflammation persisted. At 3rd–4th postoperative day, partial to full weight bearing was allowed as per tolerance. By the end of first week, peronei strengthening, range of motion at ankle and subtalar joint and calf stretching exercises were started. The patients were allowed to gradually increase activity as tolerated after first postoperative week. Patients were encouraged to use new sports shoes as soon as tolerated, making sure that the outer collar did not rub against the incision site [28].

Statistical Analysis

This study is a retrospective record analysis of longitudinal data of two groups. Statistical significance was evaluated between preoperative and final postoperative MFS scores, between initial and final follow-up MFS score of control (non-surgical) group and between the final MFS scores of both operative and control group. Statistical significance was also calculated between relevant clinical and radiological parameters before surgery and at final postoperative follow-up. A paired student's t test was applied when comparing data within the same group while single t test was applied when two groups were being compared.

Results

There was a significant improvement in MFS at final follow-up of EOTTS group patients (Table 3) in comparison to non-operative group (Table 4). MFS improved from 67.31 ± 16.04 to 95.47 ± 4.36 over a mean follow-up period of 30.66 ± 7.09 months. Pain, shoe wear and looks improved maximally. Rear foot and forefoot FPI improved by 97.01 ± 7.10% and total FPI improved by 96.83 ± 4.80% at final follow-up of EOTTS group (Fig. 5, Table 2). Radiological parameters like talar declination angle, talocalcaneal valgus angle and talar-second metatarsal angle improved significantly (Fig. 6, Table 2). Maximum correction achieved was in coronal plane (93.07 ± 30.05%) followed by axial plane (54.84 ± 16.08%) followed by sagittal plane (34.99 ± 9.1%). This suggests that EOTTS has a definite positive impact in functional and clinico-radiological outcome of patients suffering from RTTJD. The patient satisfaction scores showed excellent short-term results with overall good tolerance to the implant and improved quality of life.

Complication rate was 4% with one deep infection leading to permanent implant removal.

One patient had device displacement within 2 months of surgery. Following a revision surgery which essentially involved more thorough cut of talocalcaneal interosseous ligament and replacement of same device, patient did well at final follow-up. It was interesting to observe that while the device was partially displaced, the corrected radiological angles were still maintained.

Short term self-resolving complications like abnormal gait, sprain like feeling over lateral aspect of ankle and appearance of overcorrection disappeared once swelling, pain and inflammation were resolved.

In the non-surgical group, MFS had fallen from 76.16 to 68.36 over a mean follow-up of 35.23 ± 7.32 months. All parameters deteriorated significantly except looks, terrain and motion. This study clearly demonstrated that non-surgical treatment is not effective and leads to deterioration of function with poor outcomes.

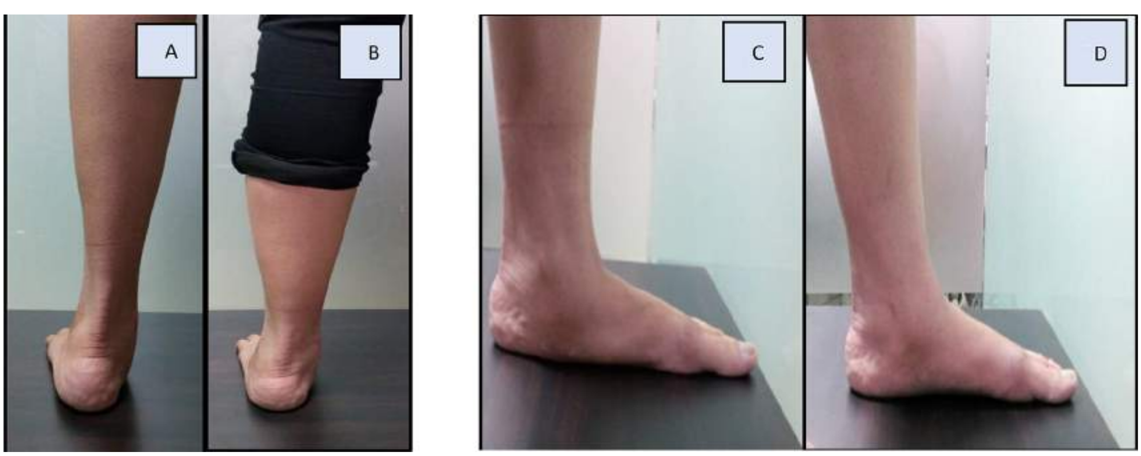
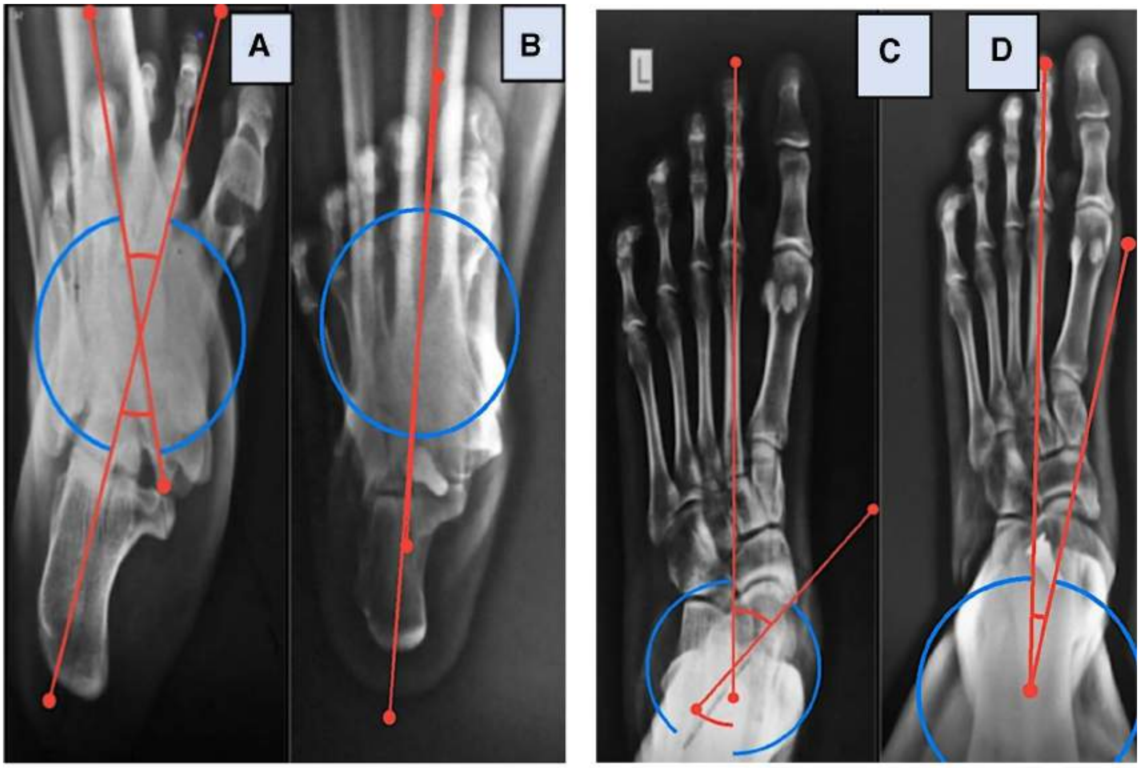


Fig. 5 Preoperative and postoperative clinical picture. (**A**,**B**) Pre & postoperative improvement in heel valgus, (**C**,**D**) Pre & postoperative improvement in medial longitudinal arch



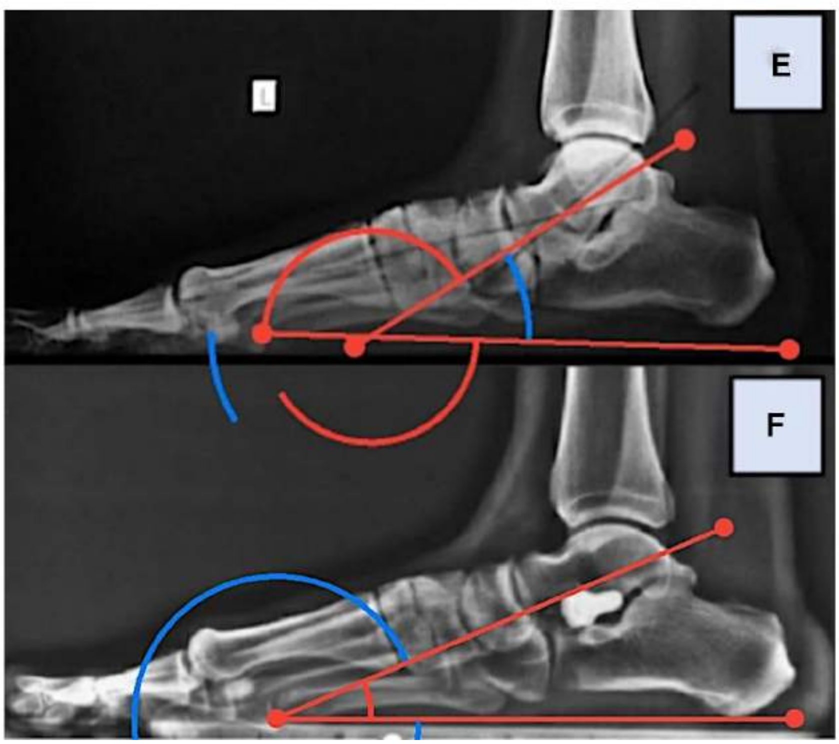


Fig. 6 Weight bearing preoperative & postoperative views. (**A**,**B**) Pre & postoperative Talocalcaneal valgus angle 26 deg and 1.2 deg. (**C**,**D**) Pre & postoperative Talo-second metatarsal angle 35 deg and 12 deg. (**E**,**F**) Pre & postoperative Talar declination angle 34.5 and 23 deg. Significant correction is noted in radiological angles in all the plane

Discussion

In recent times, many studies have been published on subtalar minimally invasive intervention for correction of mis-aligned foot.

Vedantam et al. gave satisfactory results in 96% of feet in a study of 78 children who had flexible flatfoot caused by neuromuscular disorders, in whom 140 arthroereisis procedures were performed [29]. Giannini and colleagues reported the 4-year results of subtalar arthroereisis for 21 children who had bilateral flexible flatfoot deformity using a bioresorbable implant. In selected cases, Achilles tendon lengthening and Kidner procedure were added [30]. Needleman did subtalar arthroereisis along with other surgical corrections of flexible flat foot deformity with average follow-up of 44 months. Significant improvements were found in radiographic parameters with high patient satisfaction despite the removal of 11 of 28 implants for sinus tarsi pain [31].

A retrospective study by Graham et al. [28] showed positive outcomes of EOTTS in 83 patients with less than 6% incidence of implant removal and few postoperative complications. Bresnahan [32], in his study concluded that EOTTS using type II subtalar device effectively stabilized the talo-tarsal mechanism and reduced the symptoms associated with talo-tarsal instability.

The intent of the implant is to stay in situ as long as possible. The implant has been used in USA since 2004, and since that time there has been no published reports of ill-effects to the talus or calcaneus. The implant is absolutely extra-articular and is not known to cause arthritis to subtalar joint. So far, the published reports only discuss removal due to persistent pain and upon removal of the implant the pain has resolved.

The present study is the first to report subjective as well as objective short- term outcome on the use of type II subtalar device from Asia for treatment of talo-tarsal joint instability and its associated pathologies. We conclude that appropriate patient selection is the key to success of EOTTS as a stand-alone procedure in mild to moderate cases. For severe cases, adjunctive bony and soft tissue procedures can be added. The inclusion criteria were deliberately kept narrow to asses improvement with isolated EOTTS and offer early rehabilitation to the patients.

There have been other modalities for treating flat foot. Soft tissue and bony procedures result in extensive surgical dissection, big & cosmetically challenging scars, long recovery periods with plasters and non- weight bearing instruction and sometimes inadvertent damage to adjacent joints. The compliance with custom made orthotic supports, braces and shoe inserts is very poor in this part of the world. Also, there is no proven clinical evidence that externally applied foot orthotics realigns the osseous structure and restore the normal biomechanics of foot. With EOTTS, all the above problems are bypassed & the most important advantage is its reversibility. In case of any complication, it can be easily removed without any further loss.

However, EOTTS has its own limitations and cost of implant is the most important one. Most insurance company did not cover the treatment for congenital flat foot. The training and understanding required to do EOTTS was not available in India for many years.

The limitation of the present study is that it has a short-term follow-up with limited number of patients. Our inclusion criteria are narrow. MFS scoring of conservative group and few surgical patients at the end of study were done on phone or using text messages.

Conclusion

EOTTS, as a standalone procedure using type II device resulted in excellent results in presence of competent spring ligament and posterior tibial tendon. The procedure improved the foot radiological angles and was able to restore the normal foot biomechanics significantly. The present study opens a gateway for further research into EOTTS wherein long-term study can be done with broader inclusion criteria and added procedures on a larger group of patients.

Author contributions AJ: Study design, performed measurements, manuscript preparation. GG: Study design, performed measurements, manuscript preparation. AG: Statistical analysis, manuscript preparation.

Declarations

Conflict of interest The author declares that they have no competeing interest.

Ethical approval Ethical committee approval was taken for the study.

Informed consent A written informed consent was taken from the patients willing for surgery and from both the groups using their clinicoradiological data for the study.

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ORIGINAL ARTICLE

Should We Use Intra-articular Tranexamic Acid Before or After Capsular Closure During Total Knee Replacement? A Study of 100 Knees

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Abstract

Background Intraarticular (IA) administration of tranexamic acid (TXA) is a proven way of reducing blood loss in total knee replacement (TKR). However, different methods of administration have been described in literature such as placement of an intra-articular swab soaked in TXA before capsular closure or injecting TXA intraarticularly after capsular closure. We decided to compare these two methods.

Materials and Methods One hundred consecutive patients planned for unilateral TKR between December 2018 and March 2019 were selected for the study and divided into 2 groups of 50 patients each. All patients received IV and oral TXA identically—15 mg/kg TXA IV preoperatively, 10 mg/kg IV TXA at 3 and 6 h postoperatively, and 1 g oral TXA for the next 2 days. Group A was given IA TXA via swab soaked with 1 g TXA in 100 ml normal saline (NS) before closure of arthtrotomy, while Group B was given 1 g of IA TXA via injection in the knee after capsular closure. Preoperative haemoglobin (Hb) and post-operative day 4 Hb values were measured. Blood loss was calculated and compared in both groups using Mann Whitney test.

Result The mean blood loss was 652.23 ± 64.36 ml in Group A and 542.68 ± 266.23 ml in Group B. The difference in blood loss between both groups was found to be clinically significant with a *p*-value of 0.03236 (significant, $p < 0.05$).

Conclusion Injecting TXA intraarticularly after capsular closure is more effective than using an intra-articular swab containing TXA.

Level of Evidence Level III Retrospective Comparative study.

Keywords Tranexamic acid · Intraarticular · Swab · Haemoglobin · Blood loss

Abbreviations

TKR	Total knee replacement
TXA	Tranexamic acid
DVT	Deep vein thrombosis
PE	Pulmonary embolism
IV	Intra-venous
IA	Intra-articular
tPA	Tissue plasminogen activator
Hb	Haemoglobin
BMI	Body mass index
PBV	Patient's blood volume
DM	Diabetes mellitus
HTN	Hypertension
CABG	Coronary Artery Bypass Graft
ACB	Adductor Canal Block
TED	Thrombo Embolic Deterrent
SC	Subcutaneous
LMWH	Low molecular weight heparin
GI	Gastro-intestinal
NS	Normal saline
ROM	Range of movement
RBCs	Red blood cells
Kg	Kilogram
g	Gram
mg	Milligram

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Introduction

Total knee replacement (TKR) can be linked with considerable perioperative blood loss, ranging from 1000 to 1790 ml [1–4]. Several techniques have been described to reduce this blood loss. These include various preoperative, intraoperative and postoperative modifications [3, 5]. Currently, the perioperative use of tranexamic acid (TXA) is one of the favored methods to reduce blood loss during and following TKR.

TXA is an antifibrinolytic agent. It is an artificial molecule derived from the amino acid lysine. It blocks lysine binding sites on plasminogen molecules in a reversible manner. It prolongs clot life by impeding fibrinolysis. This reduces blood loss. The routine use of TXA in recent years has resulted in an overall decreased reported blood loss and transfusion requirements in patients undergoing TKR [6].

The blood loss following TKR occurs from cut vessels and bony surfaces. To address this intraoperatively, several studies have been performed advocating the use of intra-articular (IA) administration of tranexamic acid (TXA) in total knee replacement surgery (TKR).

However, different ways of administration of IA TXA have been described by different Surgeons. While few surgeons prefer the placement of an intra-articular swab soaked in TXA before closure of the arthrotomy [7, 8], others inject TXA intraarticularly after its closure [9].

We have conducted this study with the objective to assess and evaluate the efficacy of both these methods on postoperative blood loss in patients undergoing primary unilateral total knee arthroplasty.

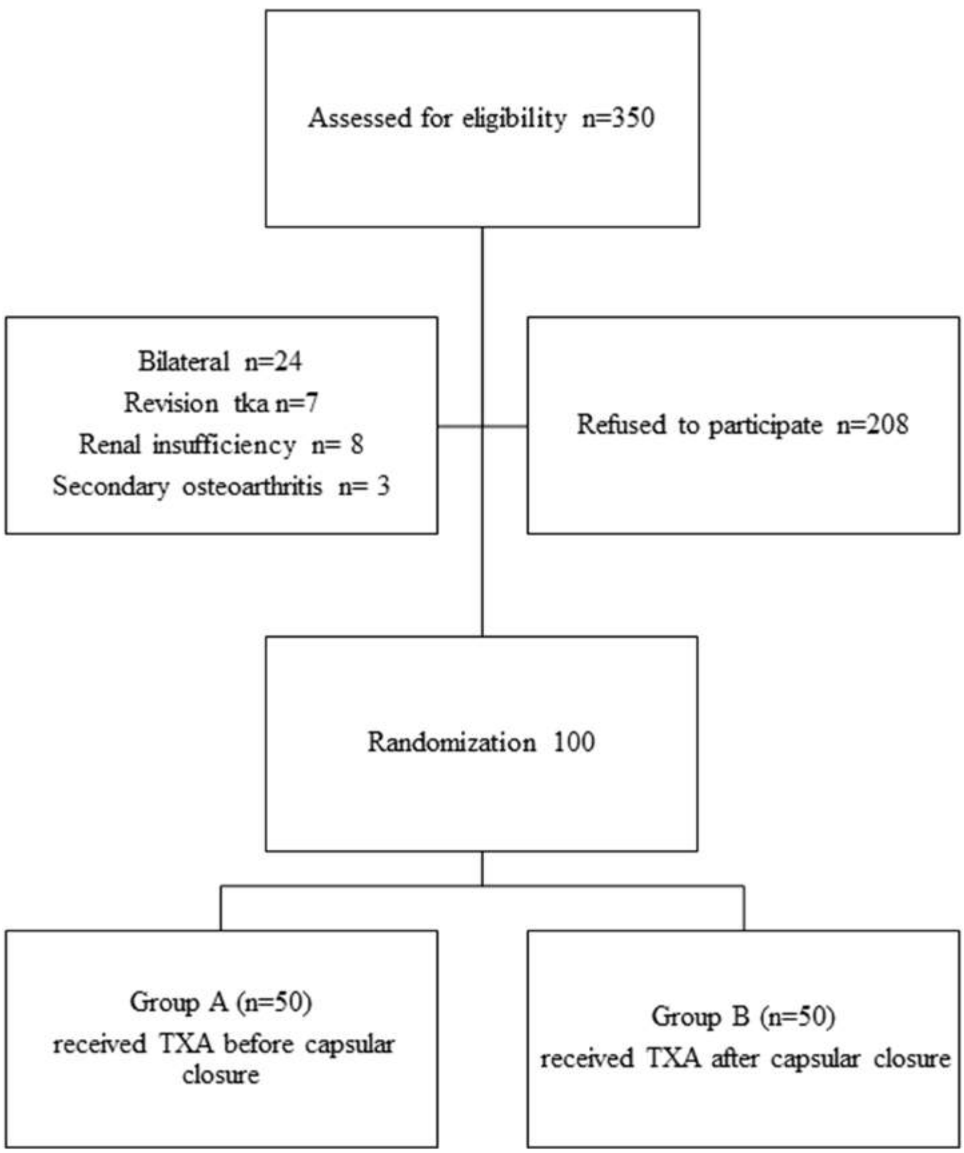
Materials and Methods

Study Design

This study is a retrospective analysis of prospectively collected data in a case control design.

Approval for the study was obtained from the Institutional Review Board.

A total of 350 patients were operated between December 2018 and March 2019, out of which 100 consecutive patients planned for unilateral total knee replacement were selected for the study.



Each patient was randomized in one of two groups:

Group A ($n = 50$), received intra-articular 1gm TXA via a swab (1 g TXA in 100 ml NS) for 5 min before closure of capsule.

Group B ($n = 50$) received an injection of 1gm TXA intra-articularly after closure of capsule.

Randomization was done based on the date of surgery. Patients operated in December 2018 and January 2019 were kept in group A while those operated in February and March 2019 were placed in group B.

Informed consent was obtained from each patient.

Inclusion criteria,

- Unilateral TKR.
- Minimum 6 weeks follow-up.

Exclusion criteria,

- Unwilling patient.
- Bilateral TKR.
- Diagnosis other than Primary osteoarthritis (OA) of the knee.
- Renal dysfunction.
- History of deep vein thrombosis (DVT)/pulmonary embolism (PE).

Preoperative hemoglobin (Hb) and postoperative day 4 Hb value were recorded in each case. Loss in blood volume was calculated using Hb balance method. This loss was then compared in two groups and statistically analysed.

Surgical Technique

All surgeries were performed by the senior author (NAS) using a mini-subvastus approach as described previously [10] without the use of a tourniquet.

All surgeries were performed under spinal anesthesia (0.5% Bupivacaine) and Adductor Canal Block (ACB) was utilised for post-operative pain relief.

30 mL of saline with adrenaline (1:300,000) was infiltrated into the skin, subcutaneous tissues and joint capsule before making the surgical incision. Standard surgical techniques were used for intraoperative haemostasis. Tourniquet was not applied.

The NexGen (Zimmer, USA), Legion (Smith and Nephew, USA), Freedom (Maxx, USA) cemented total knee endoprosthesis systems were used for total knee replacements.

In Group A, after final implantation and prior to capsular closure, wash with normal saline was given and a swab soaked in TXA and isotonic saline solution (1 g TXA in 100 ml NS) was applied for 5 min [7, 8].

In Group B, 1 g TXA was injected in the knee joint intra-articularly after closure of the capsule [9].

No surgical drains were used.

Prophylactic antibiotic therapy consisted of IV administration of 1.5 g cephalosporin (cefuroxime) pre-op followed by 2 more doses of 750 mg IV at 8 and 16 h post-op.

15 mg/kg TXA was given IV preoperatively and 10 mg/kg TXA was administered IV at 3 and 6 h postoperatively. 1 g oral TXA was administered for the next 2 days, in two divided doses.

The knee was kept in 40 degrees flexion post-operatively for the first 4 h after surgery [11].

For DVT prophylaxis,we used bilateral TED stockings and chemoprophylaxis for all patients. Chemoprophylaxis consisted of subcutaneous (SC) dose of low molecular weight heparin (LMWH) (inj. Enoxaparin) 12 h postoperatively (0.4 ml if patient's weight < 60 kg and 0.6 ml if weight > 60 kg). This was followed by a Factor Xa inhibitor (tablet Rivaroxaban 10 mg) for the first 2 weeks followed by tablet Aspirin 75 mg for the next 4 weeks.

While in the hospital, patients were examined daily for any clinical symptoms and signs of DVT. All surgical and medical adverse events and thromboembolic events occurring (if any) during the first 6 weeks after surgery were recorded at the time of the follow-up.

Postoperatively, mobilization was early and aggressive in both the groups. Static quadriceps exercises, straight leg raising exercises and range of motion (ROM) exercises were started from day 0. Patients were encouraged to get out of bed and walk as tolerated from day 0 after the first 6 h.

Blood was transfused to patients if hemoglobin level fell to 7.5 gm/dl or lower and if there were systemic symptoms of anemia [12].

Assessment of Intraoperative and Postoperative Blood Loss

All patients were evaluated with a complete blood count before surgery and on the fourth day after the procedure. By this time, the patients were hemodynamically stable and thus fluid shifts would have been largely completed. The height and weight of the patients were recorded pre-operatively and the body mass index (BMI) was calculated.

Calculation of Blood Loss

In our series, the patient's blood volume (PBV) was calculated using the formula of Nadler and colleagues [13].

$$\text{PBV} = k_1 \times \text{height}^3\left(\text{m}^3\right) + k_2 \times \text{weight (kg)} + k_3.$$

where $k_1 = 0.3669$, $k_2 = 0.03219$, $k_3 = 0.6041$ for men, and $k_1 = 0.3561$, $k_2 = 0.03308$, $k_3 = 0.1833$ for women.

Using this formula, all patients' blood volume and perioperative blood loss was calculated by the hemoglobin balance method indirectly [14].

It has been proven that direct blood loss estimation is not accurate and denotes a much lesser blood loss than what is estimated by indirect evaluation as the indirect method also takes into account the hidden blood loss.

Patients were evaluated for deep vein thrombosis whilst in the hospital and at follow-up for 6 weeks post TKR and if they presented with any symptoms.

Statistical Analysis

Statistical analysis was carried out using paired student's z test and Mann Whitney test. Differences were considered statistically significant at $p < 0.05$. Statistical analysis was done using SPSS software 20.0 (SPSS inc., Chicago, IL).

Results

The demographic parameters in both groups like age, height, weight, male:female ratio and BMI were comparable (Table 1).

The mean perioperative blood loss in Group A was 652.23 ± 64.36 ml as compared to 542.68 ± 266.23 ml in Group B. It was found to be significant with a z-value of 2.14 and p-value of 0.03236, i.e. $p < 0.05$ with confidence interval of 95%.

The mean reduction in hemoglobin level was 1.9 ± 0.8 gm/dl in group A compared to 2.1 ± 0.7 gm/dl in group B. None of the patients developed DVT or any other thromboembolic episodes.

The following Table 2 shows the distribution of comorbidities:

Table 2 Comorbidities in patients of both groups

Comorbidity	Number of patients in Group A	Number of patients in Group B
Diabetes mellitus (DM)	10	11
Hypertension (HTN)	18	25
Dyslipidemia	2	2
Hypothyroidism	6	2

Eighteen patients in group A and twenty-five patients in group B were hypertensives. The mean blood loss in this hypertensive subgroups of patients was 649.78 ± 61.959 ml in Group A against 550.025 ± 265.238 ml in Group B, which was also found to be statistically significant ($p < 0.05$).

Discussion

Physiologically, human vascular system is responsible for effective circulation of blood as well as minimizing blood loss from any injured vessel. This is attained by a balance between the two processes- thrombus formation to prevent blood loss, and fibrinolysis for clot dissolution. The intrinsic clotting cascade leads to thrombus formation. Activation of plasminogen is triggered by tissue plasminogen activator (tPA), which forms a complex with fibrin and stops it from forming a clot. Normally, there is a homeostasis between these two processes that prevent spontaneous thrombosis intravascularly. But, a vascular injury inclines the equilibrium towards clot formation.

During surgery and healing, we desire the formation of clots in order to prevent blood loss. tPA slows down this process by dissolving the small clots that form on cut vessels and bony surfaces, thus, prolonging bleeding.

Anderson et al. [15] ascertained that TXA indirectly prevents the dissolution of clots.

Table 1 Demographic parameters in both groups

	Parameters	Group A	Group B
1	*N* (number of subjects)	50	50
2	Age (in years)	67.26 ± 8.48	67.48 ± 6.38
3	Male:Female	9:41	12:38
4	Height (in cm)	151.56 ± 8.08	155.62 ± 8.28
5	Weight (in kg)	71.64 ± 12.15	72.93 ± 13.33
6	Body mass index (BMI)	31.32 ± 7.37	29.73 ± 4.78
7	Total blood loss (in mL)	652.23 ± 64.36	542.68 ± 266.23
8	Hemoglobin (Hb) difference (in gm/dl)	1.59 ± 0.69	1.75 ± 0.97
9	Preoperative Hb (in gm/dL)	12.02 ± 1.05	12.35 ± 1.17
10	Hb on post-op day 4 (in gm/dL)	9.96 ± 1.16	10.59 ± 1.13
11	Mean operative time(in mins)	62.9 ± 8.0	59.5 ± 11.5

TXA is a synthetic derivative of lysine with a higher affinity for the lysine-binding sites on plasminogen. It disrupts fibrinolysis by blocking the lysine binding sites which in turn inhibits the activation of plasminogen. Thereby, preventing complex formation between plasminogen and fibrin and clot dissolution does not occur. Its elimination half-life is 2 h.

TXA can therefore be used to prevent, arrest or reduce perioperative blood loss [16] by delaying clot dissolution. Also, it is relatively low-cost and easily available [17].

Since 1968, a lot of data has been published that shows that TXA reduces blood loss in various surgical procedures [18] including cardiopulmonary bypass [19], thoracic surgeries [20], as mouthwash in oral surgeries [21], epistaxis [22], upper GI bleed due to peptic ulcers [23] and total hip and knee replacement [24].

During TKR surgery, hemorrhage occurs directly from vessels. Postoperative hemorrhage is usually in the form of concealed haemorrhage [17] which leads to hematoma formation. There is a sequestration of red blood cells (RBCs) in such hematomas and a further drop in hemoglobin levels is seen.

Use of intravenous and oral formulations of TXA are well established [25–27].

The use of topical tranexamic acid has been explored in the last 20 years [7, 28–30]. In a retrospective study, Chimento et al. [30] reviewed 683 cases of primary TKR and compared the use of intra-articular TXA to placebo. Out of 683 patients, the case group ($n = 310$) received topical intra-articular application of 3 gm TXA in 100 ml saline following cementing, and control group ($n = 373$) did not receive it (placebo). The case group reported a significantly higher postoperative hemoglobin level and lower transfusion rates compared to the control group.

In a meta analysis, Panteli et al. [29] found that use of topical TXA in TKR was associated with significant reduction in postoperative drain output and hemoglobin drop.

Zecker et al. [31] demonstrated the safety of topical route without any increase in incidence of DVT or PE.

Some studies have used combinations of topical TXA with IV and oral formulations [6, 32]. Studies comparing all the three routes are also available [33, 34].

Intra-aticular Tranexamic acid (topical TXA) has been used in different ways by different authors. Wong et al [7] used TXA to the open joint surface (before the capsule was closed) for 5 min, while Martin et al. [8] bathed the wound for 2 min (again before capsular closure) and sucked out the extra fluid and closed the knee. In the study by Kim et al. they infused joint with 1 gm TXA using a drain post a water-tight capsular closure and clamped it for 48 h [9]. Roy et al. administered 500 mg TXA in 5 ml NS via the drain, and Ishida et al. administered 2 gm TXA in 20 ml NS via the drain and clamped it for 30 min. Sa-Ngasoongsong et al. injected 250 mg TXA in 25 ml NS intraarticularly after fascia closure and clamped the drain for 2 h [29]. Chen-guang Wang et al. [35] used topical TXA by injecting 0.5 g of TXA in 10 ml saline intra-articularly after capsular closure. The different ways of using topical TXA have not been compared in the literature and the optimum or the minimum duration that TXA needs to be in the intra-articular cavity to be effective has also not been established.

In the present study, we compared the two methods of using TXA topically (available to us as we do not use drains) and found that the application of TXA after capsular closure was better in reducing blood loss.

From our study, it appears that topical TXA applied before capsular closure has a limited action while TXA injected after closure of capsule acts for a longer duration due to prolonged contact with the wound and vessels and has a better effect in reducing blood loss. Obviously, blood loss following a TKR can also depend upon the total operative time, but in our study the duration of surgery for the two groups was similar. We mobilised the patients early in both the groups (on the same day) and there was no difference in the blood loss in the two groups based on when were the patients mobilised after surgery.

However, there are certain limitations to our study. It has been performed at a single center with all patients operated by a single surgeon using a subvastus approach without a tourniquet or post-operative drains. Whether or not the same results can be achieved when a tourniquet and drains are used or if they can be replicated with a different surgical approach can be the subject of further research. But the study shows that intrarticular TXA in TKR is best utilised after capsular closure.

Conclusion

Injecting intra-articular tranexamic acid after capsular closure is more effective than applying tranexamic acid via swab before capsular closure in reducing the blood loss after TKR, without increasing the rate of complications.

Author Contributions VK: data collection, analysis and paper writing. NS: senior surgeon, paper editing. PP: data collection. This manuscript has been read and approved by all authors. This article is our original work.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest.

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ORIGINAL ARTICLE

An Early Experience with a Novel Technique of Total Knee Arthroplasty for Osteoarthritic Knee with Coexistent Traumatic Tibia Diaphysis Fracture

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Abstract

Background Treatment of tibia (upper third and diaphysis) fracture together with severe osteoarthritis (OA) poses challenge to an orthopedic surgeon. Traditionally, it is treated through three-stage surgeries, first fracture fixation followed by implant removal and finally surgery of total knee arthroplasty (TKA). Herein, we describe a novel TKA procedure using long-stemmed tibia component. This one-step technique not only addresses arthritis of the knee joint but also helps in assisting fixation of the fracture.

Materials and Methods We reported outcomes of three female non-diabetic patients with OA who developed tibia shaft fracture following trauma. Range of motion and quadriceps strengthening exercise were initiated immediately after the procedure. X-rays anteroposterior and lateral views of the operated limbs were obtained at post-operative week-6 and week-12. We allowed the patients' toe touch weight-bearing immediately after the surgery. The patients were progressed to full weight-bearing after confirming radiological union on the X-rays.

Results At follow-up, all treated patients were able to mobilize with good range of motion of the operated knee and with union of the fracture. The American Knee society scores and WOMAC pain and stiffness scores improved significantly.

Conclusion This novel technique offers one-stage solution to the complex situation of osteoarthritis of the knee with associated tibia shaft fracture, thereby reducing future hospital admissions/surgeries and associated costs and complications. Further, it allows faster rehabilitation.

Keywords Osteoarthritis · Tibia shaft fracture · Long-stemmed tibia · One-staged total knee arthroplasty · Novel technique

Abbreviations

OA Osteoarthritis
TKA Total knee arthroploasty
IM Intramedullary
AP Antero-posterior

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Introduction

The most common long bone injuries include fractures of the tibia shaft or tibia diaphysis which usually occur as a result of accident, falls, direct trauma and/or combined bending and torsion forces [1–3]. Among several factors identified, smoking habit, lack of physical activity, menopause, family history and osteoporosis have been reported frequently [4]. Clement et al. [5] in a study of 233 tibial diaphyseal fractures in the elderly (> 65 years of age) reported a greater rate of non-union i.e. 10%. These elderly patients often present challenge to the surgeon as malalignment secondary to osteoarthritis predisposes to delayed union or non-union due to increased stress at the fracture site. Furthermore, factors associated with osteoarthritis including osteopenia, corticosteroid use and abnormalities of calcium metabolism affect the strength of the bone and thereby make them liable to non-union [6]. Being a load sharing implant, intramedullary (IM) nailing causes less stress shielding and facilitates early loading and weight-bearing which make it more beneficial over cast immobilisation and plating [7–9]. The procedure of IM nailing not only preserves hematoma and cambium layer of periosteal required for bone healing but also reduces the rate of infection [9]. These together attribute to higher union rate and reduced risk of implant failure. Furthermore, the operative and healing time can be reduced to a great extent which ultimately enables mobilisation of the patients in a short span of time. However, literature describing surgical methodology for the treatment of tibial shaft fracture or diaphysis fracture of tibia co-existing with OA is limited. We developed a novel technique to manage traumatic closed tibia shaft fracture with co-existent severe OA of knee joint. In our technique, we attempted to manage both the problems using one-stage total knee arthroplasty together with a long-stemmed tibia component having a good diaphysis fit.

Fig. 1 Implant used

Materials and Methods

We share our experience of treating patients ($n = 3$) with one-stage total knee arthroplasty (TKA) with a long-stemmed tibia component for closed traumatic tibia shaft fracture and concomitant severe osteoarthritis of the knee joint. All the patients had low energy type of trauma. We conducted this retrospective review of the three operated cases with local ethics committee approval. Informed consent was also received from all the included patients. A single team of experienced orthopedic surgeons performed all three surgeries. All the patients had a clinical follow-up at day 2, week 6, week 12, week 24, 1 year and 2 year post procedures and a radiological follow-up at 6 weeks and 12 weeks post surgery. American Knee Society Score (AKSS) for clinical and functional outcomes and WOMAC score for pain and stiffness assessments were performed at post-procedural day-2, week-6, week-12, week-24, 1-year and 2-year follow-up by an independent observer.

Procedure

The surgery was performed under combined spinal and epidural anesthesia. TKA was performed through medial para patellar approach. Tourniquet was used in all the cases. In all three patients maxx freedom knee system posterior-stabilized implant (maxx orthopedics Inc., Pensylvania, USA) was used. This particular implant is selected because it offers more variables of the available tibia stems, both for the diameter and length in Indian patient morphology than any other implant system. (The stem provides a choice of 24 straight stem extensions ranging from 7.5 to 16.5 mm and lengths of 40–150 mm) (Fig. 1). Upper tibia preparation was done using intramedullary rod alignment technique. The position of the IM rod across the tibia fracture was confirmed through anteroposterior (AP) and lateral projections on the image intensifier. IM reamers of increasing diameters were used to ream the tibia until a good diaphysis fit was achieved. Long-stemmed tibia trial component was introduced. The position of the tibia tray and stem was determined through AP and lateral views. Distal femur was prepared in a routine fashion and a trial reduction was carried out. Intraoperatively anteroposterior stability and mediolateral stability of the trial implants were checked by the operating surgeon. Prior to cementing the implant, pulse lavage wash was given. However, tibia stem was not cemented. The bone graft obtained from the distal femoral condyle cut, notch/chamfer cut was utilized for grafting the fractured tibia site, (through a small separate incision or the primary TKA incision). The operative wound was closed in layers over a negative suction drain. All the three patients in this case series had associated fibula fracture. Hence, resection of the fibula was not required to be done to allow good collapse at the fracture site. None of the patient preoperatively was diagnosed to have osteoporosis nor was any one of them on long term bisphosphonate therapy. They had their DEXA scan post-operatively which showed osteoporosis and hence were treated with calcium and vitamin D supplementation and 12 months of injectable terriparetide treatment.

Post-operative Rehabilitation

Routine knee range of motion and quadriceps muscle strengthening exercises were commenced immediately after the surgery. We allowed the patients' toe touch weight-bearing immediately after the surgery protected with a short knee brace for the tibia acting as a Sarmiento type of corset. The patients were progressed to full weight-bearing after confirming radiological union on the X-rays. The reason for cautious approach for weight-bearing is the extended tibial stem has no locking

Fig. 2 Pre-operative and post-operative x-rays of patient A

Fig. 3 Pre-operative and post-operative x-rays of patient B

Fig. 4 Pre-operative and post-operative x-rays of patient C

Table 1 Implant sizing for the patients

Patient	Age	Limb operated	Femoral component	Tibia base plate	Tibia liner	Stem extension
A	72 years	Right	Size C	Size 2	C1-2 11 mm	13.5 mm × 150 mm
B	84 years	Left	Size C	Size 1	C1-2 14 mm	12 mm × 150 mm
C	73 years	Right	Size B	Size 2	B1-2 11 mm	9 mm × 150 mm

option distally (As is available in certain revision hip systems). Follow-up was continued till 2 years of the surgery. Pre-operative and post-operative radiographs are shown in Figs. 2, 3, 4.

Results

The present case series includes three female patients diagnosed with tibia shaft fracture following trauma with co-existent severe knee OA. All the patients were non-smoker, non-diabetic and at post-menopausal age. Long-stemmed tibia component was utilized during one-stage total knee arthroplasty. Posterior stabilized fixed-bearing (PS/FB) knee implants were implanted in all three cases with valgus alignment of 4–5°. The details of component sizing are depicted in Table 1.

Pre-procedural clinical characteristics like range of motion, American Knee Society Score (AKSS) for clinical and functional outcomes, and WOMAC score for pain and stiffness could not be obtained due to advanced age of the patients, the intensity of pain due to fracture and unwillingness of the patients to go for physical examination. Hence, all the aforementioned assessments were performed at post-procedural day-2, week-6, week-12, week-24, 1-year and 2-year follow-up. Range of motion improved consistently throughout 2-year follow-up. Clinical AKSS score improved after the surgery suggesting reduced intensity and frequency of the pain with appropriate varus-valgus alignment. Likewise, improvement in functional AKSS scores was also noted at follow-up. The WOMAC pain and stiffness score at follow-up were suggestive of improvement in the pain and stiffness (Tables 2, 3, 4).

Discussion

The fractures of tibia shaft or tibia diaphysis need to be treated on an urgent basis. The available treatment modalities include cast immobilisation, IM nails and plates. Open reduction and internal fixation with the plate is one of the treatment options for these fractures. However, the prolonged healing period and restriction for weight-bearing make the patients immobilize for at least 3 months after the procedure [10]. Infection at operative site and skin necrosis are other discouraging factors that limit its acceptance as a preferred treatment approach [10]. Owing to the prolonged healing time, plating delays subsequent TKA, it is noteworthy that treatment of tibia shaft fracture further requires removal of hardware at the time of TKA which impart high treatment cost to the patient. Similarly, the presence of IM nails hinders the placement of tibia component of TKA. Hence, an IM nail also needs to be removed surgically before TKA. One-stage TKA with the long-stemmed tibia component can address this unmet clinical need as it eliminates need for multiple surgeries required for the management of tibial shaft fracture and at the same time allow TKA for co-existing knee osteoarthritis. Long-stem extension of the tibial component implantation during the same TKA surgery would bypass the fracture site and simultaneously stabilize and repair the fracture. Requirement of anesthesia only during one surgery reduced surgical/anesthetic risk as well as lowers the hospital expenditure and risk of infection.

Table 2 Assessment of patient A

Patient A	ROM	Clinical AKSS	Functional AKSS	WOMAC pain score	WOMAC stiffness score
Day 2	98°	47	0	3	4
Week 6	110°	62	30	2	2
Week 12	122°	90	75	1	1
Week 24	122°	90	75	1	1
One year	122°	90	75	1	1
Two year	122°	90	75	1	1

Table 3 Assessment of patient B

Patient B	ROM	Clinical AKSS	Functional AKSS	WOMAC pain score	WOMAC stiffness score
Day 2	98°	45	0	3	3
Week 6	106°	61	35	2	1
Week 12	122°	90	90	0	0
Week 24	122°	90	90	0	0
One year	122°	90	90	0	0
Two year	122°	90	90	0	0

Table 4 Assessment of patient C

Patient C	ROM	Clinical AKSS	Functional AKSS	WOMAC pain score	WOMAC stiffness score
Day 2	92°	39	0	4	4
Week 6	96°	63	15	3	2
Week 12	118°	77	70	1	1
Week 24	118°	77	70	1	1
One year	118°	77	70	1	1
Two year	118°	77	70	1	1

Several studies have evaluated one-stage TKA surgery with implantation of long-stem tibia component for stress fractures of the tibia in patients with severe OA [6, 11–15]. To the best of our knowledge, there are no reported studies of the use of single-stage TKA with long-stem tibia component for traumatic fracture of the diaphysis of the tibia with co-existent OA of the knee. In our study, all the three patients had a fracture of the tibia following a fall (trauma/injury).

Mittal et al. [6] reported the outcomes of 11 men and 18 women who were treated with fixed-bearing posterior-stabilized TKA for OA or rheumatoid arthritis. The patients had associated tibial ($n=31$) and femoral ($n=3$) stress fractures. Clinical outcomes at an average follow-up of 51 months were encouraging with significant improvement of Knee Society clinical and functional score together with united fractures. Moskal et al. [13] reported a unique technique for managing three patients who had non-union of a proximal tibial stress fracture adjacent to an arthritic knee joint. The patients were treated with concomitant TKA involving angular correction at the stress fracture non-union site, bone grafting, and stabilization of the non-union site with a long-stemmed tibial component and a unicortical plate. In two instances, fibular osteotomy was needed to achieve the preferred angular correction. Another case series reported satisfactory early functional outcomes of the 34 patients treated with TKA. Stress fracture of tibia and associated arthritis was addressed through single surgical procedure using long-stem tibial component, metal augments, corrective osteotomy [14]. Similarly, radiological and functional outcome of one-stage TKA with long stem for 20 patients with varied degrees of knee arthritis and proximal tibia stress fractures confirmed restoration of limb alignment and fracture healing at mean follow-up of 28 months [15].

This is one of its kind studies that describe 2-year functional outcomes of one-stage TKA that used long-stemmed tibial component with good diaphysis fit for simultaneous treatment of severe OA and traumatic tibial fractures. Earlier reported studies [6, 11–15] are all for the simultaneous management of severe OA and associated stress fracture of the tibia and not for the fracture of the tibia following trauma/injury. It showed improved functional and clinical knee scores at 2-year follow-up. Apart from cost-effectiveness, less frequent hospital admissions/surgeries, early rehabilitation and ambulation, reduced fracture healing time, low infection rate or wound complications make this technique as an attractive treatment approach. Our study has certain limitations. The interpretation of the results needs careful consideration of small sample size and lack of metabolic workup of the patients. Notably, all the fractures treated in this study were extra-articular fractures. Other limitation of our study is we did not have radiographs of the knee prior to the patient sustaining trauma. Presence of pre-trauma radiographs would have made sure that these were not stress fractures of tibia (which happens in severe varus OA knee) which became displaced fracture due to trivial trauma.

Conclusion

One-stage TKA with the use of long-stemmed tibial component can be considered as a combined treatment approach for traumatic tibial fracture with co-existent knee OA. Single surgical procedure reduces hospital admissions, multiple surgeries and thereby associated costs and complications. Faster rehabilitation is an added advantage of this novel procedure. However, larger randomized study is required to reciprocate similar findings.

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Availability of Data and Materials Not applicable.

Declarations

Conflict of Interest There are no competing interests.

Ethical Approval Institutional review board approval was obtained before the study. Also all patients were consented.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed Consent Informed consent was obtained from all individual participants included in the study.

Consent for Publication We hereby give our consent for publication.

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ORIGINAL ARTICLE

Poor Accuracy of Clinical Diagnosis in Pes Anserine Tendinitis Bursitis Syndrome

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Abstract

Objectives To investigate the characteristics of the patients who are clinically diagnosed with pes anserine tendinitis bursitis syndrome (PATBS), and to determine the sensitivity and specificity of clinical diagnose based on magnetic resonance imaging (MRI).

Methods Included in this cross-sectional clinical study were 156 patients who were evaluated based on the clinical presence or absence of PATBS. All patients underwent Q-angle measurement, knee osteoarthritis (OA) grading according to the Kellgren–Lawrence classification, and medial joint space measurement, and their cartilage thickness, and any periarticular and intraarticular knee pathologies were recorded from an assessment of knee MRIs.

Results Of the total, 64 cases (41%) were diagnosed clinically with PATBS and 92 (59%) were not. There was no difference in the Q angles of the two groups ($p > 0.05$), while the medial joint spaces were significantly lower in the PATBS patients ($p < 0.05$). There were no significant differences between the two groups in an MRI assessment of meniscus and ligament lesions, chondromalacia patella, cyst, bursitis, effusion and synovial pathologies ($p > 0.05$). The sensitivity and specificity of the PATBS clinical diagnoses relative to the MRI findings were determined as 41.2% and 59.5%, respectively.

Conclusion The medial joint space was found to be significantly lower in patients with PATBS, while there was no difference in any other knee pathologies between the two groups. The sensitivity and specificity of a PATBS clinical diagnosis were found to be low, and so it was concluded that clinical PATBS diagnoses may be inaccurate, particularly in the presence of such invasive therapies as injection, and that diagnoses based on imaging methods would be more accurate.

Keywords Knee · Magnetic resonance imaging · Pes anserine tendinitis bursitis syndrome

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Introduction

Pes anserine tendinitis bursitis syndrome (PATBS) is one of the most frequently encountered soft tissue pain syndromes of the knee, and often accompanies knee osteoarthritis (OA) [1, 2]. PATBS increases knee pain, and thus effects the quality of life of patients with OA [3, 4]. Conjoined gracilis, sartorius and semitendinosus tendons form the pes anserine tendon and insert the proximal anteromedial tibia 5 cm distal to the medial tibial joint line. Pes anserine bursa lies deep in the pes anserinus tendon and medial collateral ligament [5]. The proximity of the tendon and bursa make it difficult to differentiate pes anserine tendinitis (PAT) from pes anserine bursitis (PAB) by clinical examination alone. Since the treatments are identical, the term PATBS term has been adopted for the clinical condition [6].

PATBS may cause tenderness and sometimes swelling over the pes anserine, along with anteromedial knee pain [7]. Repetitive friction over the bursa, overuse of the bursa, direct trauma to the bursa and mechanical derangement are assumptive causes, although the pathophysiology of PATBS is still unclear and controversial [5, 7–9]. The recommended treatments for PATBS include rest, non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroid injections [7]. While these treatments are currently used, PATBS is often a clinical diagnosis. There has as yet been no study assessing the accuracy of this clinical diagnosis in the literature. The aim of our study is to determine the sensitivity and specificity of clinical diagnoses of PATBS based on magnetic resonance imaging (MRI) findings. As a further objective, we compare the characteristics of patients with knee pain with and without PATBS as a clinical diagnosis, and with other pathologies detected on a knee MRI.

Materials and Methods

One hundred ninety-eight patients between that ages of 18–75 years who presented to our Physical Medicine and Rehabilitation outpatient unit complaining of knee pain were evaluated between December 2014 and January 2016. Patients with a history of infective arthritis of the knee and knee surgery, and those with fibromyalgia, rheumatoid disease, malignancy, stroke and neuromuscular diseases, were excluded from the study.

The age, sex and body mass index (BMI) of the patients, were ascertained, along with the presence of diabetes mellitus (DM), pain duration, engagement in sporting activities and trauma history. The patients were categorized by age as those under 40 years (18–40 years) and those over 40 years of age (41–75 years).

Knee OA diagnoses were based on the criteria of American College of Rheumatology [10]. Each patient was questioned according to the clinical diagnostic criteria of PATBS. (1) Have you experienced any knee pain in the last 2 weeks? (2) Do you experience knee pain when ascending or descending stairs? (3) Do you feel knee pain during weight-bearing activities? (4) Do you have trouble getting out of a car? After completing the questionnaire, the patients were examined in the supine position. Tenderness was checked by palpating the pes anserine tendon proximal and anteromedial to the tibia, 3–5 cm distal to the medial knee joint. PATBS was clinically diagnosed if the patient responded positively to item (1) and one of items (2), (3) or (4), and tenderness upon the examination of the pes anserine area [1, 11]. The patients who did not meet the clinical diagnostic criteria for PATBS were grouped as those without PATBS. Only the right side of the patients was considered in the assessment of patients with bilateral PATBS.

The *Q* angles were measured using a manual goniometer while the patients were in the supine position and with the knees in the extended position, with the hinge of the goniometer positioned at the center of the patella. The angle between the line passing from the anterior superior iliac spine to the center of the patella, and from center of the patella to the tibia tubercle, was measured [12].

Radiological Evaluation

A radiological evaluation was made of all patients by plain radiography and an MRI of the knee. Anteroposterior weight-bearing radiographs of both knees were taken at full extension. OA was graded according to the Kellgren–Lawrence grading system [5]. Medial joint space width was measured from the apex of the medial condyle of the femur to the tibial end plateau, radiographically. The knee MRI's of the patients were evaluated by the same radiologist who was blinded to the clinical findings of the patients. The knee MRI's of the patients were evaluated using the Picture Archiving and Communication System (PACS). All studies were performed on a 1.5 T MRI 450w system (GE Healthcare, Milwaukee, WI, USA). The T1 sequences in the sagittal plane, and the T2 fat sat/Pd fat sat sequences in the coronal, sagittal and axial planes were evaluated. For the evaluation of PAT, we investigated the existence of hyperintensity, thickening of the tendon, fluid and edema adjacent to the ligament based on an axial and coronal MRI [13] (Fig. 1). For the diagnosis of PAB, increased fluid within the bursa was evaluated, along with any thickening of the bursal wall and surrounding tissue edema [6] (Fig. 2). The medial cartilage thickness and chondral erosion evaluation was made from a coronal MRI. Cartilage thickness was described as the

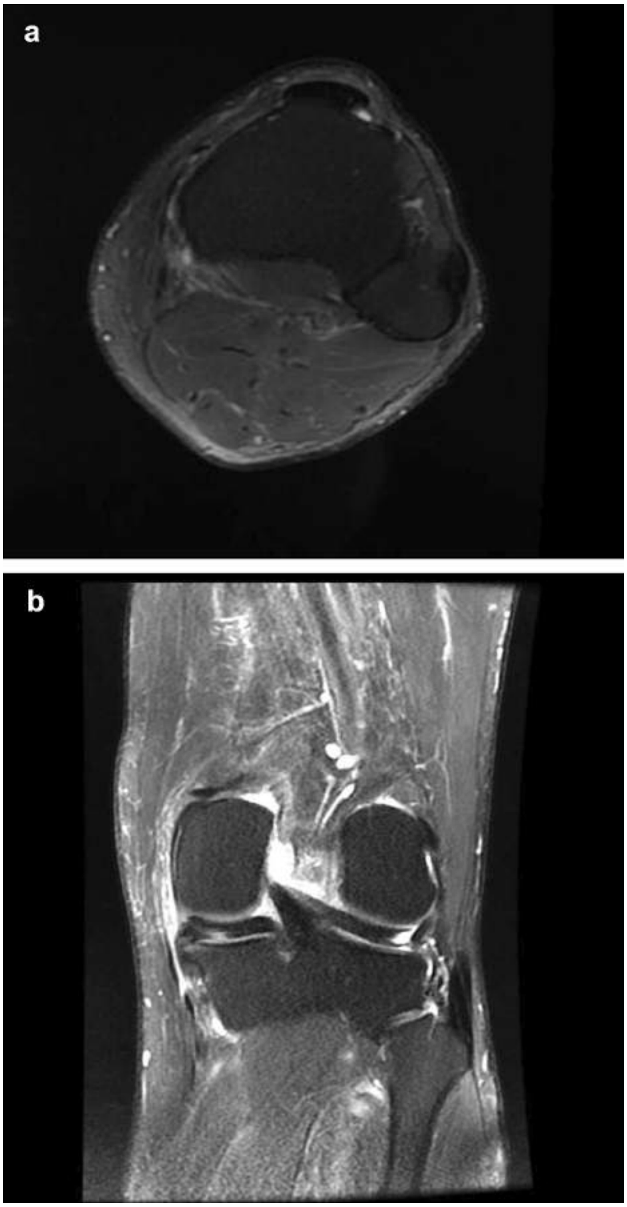

Fig. 1 Axial (**a**) and coronal (**b**) FS PD-weighted MR images of the knee in a 67-year-old male patient showed thickened pes anserine tendons which have with increased intrasubstance signals and edema with minimal effusion adjacent to the tendon

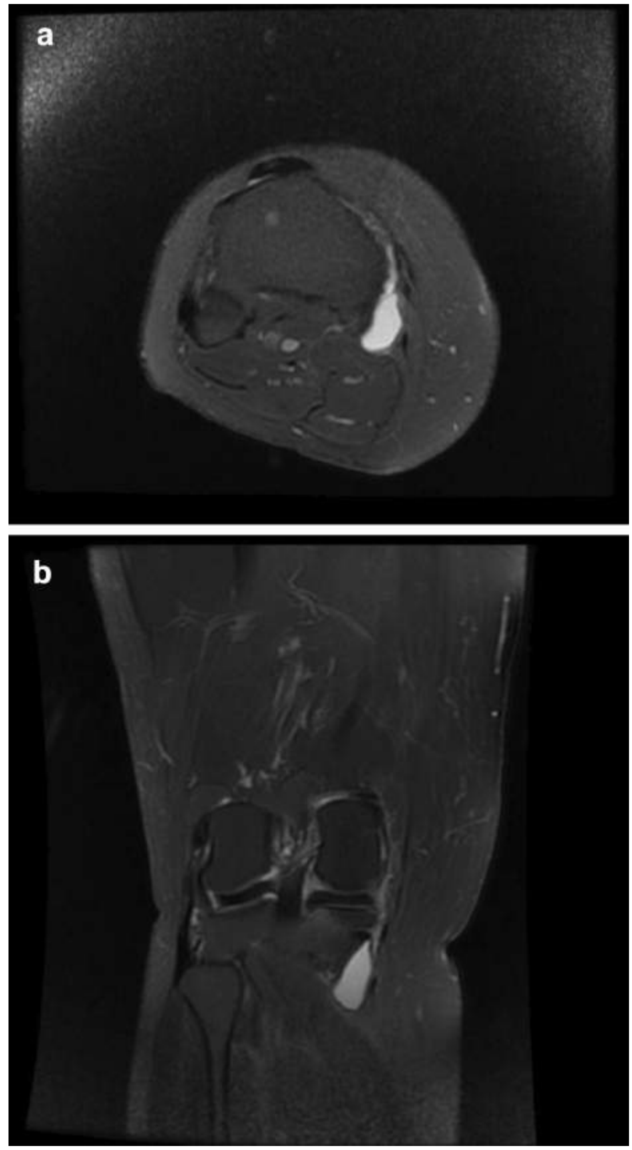

Fig. 2 Axial (**a**) and coronal (**b**) FS PD-weighted MR images of the knee in a 52-year-old female patient with medial joint pain, showings hyperintense fluid collection adjacent to the distal aspect of the pes anserinus

distance between tibia surface and the cartilage surface at the medial tibia plateau in the tibiofemoral joint space.

The medial meniscal lesion evaluation was made from coronal and sagittal MRI, with lesions in the menisci on MRI divided into four grades [14]. The chondromalacia patella was evaluated from an axial MRI.

The study was approved by Ethics Committee of our hospital. The patients were informed about the nature of the study, and written consent was obtained.

Statistical Analysis

The calculations of the estimated sample size were based on a previous study by Alverez et al. [2]. When the difference in the incidence of valgus knee deformation between those with and without the PATBS groups was 27.6%, the minimum sample size was calculated as n: 84 with a power of: 0.80 and α: 0.05. This calculation was performed using G*Power software. IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. The conformity of the parameters with normal distribution data was calculated using a Shapiro Wilks test;

a Student's *t* test was used for the comparison of descriptive statistical data (mean, standard deviation, and frequency) and quantitative data with normal distribution between two groups, and a Mann–Whitney *U* test was used for the comparison of data with non-normal distribution. A Chi-square test, Yates' continuity correction, and Fisher's exact and the Ficher Freeman Halton tests were used for the assessment of qualitative data. Diagnostic screening tests were conducted to calculate sensitivity and specificity. $p < 0.05$ was set as the significance level.

Results

Of the 198 patients who presented to our outpatient unit with knee pain, 27 were excluded from the study due to fibromyalgia, 4 due to inflammatory rheumatoid disease and 11 due to previous knee operations. Subsequently, 156 patients were included in the study, of which 121 were female (77.6%) and 35 were male (22.4%). The ages of the cases were in the 18–75 years age range, with a mean age of 53.73 ± 12.12 years.

Of the total, 27 patients were between 18 and 40 years of age (mean 34.26 ± 5.52 years), and 129 patients were over 40 years of age (mean 57.81 ± 8.66 years).

Furthermore, 64 (41%) of the patients were clinically diagnosed with PATBS (seven patients aged 18–40 years, 57 patients aged 40 years older) and in 92 (59%) of them this clinical diagnosis could not be established (20 patients were 18–40 years, 72 patients were over 40 years of age). PATBS was unilateral in 32 (50%) patients and bilateral in the other 32 (50%).

Clinical diagnoses of PATBS was found significantly higher in females than in males ($p < 0.05$). There was no significant difference between the two groups in terms of age, BMI, DM, trauma, pain at night and age group (Table 1). None of the patients were engaged in active sports. The duration of knee pain was significantly longer in patients with PATBS ($p < 0.05$). There was no difference in the *Q* angles recorded in the two groups ($p > 0.05$). Among the PATBS patients, grade II OA based on Kellgren–Lawrence

Table 1 General and clinical characteristics of patients with and without a clinical diagnosis of PATBS

	Patients with PATBS, (*n* = 64)	Patients without PATBS, (*n* = 92)	*p*
Sex (*n*) (%)			0.001**
Female	61 (95.3%)	60 (65.2%)	
Male	3 (4.7%)	32 (34.8%)	
Age (year) (mean ± SD)	54.91 ± 10.57	52.91 ± 13.08	0.296
Age groups			0.124
40 years and younger (*n*) (%)	7 (10.9%)	20 (21.7%)	
Over 40 years of age (*n*) (%)	57 (89.1%)	72 (78.3%)	
BMI (kg/m^2)	30.62 ± 4.49	29.80 ± 5.14	0.304
History of DM (*n*) (%)	15 (23.5%)	19 (20.7%)	0.679
Duration of pain (months) (mean ± SD) (median)	46.71 ± 57.45 (36)	34.29 ± 58.42 (12)	0.001**
Pain at night (*n*) (%)	47 (73.4%)	54 (58.7%)	0.084
History of trauma (*n*) (%)	10 (15.6%)	13 (14.1%)	0.977
Extremity (*n*) (%)			0.442
Right	28 (43.8%)	46 (50%)	
Left	36 (56.3%)	46 (50%)	
Q angle	15.95 ± 4.21	14.66 ± 4.52	0.074
Kellgren–Lawrence grading (*n*) (%)			0.026*
No osteoarthritis	1 (1.6%)	8 (8.7%)	
Grade I	14 (21.9%)	35 (38%)	
Grade II	27 (42.2%)	27 (29.3%)	
Grade III	19 (29.7%)	16 (17.4%)	
Grade IV	3 (4.7%)	6 (6.5%)	
Medial joint space (mm) (Mean ± SD)	3.10 ± 1.10	3.46 ± 0.88	0.023*

DM diabetes mellitus, *mm* millimeter, *PATBS* Pes anserine tendinitis bursitis syndrome

*$p < 0.05$

**$p < 0.001$

staging was significantly more common than the other grades ($p < 0.05$) (Table 1). However, when we compared the patients with and without PATBS in both age groups in terms of Kellgren–Lawrence grading, no significant difference was identified. Furthermore, the medial joint space was significantly narrower in patients with clinically diagnosed PATBS ($p < 0.05$). When examined in the different age groups, the medial joint space was found to be statistically significantly narrower in patients with a clinical diagnosis of PATBS when compared to those without PATBS in patients over 40 years of age (Table 2).

In an analysis of the MRIs, no statistically significant difference was noted in cartilage thickness, cartilage erosion, medial meniscus lesion, medial collateral ligament (MCL) sprain or rupture with and without a clinical diagnosis of PATBS of the two age groups ($p > 0.05$) (Table 3 and Table 4), and no statistically significant difference between the two groups in terms of anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), lateral meniscus and lateral collateral ligament (LCL) lesions, chondromalacia patella, synovial hypertrophy, suprapatellar effusion, Baker cyst, infrapatellar and prepatellar bursitis, semimembranous bursa effusion, popliteal tendon tenosynovitis, meniscus and parameniscus cysts ($p > 0.05$) (Tables 3 and 4).

Of the 64 patients clinically diagnosed with PATBS, 49 had a PATBS finding on MRI and 15 patients had no PATBS finding on MRI. Of the 92 patients who were not clinically diagnosed with PATBS, 70 had PATBS findings on MRI, and 22 patients had no PATBS finding on MRI. The distribution of cases based on MRI PATBS findings is presented in Table 5. The sensitivity, specificity, positive predictive value and negative predictive value of clinically established PATBS diagnoses were 41.2%, 59.5%, 76.6% and 23.9%, respectively, with an accuracy rate of 45.5% (Table 6).

Discussion

The sensitivity and specificity of the clinical diagnoses of PATBS relative to the MRI findings were found to be low in the present study. In patients with PATBS, the medial joint space was statistically significantly narrower, and duration of knee pain was statistically significantly longer.

PATBS is a condition that is characterized by pain at the medial of the knee while descending or ascending stairs, and is usually a clinically established diagnosis [1]. PATBS is reported to be more common among overweight females and patients with DM [15–17]. In the present study, its incidence was significantly higher in females, while there was no difference between the patients with and without PATBS in terms of BMI and DM.

The sartorius, gracilis, and semitendinous muscles, as flexors of the knee, form the pes anserine tendon, and have the additional function of protecting the knee against rotator and valgus stress by having an impact on the internal rotation of tibia [6, 8]. In a study investigating risk factors

Table 2 Comparison of Q angles, Kellgren-Lawrence grading and medial joint spacing of patients with and without a clinical diagnosis of PATBS according to age groups

	Patients with PATBS	Patients without PATBS	*p*
Q angle (mean ± SD) (median)			
40 years and younger	17.71 ± 4.35 (18)	14.9 ± 3.49 (14)	0.144
Over 40 years of age	15.74 ± 4.19 (15)	14.6 ± 4.79 (14)	0.120
Kellgren–Lawrence grading (*n*) (%)			0.100
40 years and younger			
No osteoarthritis	1 (1.4.3%)	7 (35%)	
Grade I	2 (28.6%)	10 (50%)	
Grade II	4 (57.1%)	2 (10%)	
Grade III	0 (0%)	1 (5%)	
Grade IV	0 (0%)	0 (0%)	
Over 40 years of age			0.225
No osteoarthritis	0 (0%)	1 (1.4%)	
Grade I	12 (21.1%)	25 (34.7%)	
Grade II	23 (40.4%)	25 (34.7%)	
Grade III	19 (33.3%)	15 (20.8%)	
Grade IV	3 (5.3%)	6 (8.3%)	
Medial joint space (mm) (mean ± SD)			
40 years and younger	3.74 ± 1.47	3.70 ± 0.78	0.524
Over 40 years old of age	3.02 ± 1.04	3.4 ± 0.90	0.032*

PATBS Pes anserine tendinitis bursitis syndrome

*$p < 0.05$

Table 3 Comparison of MRI findings of patients aged 18–40 years with and without a clinical diagnosis of PATBS

	Patients with PATBS, ($n=7$)	Patients without PATBS, ($n=20$)	p
Cartilage thickness (mm) (mean ± SD) (median)	1.54 ± 1.04 (1.4)	1.45 ± 0.53 (1.5)	0.802
	n (%)	*n* (%)	
Erosion (*n*)			0.307
No	6 (85.7%)	18 (90%)	
Focal erosion	0 (0%)	2 (10%)	
Erosion	1 (14.3%)	0 (0%)	
Medial meniscus lesion (*n*)			1.000
No	1 (14.3%)	2 (10%)	
Grade 1	1 (14.3%)	1 (5%)	
Grade 2	4 (57.1%)	13 (65%)	
Grade 3	1 (14.3%)	4 (20%)	
MCL sprain	1 (14.2%)	3 (15%)	1.000
LCL sprain	0 (%0)	1 (5%)	1.000
ACL sprain	0 (0%)	4 (20%)	0.545
Partial ACL tear	1 (14.3%)	1 (5%)	0.459
ACL full layer tear	0 (0%)	1 (5%)	1.000
Baker cyst	2 (28.6%)	5 (25%)	1.000
Suprapatellar effusion	1 (14.3%)	1 (5%)	0.459
Synovial hypertrophy	1 (14.3%)	0 (0%)	0.259
Chondromalacia patella	1 (14.3%)	4 (20%)	1.000
Prepatellar bursitis	0 (0%)	1 (5%)	1.000
Meniscal or parameniscal cysts	0 (0%)	2 (5%)	1.000

ACL anterior cruciate ligament, *LCL* lateral collateral ligament, *MCL* medial collateral ligament, *mm* milimeter *PCL* posterior cruciate ligament, *PATBS* Pes anserine tendinitis bursitis syndrome

*$p<0.05$

for PATBS, it was determined that valgus deformities of the knee and collateral ligament instability, along with valgus deformities of the knee, were significantly more common in patients with PATBS [2]. The Q angle is used to measure the alignment and biomechanics of the lower extremities [12, 18, 19]. Our review of literature failed to identify any study to date assessing the Q angle in PATBS cases. In the present study, we measured the Q angle, but could find no statistically significant difference between the two groups.

PATBS is often associated with knee OA. In patients with symptomatic knee OA, PATBS of 17.5–58.3% have been reported in various studies [1, 8, 20, 21]. We found mostly grade II OA (42.2%) in patients with PATBS and grade I OA (38%) in non-PATBS patients, but no significant difference in the Kellgren-Lawrence grading of patients with and without PATBS in either age group. Different from previous studies, we measured the medial joint space and cartilage thickness, and found the medial joint space to be statistically significantly narrower in those aged over 40 years with a diagnosis of PATBS. This led us to assume that in patients with PATBS and without MRI findings, a diagnosis of PATBS may be confused with medial knee OA.

Medial meniscus lesions and medial collateral ligament lesions may also lead to medial knee pain [22], but we were unable to identify any significant difference between the patients with and without PATBS in terms of medial meniscus and medial collateral ligament lesions. In a study by Resorlu et al. in which a retrospective evaluation of knee MRI findings was made of 100 patients over 65 years of age, a positive correlation was identified between medial meniscus tear and knee medial bursitis [23]. Different from the present study, however, a bursitis diagnosis was established in the study from MRI findings, while a PATBS diagnosis was made clinically in the present study. We were unable to identify any difference between the two groups in our study related to other pathologies found on a knee MRI in either age group. In daily practice, PATBS diagnoses are often established clinically, although it is known that USG and MRI may also be useful diagnostic tools. Previous diagnostic studies have shown the pathology to be radiologically confirmed only in some cases with clinical PABTS symptoms and from physical exam findings [15, 24, 25]. In contrast, in a study in which 102 asymptomatic knees were evaluated, effusion of the pes anserine bursa was observed on knee MRIs in 5% of the cases [26]. In our evaluation

Table 4 Comparison of MRI findings of patients aged over 40 years with and without a clinical diagnosis of PATBS

	Patients with PATBS ($n=57$)	Patients without PATBS ($n=72$)	p
Cartilage thickness (mm) (mean ± SD) (median)	0.69 ± 0.71 (0.30)	0.90 ± 0.75 (1.05)	0.119
	n (%)	*n* (%)	0.292
Erosion (*n*)			
No	26 (45.6%)	42 (58.3%)	
Focal erosion	12 (21.1%)	14 (19.4%)	
Erosion	19 (33.3%)	16 (26.4%)	
Medial meniscus lesion (*n*)			0.465
No	1 (1.8%)	0 (0%)	
Grade 1	1 (1.8%)	0 (0%)	
Grade 2	24 (42.1%)	27 (37.5%)	
Grade 3	27 (47.4%)	36 (50%)	
Grade 4	4 (7%)	9 (12.5%)	
MCL sprain	18 (31.6%)	27 (35.5%)	0.607
MCL rupture	1 (1.8%)	1 (1.4%)	1.000
Chondromalacia patella	23 (40.1%)	39 (54.2%)	0.119
ACL sprain	6 (10.5%)	15 (20.8%)	0.182
Partial ACL tear	19 (15.8%)	10 (13.9%)	0.958
ACL full layer tear	5 (8.8%)	3 (4.2%)	0.465
PCL sprain	0 (0%)	1 (1.4%)	1.000
Baker cyst	15 (26.3%)	23 (31.9%)	0.616
Suprapatellar effusion	10 (17.5%)	15 (20.8%)	0.806
Lateral meniscus tear	2 (3.5%)	1 (1.4%)	0.583
LCL sprain	0 (%0)	3 (%4.2)	0.254
Popliteus tendon tenosynovitis	2 (3.5%)	1 (1.4%)	0.583
Synovial hypertrophy	3 (5.3%)	5 (6.9%)	1.000
Semimembranosus bursa effusion	2 (3.5%)	1 (1.4%)	0.583
Prepatellar bursitis	2 (3.5%)	3 (4.2%)	1.000
Meniscal or parameniscal cysts	1 (1.6%)	2 (4.3%)	1.000
Infrapatellar bursitis	0 (0%)	1 (1.4%)	1.000

ACL anterior cruciate ligament, *LCL* lateral collateral ligament, *MCL* medial collateral ligament, mm milimeter *PCL* posterior cruciate ligament, *PATBS* pes anserine tendinitis bursitis syndrome

*$p < 0.05$

Table 5 Assessment of clinical diagnosis of PATBS relative to MRI findings

	MRI findings of PATBS		Total
	Present	Absent	
	n (%)	*n* (%)	*n* (%)
Patients with clinical diagnosis of PATBS	49 (31.4%)	15 (9.6%)	64 (41.0%)
Patients not diagnosed with clinical PATBS	70 (44.9%)	22 (14.1%)	92 (59.0%)
Total	119 (76.3%)	37 (23.7%)	156 (100%)

PATBS pes anserine tendinitis bursitis syndrome

Table 6 Sensitivity and specificity values in clinical diagnosis of PATBS

	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Clinically diagnosed PATBS	41.2	59.5	45.5	76.6	23.9

NPV negative predictive value, *PPV* positive predictive value, *PATBS* pes anserine tendinitis bursitis syndrome

of patients with knee pain, 44.9% without clinical PATBS findings were identified with PATBS findings on MRI. We evaluated also PAT in the present study. Both knee OA and PATBS affect the quality of life of patients, although the treatment approaches to these conditions are different [3]. To ensure the correct treatment, the detection of the source of pain is of utmost importance. Our study has shown that not all patients with medial knee pain diagnosed clinically with PATBS may necessarily PATBS, as it may also stem from medial knee OA. Weight loss, cold compress, exercise, and topical and oral NSAIDs are recommended for the treatment of both knee OA and PATBS [7, 27, 28]. In PATBS, if the symptoms persist even after such treatments, and if pain occurs at night, corticosteroid injections may be applied to the pes anserine bursa [7, 25]. For the treatment of knee OA, intraarticular corticosteroid injections or genicular blocks are among the alternatives [27–29]. When injection treatment is planned in a PABTS patient whose diagnosis has been clinically established, confirmation of the diagnosis through a radiologic modality would be appropriate. Since USG is more readily available than MRI, USG-assisted PATBS injections may both confirm the diagnosis and provide guidance for the injection [30]. PABTS may also be asymptomatic, and so it will be better to plan treatment after both the clinical and radiological assessment of the patient rather than being based only on a diagnosis reached via radiologic modalities.

The limitation of our study is the lack of a control group comprising cases without knee pain.

In conclusion, we have found the sensitivity and specificity of clinical PATBS diagnosis relative to MRI findings to be low, and that the medial joint space to be narrower in patients with PATBS aged over 40 years. There were no other differences related to MRI pathologies in either group. These results indicate that PATBS is mostly confused with medial knee OA. To ensure correct treatment, it is better to make both a clinical examination and radiological imaging modalities to establish a diagnosis of PATBS.

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Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical standard statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed consent For this type of study, informed consent is not required.

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ORIGINAL ARTICLE

Reconstruction of the Posterolateral Corner of the Knee Using LaPrade and Modified Larson Technique: A Prospective Study

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Abstract

Background Posterolateral corner (PLC) injuries of the knee are often overlooked for its complex anatomy, and frequent association with cruciate ligament injuries. Overlooked injuries lead to reconstruction failure of cruciate ligaments, chronic knee pain and early arthritic changes. Many reconstruction methods are described, but the best treatment still remains elusive. In this study, we have treated grade-III PLC injuries by the 'anatomic LaPrade' technique and the 'fibula-based Modified Larson' technique, and evaluated their outcomes. Our hypothesis was that both the groups will have similar improvements after surgery.

Methods An open-label prospective comparative study was done with a total of 28 patients from August 2013 to July 2019. Patients were treated alternatively by LaPrade or Modified Larson technique using hamstring autografts. Follow-up visits were done at sixth week and subsequently at 3, 6, 12, 18 and 24 months postoperatively. Outcomes were measured by Dial Test, side-to-side difference in lateral opening on varus stress radiographs, Lysholm score and IKDC subjective score.

Results During analysis, we considered 25 patients only as three patients were lost to follow-up. Both the groups had comparable improvements in rotational stability, lateral opening on varus stress, Lysholm score and IKDC subjective score.

Conclusion Both LaPrade and Modified Larson technique showed good clinical results in restoring varus and rotational stability of knee in grade-III posterolateral corner injury of the knee.

Level of evidence II (prospective, comparative study)

Keywords Posterolateral corner of knee · PLC reconstruction · LaPrade versus modified Larson

Introduction

In recent years with increase in road-traffic accidents and sports injuries, the incidence of knee joint ligament injuries is increasing; and with improving infra-structure and surgical skills, more and more ligament reconstructions are also being done. With increase in number of reconstructive surgeries in relation to sports injuries around the knee, more and more cases of reconstructive failures are being diagnosed. In search of the causes of these failures, the "darker side of knee", i.e., the Posterolateral corner (PLC) of knee came into light as one important cause. [1, 2] Injury to PLC of knee is uncommon accounting for 16% of knee ligament injuries [2] and it is frequently related to high energy trauma. Isolated injuries are even rarer accounting for 2% of injuries [3, 4]. PLC provides both static and dynamic stability to knee. Injuries to these structures are often overlooked for their complex anatomy, and frequent association with cruciate ligament injuries. Overlooked injuries lead to

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reconstruction failure of cruciate ligaments, persistent posterolateral instability with varus thrust gait, chronic knee pain and early arthritic changes [5–7]. Many reconstruction methods are described in the literature, ranging from augmentations and non-anatomic reconstructions like biceps tenodesis, to more anatomic ones like the combined tibia- and fibula-based anatomic reconstruction as described by LaPrade et al. [8–12] and the femur- and fibula-based anatomic reconstruction such as Modified Larson technique; but the best treatment still remains elusive. The LaPrade anatomic technique aims at reconstruction of the three main stabilizers of the PLC of knee, namely the lateral collateral ligament (LCL), popliteus tendon (PT), and popliteofibular ligament (PFL); whereas, only LCL and PFL are reconstructed in the modified Larson technique. In this study, we have treated grade-III PLC injuries by the 'anatomic LaPrade' technique and the 'fibula-based Modified Larson' technique, and evaluated their outcomes. Our hypothesis was that both the groups will have similar improvements after surgery.

Methods

Our study was conducted from August 2013 to July 2019 after approval by the institutional ethical committee. It was an open-label, prospective, non-randomized, comparative study. Inclusion criteria were: symptomatic grade-III PLC injury with or without other ligament injuries of the knee. All the patients were explained about their inclusion in the study and informed consents were taken.

Exclusion criteria were: hyperlaxity symptoms, bilateral knee injuries, elderly patients with low functional demand, associated major fractures around same/opposite knee, ligament avulsion fractures, significant meniscus injury requiring balancing or repair and chronic cases with varus malalignment who required high tibial osteotomy to correct limb alignment before PLC reconstruction.

Only 28 patients fulfilled our inclusion and exclusion criteria. Allocation into 'LaPrade group' or 'Modified Larson group' was done alternatively (i.e., every even number patient underwent PLC reconstruction using Modified Larson's technique). Thus, the groups were allocated 14 patients each.

All the patients were examined clinically using standard tests for knee instability and associated injuries specially Varus–Valgus stress test, anterior and posterior Drawer test, posterolateral Drawer test, dial test, external rotation recurvatum test and their findings were recorded.

The knees were further examined carefully for any signs of bony varus malalignment and varus thrust during stance phase of ambulation. This was further clarified with standing full length anteroposterior radiograph or scanogram.

All the knees were evaluated with standard radiograph (AP and lateral view), Varus–Valgus stress radiograph and MRI (Fig. 1); and findings were recorded accordingly.

In the operation theater, after examination under anesthesia (EUA), the patients were positioned supine with the affected knee and leg hanging from the edge of the table. Under tourniquet control, diagnostic arthroscopy was done to look for any menisco-ligamentous injury; cartilage injury (especially medial compartment) and presence of 'lateral drive through' sign, i.e., greater than 1 cm of lateral joint line opening to a varus stress applied to the joint at the time of arthroscopic evaluation (Fig. 2).

After confirmation of the preoperative planning by EUA and diagnostic arthroscopy, regarding the ligaments to be reconstructed, grafts were harvested as per requirement. We used autografts for our procedures: ipsilateral hamstrings for PLC reconstructions (a single-stranded semitendinosus graft with average length of 20–24 cm for reconstruction of both LCL and PFL in modified Larson group; whereas, a single-stranded semitendinosus graft for LCL and PFL, and double stranded gracillis for PT reconstruction in the LaPrade group); and contralateral hamstrings for reconstruction of associated ACL/PCL injuries. In one patient with combined PLC, PCL and ACL injuries, contralateral hamstrings were used for PCL reconstruction and ipsilateral quadriceps for ACL. One patient with PLC and ACL injury refused graft harvest from opposite limb, where ipsilateral bone patellar tendon bone graft was used for ACL reconstruction.

Our sequence of reconstructions was single-bundle PCL first (if present), followed by PLC and single-bundle ACL simultaneously. A gently curved, L-shaped incision was made on the lateral aspect of the knee starting proximal to the lateral femoral condyle and continuing distally to midpoint between the fibular head and Gerdy's tubercle. After dissection through subcutaneous layers, three fascial incisions described by LaPrade et al. [13] were used for both the groups. The first posterior-most fascial incision was made posterior and parallel to the biceps femoris tendon to expose and mobilize the common peroneal nerve (CPN). This was protected throughout the procedure. Through this incision, the posterior aspect of the proximal fibula and the proximal tibio-fibular joint could be exposed. Then, the fibular tunnel was drilled at the LCL attachment site from anterolateral to posteromedial direction first with a Beath pin followed by a 6- or 7-mm reamer. A looped passing suture was then placed through this tunnel for future use.

A second fascial incision was made in between the biceps femoris tendon and the iliotibial band. Developing this interval would expose the posterior aspect of the lateral tibial plateau for tibial tunnel preparation for attachment of the PFL and PT. Through this interval we could identify the LCL, and trace to its femoral and fibular attachment sites. However, this fascial plane was not compulsory for the

Fig. 1 19 years old male patient with ACL and PLC injury in left knee. **a** MR images confirming the diagnosis (red arrow), **b**, **c** clinical, and **d** radiological images at final follow-up after PLC reconstruction by modified Larson technique

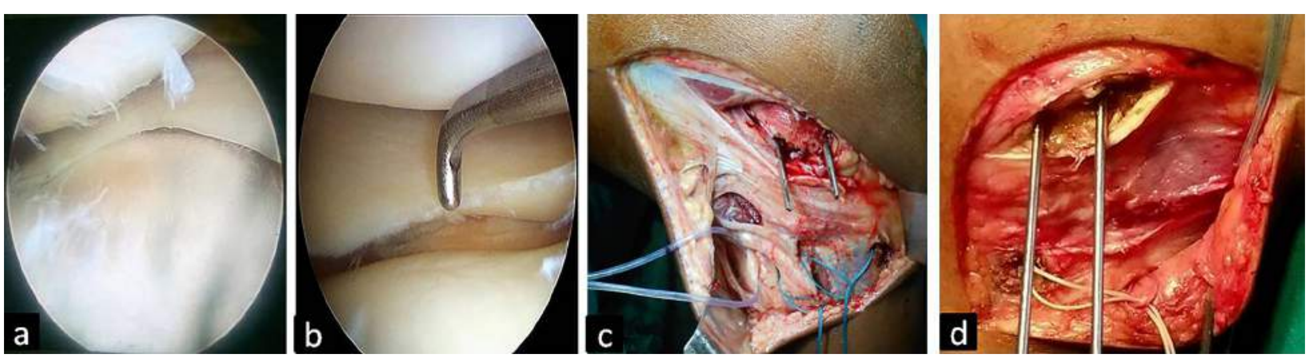

Fig. 2 Intraoperative images showing: **a** cartilage damage at medial compartment of left knee, **b** positive lateral drive through sign on diagnostic arthroscopy, **c** PLC reconstruction by LaPrade anatomical technique in right knee. Note the fibular and tibial tunnels marked by suture loops after dissection and retraction of the common peroneal nerve and guide wires for femoral tunnels of LCL and PT placed about 18 mm apart, **d** PLC reconstruction by modified Larson technique in left knee. Fibular tunnel marked by suture loop in similar way

modified Larson technique. Then, the 8- or 9-mm diameter tibial tunnel was prepared in the LaPrade group, with the help of a PCL femoral tunnel-aiming device, 10 mm distal and parallel to the tibial articular surface, starting at the flat spot just distal and medial to the Gerdy's tubercle, directing posteriorly to the popliteal sulcus of tibia which marks the location of the musculotendinous junction of the popliteus. A looped passing suture was then placed through this tunnel for future use.

The third fascial incision was made through the iliotibial band, in line with its fibers, centered over the lateral femoral epicondyle. The femoral attachments of the LCL (slightly proximal and posterior to the lateral epicondyle) and PT (at anterior aspect of the popliteal groove) were identified; and two eyelet-tipped guide pins were introduced approximately 18 mm apart from lateral to medial, directing superiorly (to avoid convergence with femoral tunnel of PCL) and anteriorly (to avoid convergence with femoral tunnel of ACL). A 7- or 8-mm femoral tunnel was then reamed over each guide pin to a depth of 25–30 mm. The medial cortices were drilled with a 4.5 mm cortical breaker over the guide pins to facilitate graft passage.

The grafts were then passed through the ligaments' normal anatomical courses, which were developed bluntly with the use of a curved hemostat. The sequences of graft fixations were slightly different in the two groups, as described by the original authors of the two techniques [13, 14]. In the LaPrade group, grafts were fixed to the femoral tunnels of LCL and PT first, followed by the fibular tunnel with the knee at 30° of flexion and neutral rotation and a slight valgus stress, and lastly the tibial tunnels at 60° of flexion and 5° of internal rotation of the knee. In the modified Larson group, grafts were first fixed to the fibular tunnels, followed by the femoral tunnels in 30° of flexion of the knee with slight internal rotation and valgus stress. We used metal or bio-absorbable interference screws (7 mm for fibular tunnel, 8 mm for femoral tunnels and 9 mm for tibial tunnel) for securing the grafts during PLC reconstruction (Depuy or Smith–Nephew).

Conscious efforts were made to keep the tourniquet time within 2 h. If more time was required, a 15-min interval was allowed before re-inflating the tourniquet.

Postoperative Management

A common rehabilitation protocol was followed for both the groups of patients. Postoperatively, they were given a long knee brace for temporary immobilization. No prophylaxis was given for deep vein thrombosis.

Isometric quadriceps exercise was started from second day onwards along with knee range of motion (ROM) exercises as tolerated. They were discharged from the hospital on third day; and were supervised once a week on outpatient basis to achieve a minimum target ROM of 90° by 3 weeks, thereafter, as much and as early as possible.

All patients were put on gradual non-weight bearing mobilization using two axillary crutches for the initial 6 weeks. Then partial weight bearing was allowed, progressing gradually to full weight bearing by 3 months postoperatively.

Quadriceps and hamstring strengthening exercises were introduced sixth week onwards. Jogging on plain surface was started after 4 months.

All day-to-day activities were allowed by 6 months. Return to sports activities were permitted only after 9 months when normal strength, stability, and knee range of motion comparable to the contralateral side have been achieved.

Follow-Up

All patients were reviewed at the outpatient department at 6th week, and 3, 6, 12, 18 and 24 months after surgery and yearly thereafter. At each visit, patients were assessed clinically, along with functional assessment with IKDC Subjective score and Lysholm knee score.

Statistical Analysis

During analysis of data, only those patients were considered who completed at least 2-year follow-up after surgery. Statistical analysis was conducted by an independent statistician who was not associated with the surgical team. All the data were tested for 'Normality' by Kolmogorov–Smirnov test. The normally distributed data like age and operating time were compared for significance using unpaired *t* test. The differences between the preoperative and final follow-up variables of side-to-side difference on varus stress radiograph, Lysholm score and IKDC subjective score were calculated; and were compared between the two groups for statistical significance using 'independent samples Mann–Whitney *U* test' (SPSS software version 16). P value < 0.05 was considered significant.

Results

During analysis of results, only 25 patients were considered as three patients (two from 'LaPrade group' and one from 'Modified Larson group') were lost to follow-up. Average age of patient at the time of surgery was 27.44 years (18–38 years). Most of the patients were male, only two being female patients. The average follow-up period was 31.3 months (24–47 months).

Seven patients had isolated PLC injury, while eight had associated ACL and nine had associated PCL injury. One patient had both ACL and PCL injury additionally (Table 1). Twelve of them were treated by LaPrade technique, while the rest by Modified Larson technique.

The preoperative mean side-to-side difference in lateral opening seen on varus stress radiograph in the LaPrade

Table 1 Comparison of ligaments injured

	LaPrade group	Modified Larson group	Total
Isolated PLC	3	4	7 (28%)
PLC + PCL	3	6	9 (36%)
PLC + ACL	5	3	8 (32%)
PLC + PCL + ACL	1	0	1 (4%)
Total	12	13	25

Table 2 Details of preoperative and final follow-up data

		LaPrade group	Modified Larson group
Side-to-side difference seen on varus stress radiograph (in mm)	Preoperative	5.50 ± 0.90	5.31 ± 0.85
	at final follow-up	0.50 ± 0.52	0.77 ± 0.60
Lysholm scores	Preoperative	36.67 ± 6.24	37.85 ± 5.05
	at final follow-up	89.00 ± 7.76	91.54 ± 3.93
IKDC subjective scores	Preoperative	36.29 ± 5.89	39.69 ± 4.19
	At final follow-up	79.70 ± 8.65	83.31 ± 6.05

Table 3 Comparison of difference in preoperative and final follow-up data between groups

	LaPrade group	Modified Larson group	*P* value
Side-to-side difference seen on varus stress radiograph (in mm)	5.00 ± 0.74	4.54 ± 0.52	0.15
Lysholm scores	52.33 ± 6.67	53.69 ± 3.09	0.81
IKDC subjective scores	43.41 ± 8.07	43.62 ± 3.03	0.41

Table 4 Comparison of other relevant data between groups

	LaPrade group	Modified Larson group	*P* value	Statistical method
Age (years)	27.33 ± 7.14	27.54 ± 5.85	0.94	Unpaired *t* test
Operating time (min)	127.08 ± 26.58	115.77 ± 12.39	0.18	Unpaired *t* test
Hospital stay (days)	5.08 ± 0.52	4.77 ± 0.44	0.25	Mann–Whitney *U* test

group was 5.50 ± 0.90 mm (4–7 mm); and at final follow-up, it was 0.50 ± 0.52 mm (0–1 mm). In the Modified Larson group, before surgery it was 5.31 ± 0.85 mm (4–7 mm); and at last follow-up it was 0.77 ± 0.60 mm (0–2 mm) (Table 2). Postoperatively, all the patients had negative dial test, which were positive before surgery.

The average Lysholm score in the LaPrade group improved from 36.67 ± 6.24 preoperatively to 89.00 ± 7.76 at last follow-up, and in the Modified Larson group from 37.85 ± 5.05 preoperatively to 91.54 ± 3.93 at last follow-up. Preoperatively, the IKDC subjective knee score was 36.29 ± 5.89 in the LaPrade group and 39.69 ± 4.19 in the Modified Larson group, and became 79.70 ± 8.65 and 83.31 ± 6.05, respectively, at final follow-up (Table 2).

The differences between the preoperative and final follow-up data are mentioned in Table 3. No statistically significant difference was noted between the two groups in operating time and hospital stay (Table 4).

We had three complications in two patients in our study: stiffness with surgical site infection in one patient, and stiffness with heterotopic ossification in the other. Both of them belonged to the LaPrade group.

Discussion

Many studies have reported several techniques of PLC reconstruction with their biomechanical as well as clinical results, but the best surgical technique remains a matter of debate [8–12]. Many surgical techniques including repairs, augmentations and non-anatomic reconstructions like biceps tenodesis were done previously, but abandoned nowadays in view of poor functional outcome and high failure rates [1, 12, 15, 16].

The LCL and the PFL are the two main static stabilizers, whereas the popliteus muscle–tendon unit functions as the dynamic stabilizer of the PLC of knee. In 2004, LaPrade et al. [13, 17, 18] described an anatomic technique of the PLC reconstruction using the native attachments of the LCL, PT and PFL. This was one of the earliest descriptions of a surgical option to recreate the anatomy of the three main

Fig. 3 An 18-year-old male patient with isolated PLC injury treated by LaPrade anatomical reconstruction developing complications. **a**, **b** clinical images of knee stiffness (note the swelling over lateral femoral condyle), **c** heterotopic ossification (red arrow)

static stabilizers of the PLC. On the contrary, the fibula-based modified Larson technique was relatively simple, but still useful with reconstruction of the LCL and PFL only [2, 11, 14, 19], although the PFL attachment was slightly modified from its anatomical attachment. The modified Larson technique had mainly two modifications over the original Larson technique: (1) two separate femoral tunnels for attachments of the LCL and PFL rather than a single isometric femoral tunnel, and (2) slightly oblique orientation of the fibular tunnel from anterolateral to posteromedial direction rather than anterior to posterior. These two modifications allow recreation of more anatomic attachments of the native LCL and PFL, along with reduction in the incidence of fibular head fracture [14, 19]. In biomechanical studies, no statistically significant difference has been found in the ability of the above two reconstruction methods, the LaPrade and the modified Larson, to control posterolateral instability [20]. Therefore, the aim of this study was to compare these two currently used techniques for PLC reconstruction on clinical grounds to evaluate how closely each technique restores varus and rotational stability to normalcy, and to compare their clinical outcomes.

The collective incidence of isolated PLC injury of the knee in our series was 28% (Table 1) which was relatively high as per literature, but comparable with the original series by LaPrade et al. [17]. Associated injury to the cruciate ligaments or menisci adversely affects the functional outcome of PLC reconstruction of the knee [6, 16]. Chronic PLC injury of the knee leads to abnormal varus thrust gait, significant changes in articular contact pressure at the medial compartment and progressive secondary osteoarthritis. That is why medial compartment cartilage damage on diagnostic arthroscopy is seen as indirect evidence of PLC injury of the knee. Another confirmatory evidence of significant PLC injury of the knee is the presence of 'lateral drive through' sign, i.e., greater than 1 cm of lateral joint line opening to a varus stress applied to the joint at the time of diagnostic arthroscopy [9]. LaPrade et al. [21] have shown in 2008, in a cadaveric study, an approximately 2.7 mm increase in lateral opening on varus stress radiographs after isolated LCL injury compared to 4.0 mm increase in cases with grade-III PLC injury. These findings are comparable with those of our study, where varus and rotational instability were well controlled in both the groups (Tables 2, 3) with no statistically significant difference, with only one patient from 'Modified Larson group' showing a side-to-side difference in lateral opening of 2 mm compared to the intact knee at final follow-up [22, 23].

We found significant improvements in Lysholm scores and IKDC subjective scores after surgery, i.e., from preoperative to final follow-up scores in both the groups. But when we compared the differences [23] in the preoperative and final follow-up scores between the two groups, they were not statistically significant (Table 3). Therefore, we did not find any clinical evidence to support the use of the more complex reconstruction method similar to some other biomechanical studies [20].

We faced three complications in two patients: first one was an immediate complication in the form of infection at surgical site that was managed promptly with debridement and antibiotics; the second one was a late complication in the form of heterotopic ossification (Fig. 3), which was treated by non-operative means initially, but required excision after maturation. It is believed that reaming for the graft tunnels particularly femoral tunnels for PLC reconstruction contributes to the process [24]. Therefore, thorough lavage with normal saline should be given to remove the bone debris to prevent this complication. Both these patients developed the third complication, i.e., residual stiffness, for which they refused any further treatment. CPN injury is an important complication that needs to be avoided when one is performing lateral knee procedures. In our series, we exposed the nerve early in the procedure where the nerve passes the fibular neck. This enables nerve protection by visual confirmation during the drilling procedures that most likely could cause nerve injury. In our series no nerve injuries were observed.

Similar to any other complex surgical procedures, PLC reconstruction is also associated with significant learning curve [25]. Our experience is no different in this regard as the operating time decreased gradually in the later part of our series compared to the initial few cases.

In recent years newer arthroscopic procedures for anatomical reconstruction of the PLC have been described that could have the potential to replace open procedures in posterolateral corner surgery of the knee in the future [25–27]. However, their usefulness with regard to biomechanical stability tests and clinical implications are yet to be established.

Only a few clinical studies have presented outcomes after PLC reconstruction comparing the two techniques that have stood the test of time so far. The authors believe that this study with a minimum of 2-year follow-up should be able to reflect some light on this 'darker side of the knee'. However, our study is limited by the fact that the study population is small. Randomized controlled trials with large sample size and longer follow-ups are required to further illuminate and standardize the treatment protocols of PLC injuries in future [28].

To conclude, in institutions like ours where we are forced to rely on autografts only, owing to the lack of tissue banks and financial constraints, Modified Larson technique seems to be a better treatment option for PLC reconstruction, specially with multiple ligament injuries, in view of less graft requirement and comparable clinical outcome.

Declarations

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval The study was approved by the institutional ethical committee.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by the any of the author

Informed Consent For this type of study informed consent is not required.

Consent for Participation and Publication All the patients were explained about their inclusion in the study and that the data will be used for publication in future; and informed written consents were taken.

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ORIGINAL ARTICLE

Is It Possible to Treat Developmental Dysplasia of the Hip with Anterior Open Reduction and Pemberton Osteotomy Under 18 Months of Age?

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Abstract

Purpose of the Study The purpose of the present study is to determine the outcome success of anterior open reduction with Pemberton osteotomy in patients under 18 months of age with developmental dysplasia of the hip.

Methods We retrospectively reviewed the clinical and radiological results of 27 developmental hip dysplasia patients under 18 months of age (26 girls, 1 boy) who underwent anterior open reduction with Pemberton osteotomy. Bilateral surgery was performed in 18 patients and unilateral in nine patients. At the final follow-up, the clinical results were evaluated according to the McKay's clinical evaluation criteria, the radiological results according to the Severin's radiological evaluation criteria, and the presence of avascular necrosis according to the Kalamchi-MacEwen's classification criteria.

Results We treated 36 hips of 27 patients who were younger than 18 months of age (range 10–18 months) at the time of surgery and followed up a minimum of 5 years (mean 6.5 years). At the final follow-up, 34 (94.4%) were assessed clinically as excellent, one hip (2.7%) as good and one hip (2.7%) as fair according to the McKay's clinical classification. Radiological classification revealed that, 97.2% of the hips were Severin Type-1 and 2.8% Severin Type-3. Avascular necrosis was observed in 5 of 36 hips (13.8%). Two hips were assessed as Type-2, two hips Type-3 and one hip Type-4 according to the Kalamchi-MacEwen's classification.

Conclusion We conclude that Pemberton osteotomy with anterior open reduction is useful technique for developmental hip dysplasia treatment of patients under the age of 18 months with good clinical and radiological results as well as with low complication rates.

Keywords Developmental dysplasia of the hip · Anterior open reduction · Pemberton osteotomy

Introduction

Developmental dysplasia of the hip (DDH) is one of the most challenging diseases for orthopedic surgeons. Its incidence, ranging from 0.06 to 76.1 per 1000 live births, varies significantly between and within racial groups and geographic locations [1]. Similarly, treatment methods to be applied differ depending on the age of the patient [2]. The fundamental goal of the treatment is to obtain a concentric reduction as early as possible. Early detection of the disease may facilitate treatment and can prevent operative procedures [3]. In early periods (before 6 months of age), the use of pavlik harness is the treatment of choice among other modalities [4], while surgical intervention usually begins to predominate after 6 months [2].

Concentric reduction of the femoral head in the acetabulum stimulates innominate bone remodeling in terms of congruency and containment over the time especially in the first year after reduction [5]. Medial or anterior approaches can be used for treatment after 6 months. Medial approach offers adequate access to the adductor musculature, transverse ligament, and anteroinferior capsule and typically leads to less blood loss but anterior approaches allows access to capsular plication and pelvic osteotomy site, and can be performed in patients of any age [6]. But normal hip joint development can-not be achieved by applying only these procedures.

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The application of open reduction alone has higher risks for further surgeries compared to combined procedures especially after 12 months of age [7]. Depending on the age of the patient, failure rates can reach up to 70%. Pollet et al. in a long-term follow-up study, reported that medial open reduction had poor results, especially after 8.6 months, and that additional surgical interventions were needed in 22% of the cases due to residual dysplasia [8]. Isiklar et al. in their study evaluating the effectiveness of medial open reduction according to age of the patients, stated that the need for additional bone procedures was higher in patients older than 12 months [9]. Szepesi et al. observed similar results in anterior open reduction [10]. In studies comparing anterior open reduction with medial open reduction, no difference was found in terms of treatment efficacy and complications [11, 12]. High reoperation rates of isolated open reduction, especially in patients older than 12 months, necessitate new strategies to be developed.

In general, bony procedures are advised in neglected cases of DDH or for revision surgeries [2]. Pemberton suggested his periacetabular osteotomy method for patients older than 12 months or at least after walking age [13]. He treated 115 hips with this method and reported only five reoperations due to redislocations. The author did not suggest his method to patients under 12 months of age because of the risk of collapse during the osteotomy of the soft and thin pelvic bone. In older children, several successful results were published [13–15]. This method can be used bilaterally in the same session without alteration of the inner pelvis and leg length. However, some surgeons consider that the method decreases acetabular volume [16].

Considering the failure rates of open reductions and the necessity of secondary surgery [6–10], we are of the opinion that anterior open reduction and Pemberton osteotomy is an alternative treatment option in children less than 18 months of age. As suggested by Pemberton [13], we performed anterior open reduction and Pemberton osteotomy in 12–18 months of age walking children, whose treatment with any conservative approach failed or who were neglected. The purpose of the present study is to determine the success of anterior open reduction and Pemberton osteotomy in patients 12–18 months of age.

Materials and Methods

Between 2008 and 2014, 52 hips of 40 DDH cases were treated with anterior open reduction and Pemberton osteotomy in our clinic. The treated children between the ages of 12–18 months were either neglected patients or their treatment failed with any conservative method. We reviewed these patients using our medical records retrospectively with a minimum 5-year follow-up. The follow-up was lost in 13 patients (32.5%) before 5-years. Finally, 36 hips of 27 patients (1 male, 26 female) with satisfactory data were included in the study. Twenty-five of these 27 patients had not received any treatment before our procedure. In other healthcare institutions, closed reduction and spica casting treatment had applied for 3 months in one patient (bilateral) and a pavlik harness was used for 2 months in one patient (unilateral), but sufficient acetabular coverage was not achieved. There were 8 right and 10 left unilateral hips, while nine patients had bilateral pathologies. Preoperative standard AP pelvis radiographies were examined and we classified hips according to the Tönnis classification and measured acetabular index angles [17].

Surgical Technique

All surgeries were performed by a single senior surgeon (ET). After routine preparation, adductor tenotomy was done via mini incision in all cases. Anterior iliofemoral incision was used. In all hips, iliopsoas tenotomy was performed at the level of the trochanter minor attachment. Capsulotomy was done in 'T' shape fashion. Pulvinar tissue removal, ligamentum teres excision, and transverse acetabular ligament release were routinely performed in all patients. The stability of hips was checked during joint motion after reduction and temporary capsuloraphy. The hip was considered unstable if it dislocated, under 40° abduction in 90° flexion and neutral rotation. Pemberton osteotomy was decided for the hips with insufficient stability. Osteotomy was performed without extension to sciatic notch as recommended by Pemberton [13] and by 8 mm double thin curved osteotomes. Before completing procedures, the osteotomy site was not separated and two osteotomes were used simultaneously to allow less force to be exerted on the osteotomy sites (Fig. 1). A triangular graft taken from the iliac wing was placed in the osteotomy line. There was no need for excessive force or femoral osteotomy for reduction in any of the hips. After reduction of the hip joint, a capsulorrhaphy was performed meticulously. Femoral osteotomy was not required for excessive anteversion or to prevent forced hip reduction. Following the closure of tissues and skin, a spica cast was applied with hip in 50°–60° flexion 45° abduction and neutral rotation, knee in 60° flexion, ankle in neutral position. The cast was removed at the 6th week and a bilateral long leg cast with bar was applied for abduction for six weeks. At the 3rd month, an abduction brace was used for additional 6 weeks. All patients were followed every six weeks in the first 6 months after the surgery and annually after 6 months.

At the final follow-up, clinical examinations such as hip range of motion, lower extremity lengths, trendelenburg sign were recorded and radiographs of the pelvis in the neutral and frog leg positions were taken. Acetabular index (AI), Sharp's angle (SA) and Wiberg's center-edge (CE) angles,

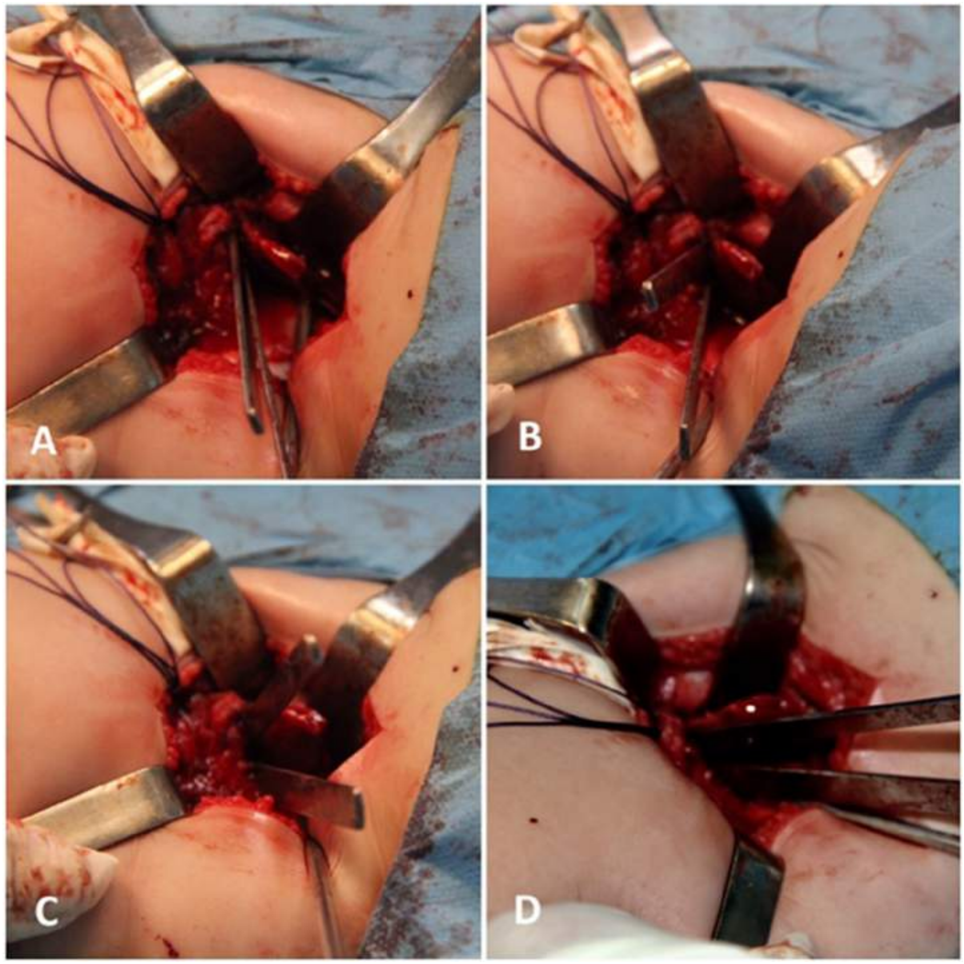

Fig. 1 **A**–**D** Pemberton osteotomy with two osteotomes technique. Osteotomy should be performed using double thin curved osteotomes. After completing the osteotomy the acetabular roof should be gently lowered with two osteotomes and to prevent acetabular roof collapse

acetabular depth-width ratios and femoral head extrusion index were measured. The McKay's clinical evaluation criteria were used in the clinical assessment for functional result [18]. The Severin's radiological criteria were used for radiological assessment of the hips [19]. In cases with avascular necrosis (AVN), the Kalamchi-MacEwen's classification was used [20] and type 1 hips were not included as they have minimal effect on the outcome. The type 1 hips show subtle changes such as delay in the appearance of the ossific nucleus and temporary, irregular ossification that has minimal clinical significance [21]. It eventuates with almost excellent clinical and radiological results [22–24].

Statistical Analysis

All analyses were performed using IBM SPSS Statistics Version 20.0 statistical software package. The categorical variables were expressed as numbers and percentages, whereas the continuous variables were summarized as mean and standard deviation. The normality distribution of continuous variables was confirmed with the Shapiro–Wilk test. For the comparison of preoperative and postoperative measurements, the paired samples t test was used. The statistical significance level used for all tests was 0.05.

Results

The patients were operated at the mean age of 14.5 ± 1.4 months (range 12–18). The mean follow-up time was 78.08 ± 14.3 months (range 60–119) and the patients' mean age were 94 ± 14 months (range 74–133) at the final follow-up. All preoperative and postoperative results are given in the Table 1. Preoperatively, 19 hips (52.7%) were Grade 2, 13 hips (36.1%) were Grade 3 and 4 hips (11.1%) were Grade 4 according to the Tönnis classification. While the mean acetabular index was 36.4° ± 4.6° (range 29–44) preoperatively it was 13.2° ± 3.1° (range 9–25) at the final follow-up. Preoperative and final follow-up acetabular index difference was statically significant ($p < 0.001$). The mean bleeding volume was 82 ± 21(range 65–150) ml for unilateral cases and 139 ± 12 (range 130–160) ml for bilateral cases during the surgery. The mean operation time that included casting was 77 ± 13 (range 65–100) minutes

Table 1 Results

Preoperative	
Tönnis classifications	
Grade 1	None
Grade 2	19 (52.7%)
Grade 3	13 (36.1%)
Grade 4	4 (11.1%)
Mean preoperative Acetabular Index Angel[a]	36.4° ± 4.6 (29°–44°)
Last follow-up	
Mean Last Follow-up Acetabular Index Angel[a]	13.2° ± 3.1 (9°–25°)
Severin's Radiological Classification of Hips	
Type 1	35 (97.2%)
Type 2	None
Type 3	1 (2.8%)
Type 4	None
McKay Clinical Classification of Patients	
Excellent	34 (94.4%)
Good	1 (2.7%)
Fair	1 (2.7%)
Poor	None
Avascular Necrosis	8 / 36 (22.2%)
Kalamachi-MacEwen Classification of Avascular Necrosis	
Type 1	3 (37.5%)
Type 2	2 (25%)
Type 3	2 (25%)
Type 4	1 (12.5%)
Total	8 (100%)

[a]Mean preoperative and final follow-up difference $p < 0.001$

for unilateral cases and 138 ± 12 (range 120–165) minutes for bilateral cases. Blood transfusion was required in two bilateral cases.

At the final follow-up, it was found that; 35 hips were Type 1 (97.2%), only one hip was Type 3 (2.8%) according to Severin's radiological classification. The patient who had Type 3 hip was re-operated at 27 months of age (Salter osteotomy and anterior open reduction), and CE angle was 13° at final follow up.

For ages of the patients included our study, there is no consensus in normal value of AI, Wiberg CE angle, SA, femoral head extrusion index and acetabular depth-width ratio. Therefore, in one sided patients, the hips operated were compared with contralateral normal hips. There were no statistically significant differences between operated and non-operated normal hips (Table 2).

At the final follow-up, 26 of 27 patients (96.2%) had satisfactory results. According to the McKay classification; 34 hips (94.4%) had excellent, one hip had good (2.7%) and one hip had fair (2.7%) results. Neither postoperative graft migration nor perioperative complications such as wound healing problems were encountered in our study.

Table 2 Comparison of single side affected hips between non-operated sides

	Operated hips	Non-operated Hips	*p* value
Acetabular Index (°)	12.3 ± 1.8	13.5 ± 2.8	0.71
Sharp angle (°)	46.5° ± 2.7	47.9° ± 4.5	0.16
CE angle (°)	31° ± 5.2	29.4° ± 4.9	0.07
FHEI	14.3 ± 7.4	15.2 ± 5.7	0.72
ADWR	30.2 ± 3.8	30.6 ± 5.7	0.72

CE centre-edge angle, *FHEI* Femoral Head Extrusion Index, *ADWR* acetabular depth-width ratio

At the final follow-up, eight hips showed evidence of AVN, for an overall incidence of 22.2%. According to the Kalamchi-MacEwen classification three hips were classified as Type-1 (37.5%), two hips were classified as Type-2 (25%), two hips were classified as Type-3 (25%) and one hips as Type-4 (12.5%). Considering the development of clinically significant AVN (type 2 or higher), the rate of AVN was 13.8% 5 of 36 hips). The relationship between the Kalamchi-MacEwen classification and the Tönnis classification is given in the Table 3.

Table 3 The relationship between Kalamchi-MacEwen and Tönnis classification

	Tönnis grade of hips				*p* value
	Grade 1 *n*:0	Grade 2 *n*:19	Grade 3 *n*:13	Grade 4 *n*:4	
Kalamchi-MacEwen Classification of Hips with Avascular Necrosis					
Normal	–	16	9	3	$p > 0.05$
Type 1	–	1	1	1	
Type 2	–	1	1	–	
Type 3	–	1	1	–	
Type 4	–	–	1	–	
Total	0	3 (15.7%)	4 (30.7%)	1 (25%)	

Discussion

Treatment strategies in DDH show specific differences by age [2]. The primary goal of the treatment is to obtain a concentric reduction as early as possible. Early detection of the disease after birth allows it to be treated with conservative methods such as a pavlik harness [25] After the 6th month, closed or open reduction of the hip joint and casting are commonly preferred treatment methods [2]. Closed reduction may not be preferred due to high failure rates, ranging from 30 to 48% [26, 27]. The advantage of open reduction over the closed procedure is the possibility of direct intervention to structures, such as iliopsoas and inverted labrum that prevent reduction [2, 10–12, 21–23]. Medial open reduction is more preferred due to the advantages of requiring smaller incisions, causing less blood loss, as well as providing adequate access to the adductor musculature, transverse ligament and anteroinferior capsule. The advantage of anterior open reduction is that it allows joint capsule plication and pelvic interventions when necessary [6].

Although concentric reduction of the hip joint stimulates the remodeling of the acetabulum and femoral head, it does not guarantee completely normal development of the joint in all cases [5, 8–12, 28]. In isolated anterior open reduction series, the failure rate ranges from 26 to 36% [29, 30]. Szeepesi et al. examined patients with isolated anterior open reduction by age group and observed no failures in patients treated between 6 and 9 months, while 26% failure in those treated between 15 and 18 months [10]. Increased failure rates with age in medial open reduction have also been reported in many studies. Bache et al. stated that the rate of reoperation was 24% in patients who underwent medial open reduction at the age of less than 12 months, but the failure rate increased to 70% in patients older than 12 months [22]. Pollet also stated that the average failure rate was 22% in patients who underwent medial open reduction, and the median age for poor results was 8.6 months [8]. In the studies comparing isolated medial and anterior open reductions, it was stated that there was no difference in terms of success and complications [11, 12].

Omeroglu et al. stated that acetabular development after reduction continues until the age of 7–8 years old, at most in the first year, and additional procedures should be applied if the satisfactory development is not observed at the end of the first year [5]. Bony procedures are often required in neglected patients and unsuccessful reductions in later ages [2]. The Salter's innominate osteotomy is one of the most commonly used pelvic procedures. However, it is generally recommended for patients older than 18 months because of the underdeveloped pelvic stability [2, 31, 32]. Another common pelvic procedure is Pemberton periacetabular osteotomy. Pemberton stated that the method he described can be used in patients older than 12 months or who started to walk [13]. There are many publications in the literature showing that Pemberton osteotomy is successful in later ages [13–15]. Carsi et al. compared the patients who underwent periacetabular osteotomy with open reduction and those who underwent isolated open reduction [28]. Additional surgery was required in 15 of 27 hips treated with isolated open reduction, while only 1 of 28 hips with osteotomy. Baki et al. stated that there was no need for reoperation in patients who underwent combined procedures of medial open reduction and Pemberton osteotomy [33]. We argue that the combination of Pemberton osteotomy with open reduction will increase the success, especially in 12–18 month-old patients, where isolated reduction methods often fail. In our study, excellent radiological (Severin Type-1) results were obtained in 35 of 36 hips treated with the Pemberton osteotomy combined with anterior open reduction. Only one hip required additional intervention due to residual dysplasia and dislocation. The right hip of the patient with bilateral involvement, who was 12 months old in the first operation, did not improve adequately after 15 months. Although there were no clinical and radiological differences between the procedures at the beginning, it was observed that the right hip did not heal over the time, hence a Salter innominate osteotomy was performed later. This patient had not received any treatment before the first procedure. Although an additional surgery was performed, the hip was classified as Severin Type-3 at the final follow-up. But the patient healed without limping with full range of motion and functional results were good according to the McKay criteria.

In the original article, Pemberton did not advice his technique in patients under the age of 12 months old [13]. He pointed out the soft and thin ilium as a downsizing risk for the indication of his procedure. Acetabular roof collapse would likely to occur in the cases with such osteotomy in patients who are younger than 12 months of age and not yet walking. Although we agreed on this detail in theory, we recommend a meticulously cared osteotomy with thin curved osteotomy technique (Fig. 1). Before the osteotomy was completed, we did not separate the osteotomy site to prevent additional fractures and failure. The use of two osteotomes technique provides a lower force to be exerted on osteotomy sites. We did not observe collapse or early triradiate cartilage closure in any of our patients even under 12 months of age.

AVN, which is one of the most devastating complications of DDH treatment, compromises acetabular remodeling and congruency, and negatively impacts the long-term hip function and radiographic results [34]. Unfortunately, the occurrence of AVN remains difficult to anticipate, and therefore its etiology is elusive and likely multifactorial. Injury to the medial femoral circumflex artery is a frequently proposed factor [24, 35]. Many authors reported different rates of avascular necrosis in dysplastic hip treatment surgery. It may be as low as 0% to as high as 67% [33, 35]. The studies attempting to reveal the cause of AVN have yet to identify. Pollet et al. pointed out that the older patients (> 24 months) and > 60° hip abduction angle in spica cast were at higher risk [8]. Kothari stated that a single anterior open reduction had lower risk than anterior open reduction with femoral osteotomy and pelvic osteotomy, but there was no difference between anterior reduction alone and anterior reduction with pelvic or femoral osteotomy [36]. Wu et al. indicated that age, gender, preoperative Tönnis grade and acetabular index didn't alter AVN but femoral head inferior displacement raises AVN rate [34]. The medial and anterior open reduction methods are alternative to each other in patients under 18 months of age. Hoellwarth et al. found no difference AVN rate between these two methods under 15 months of age [6]. Classically, anterior approach has been utilized more frequently than the medial approach due to access to the hip joint capsule, opportunity to perform an osteotomy, and possibly due to a general perception of increased risk of AVN with the medial approach. Böhm and Brzuske indicated that AVN was a complication of the open reduction rather than of the osteotomy [37]. In our study, AVN developed in eight hips (22.2%). According to the Kalamchi-MacEwen classification three hips were classified as Type-1 (37.5%) (Fig. 2), two hips as Type-2 (25%), two hips as Type-3 (25%) and one hip as Type-4 (12.5%) (Fig. 3). According to the Kalamchi-MacEwen Type-1 AVN, characterized by subtle changes such as delay in appearance of the ossific nucleus heals with almost excellent clinical and radiological results (Fig. 2) [22–24]. If the hips with Type-1 are excluded, we suppose that the incidence of clinically significant AVN (Type 2 to 4) of 13.8% is acceptable and correlates with the literature data [21, 24]. To achieve low AVN rates, a special

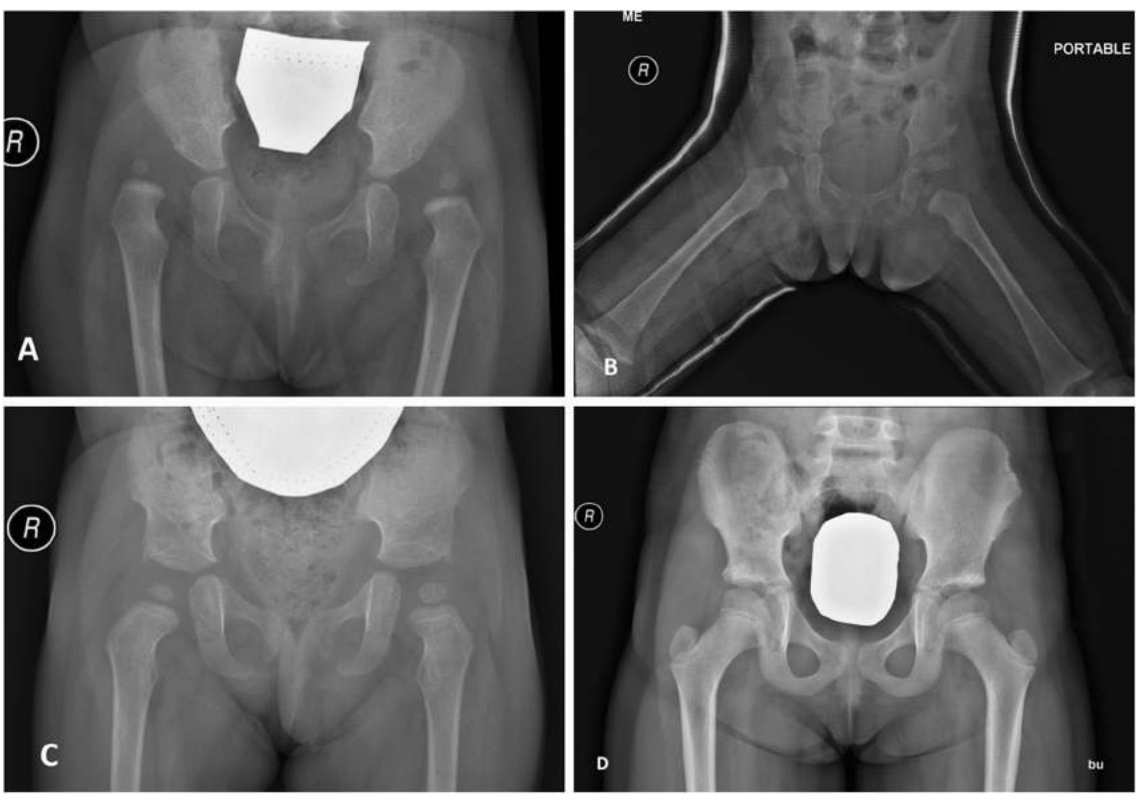

Fig. 2 **A** An anteroposterior radiograph of a thirteen month-old girl with bilateral hip dysplasia and dislocation. **B** Early postoperative radiograph in cast. **C** One year after open reduction, a Type-1 avascular necrosis of the femoral head on the right side. **D** At 89 months after the surgery, the right hip is developing normally and there is no difference compared with the left side

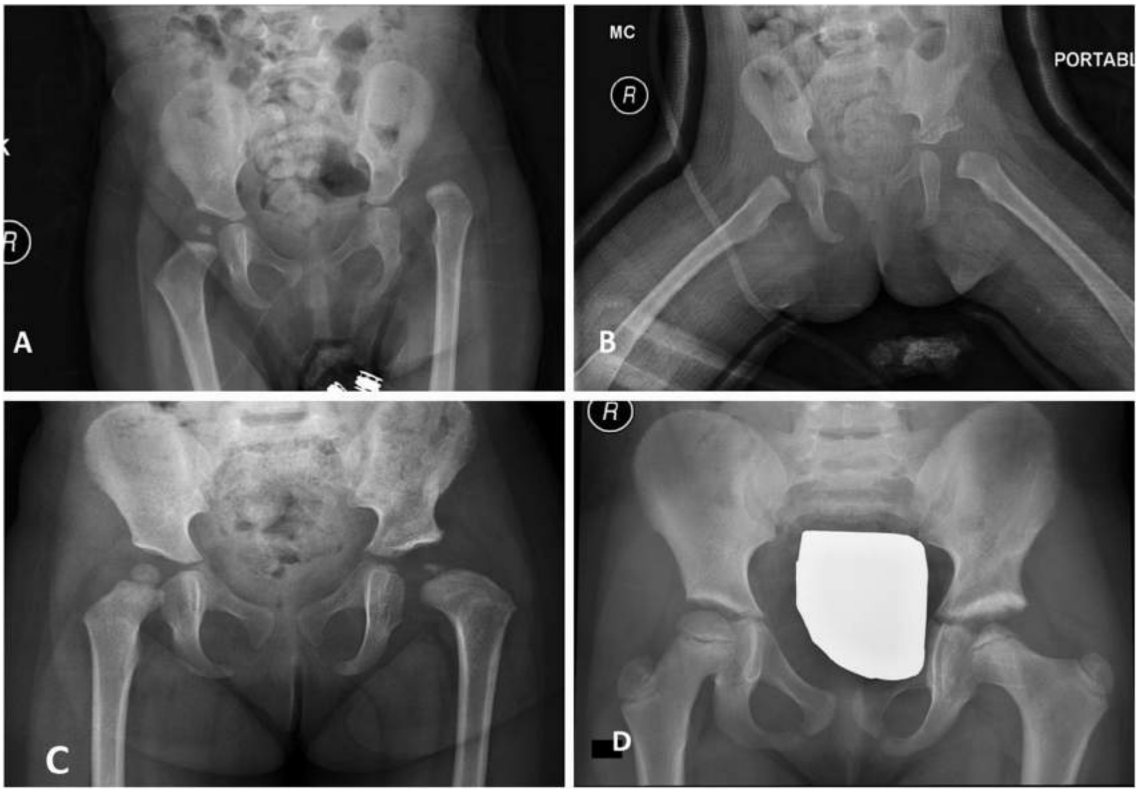

Fig. 3 **A** An anteroposterior radiograph of a fifteen month-old girl with dysplasia and dislocation on the left hip. **B** Early postoperative radiograph in cast. **C** Growth disturbances on the left side at 1 year after the surgery. **D** Significant growth disturbance of the medial plate and development of coxa vara at 74 months after the surgery

care must be taken not to injure the medial circumflex artery, to ensure concentric reduction of the hip joint and the hip must be placed under 60° abduction in cast.

There are some weaknesses in our study. First of all, our study is a retrospective study. We collected the information from our medical records. The results of 16 hips of 13 patients' were not included in the study because of insufficient follow-up. If these were included in the study the outcomes would be changed. The other weak point in our study is the fact that the results obtained were not compared with one of the other treatment methods appropriate in these ages. Prospective, randomized studies should be planned to compare at least one of the other treatment methods.

Pemberton osteotomy with anterior open reduction is a feasible alternative technique for developmental hip dysplasia treatment. We conclude that this procedure is appropriate for patients whose treatment with any conservative approach failed and who were neglected until 12 to 18 months of age and has good clinical and radiological results additional to low complication rates.

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Author Contributions RC and CO designed the study, made and classified radiological measurements analyze the data and performed the statistical analysis.

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Declarations

Conflict of Interest Remzi Caylak and Cagri Ors declare no conflict of interest.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Ethical Approval This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Clinical research ethics committee of Cukurova University approved this study.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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ORIGINAL ARTICLE

A Prospective Study Evaluating Factors Affecting Functional Outcome in Patients with Floating Elbow Injury

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Abstract

Background Floating elbow injuries are complex injuries. Due to frequent association with severe soft tissue injuries and polytrauma, they have unpredictable functional outcome. This prospective study is aimed to evaluate the factors affecting functional outcome.

Methods Thirty patients with floating elbow injuries were treated at a level 1 trauma center from July 2018 to June 2019 with minimum follow-up of 9 months. The outcome was assessed by disability for arm shoulder and hand score (DASH) and mayo elbow performance score (MEPS).

Results The overall incidence was 16.09 per 1000, mostly caused by road traffic accidents and all cases were managed surgically. Age, gender, education, occupation, arm dominance, and mechanism of injury did not significantly affect the outcomes. Open fractures and patients requiring staged procedure were associated with poorer outcomes ($p < 0.05$); however, delay in surgery for more than 24 h significantly increased the rate of complications. There was no statistical difference in the proportion of patients who had nerve injury pre operatively and post operatively on the final outcome.

Conclusion Floating elbow injuries are relatively rare but nowadays the numbers are on the rise. Timely intervention with a multimodal approach and well-supervised rehabilitation can assure better final outcome.

Keywords Floating elbow · Prognostic factor · Functional outcome · Polytrauma

Introduction

Classical floating elbow injury is a constellation of injuries involving the supracondylar or humeral diaphyseal area and proximal part of radius and ulna, initially described by Stanitski and Micheli [1]. Floating elbow variants include concomitant articular fracture or the fracture dislocation of elbow or both, fracture distal humerus with shaft radius or ulna or both that can act as functionally floating elbow [2, 3]. It has been reported to occur in combination—severe soft tissue damage and neurovascular injury [4]. As per the available literature on floating elbow, it has an unpredictable clinical outcome after treatment [5]; however, surgical treatment has been widely accepted as the best possible treatment for these injuries [2].

The outcomes of floating elbow injuries can be affected by severity, pattern of injury, type of fixation done for humerus and forearm, open fracture, multiple injuries and risk factors like age, arm dominance, level of activity [6]. Therefore, there is increased demand for such data on floating elbow injuries that can help to plan and monitor the effectiveness of measures to manage floating elbow injuries. Taking into consideration all these facts, this study was designed to evaluate the incidence, risk factors, fracture patterns, associated injuries, average delay in the treatment and the functional outcomes of floating elbow injuries

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and its variants in a tertiary care center in an Indian setup, to make suggestions regarding adequate management and rehabilitation.

Materials and Methods

This was a prospective cohort study, which included patients presenting with a floating elbow injury and its variants to Level 1 Trauma Centre [AS1] from 1 July 2018 to 30 June 2019. The patients aged more than 18 years with classical floating elbow injuries and variants such as fracture distal humerus with shaft ulna or shaft radius or both, shaft humerus fracture with proximal ulna or a radial head fracture or both, intra-articular fracture of elbow and fracture associated dislocation of the elbow were included in the study group, including both closed fractures and open grade 1, 2, 3a and 3b injuries. The patients having vascular injury (Gustilo Anderson grade 3c), preoperative brachial plexus injury, history of neuromuscular disorder, and patients not consenting to be the part of the study were excluded from this study group.

Patients who presented with floating elbow injuries were divided into three groups with subgroups in the same manner that Fraser and Hunter classified ipsilateral fractures of the femur and tibia in 1978 [7] (Fig. 1). For open fractures, Gustilo–Anderson classification [8] was used. CT scan was done in cases of intra-articular fracture patterns for better delineation of fracture pattern. Patients were shifted to the operative room as soon as possible after adequate resuscitation and stabilization.

The data were collected with special emphasis on patient demographics, functional outcomes, and complications. The management of floating elbow injuries was performed in a single stage or multiple stages, which were determined by the type of fracture, associated soft tissue injuries, and general condition of the patient. Patients requiring soft tissue coverage were managed meticulously by the plastic surgery team. Intravenous antibiotics were given as per institutional antibiotic protocol. The pain was managed with oral and intravenous analgesics. The range of motion exercises were started from day one of the postoperative period wherever feasible. Oral Indomethacin 25 mg thrice a day for 4–6 weeks was given to the patients with a high risk of heterotopic ossification like patients with fractures involving elbow joint, intra-articular fracture and patients with severe soft tissue injuries [9].

On each visit, clinical evaluation and radiology of the involved part were checked to see the progress of bony union, implant status, and any complication. The functional outcome was assessed by Mayo Elbow Performance Score (MEPS) [10] and Disability of the Arm Shoulder and

Fig. 1 Groups on basis of anatomic site of fracture in floating elbow

GROUP		TYPE OF FRACTURE
GROUP1	Group1a	Involves Shaft of humerus and shaft of radius and ulna
	Group1b	Involves shaft of humerus and either radius or ulna
GROUP2	Group2a	Shaft of humerus and intraarticular both bone forearm (Radius and ulna)
	Group2b	Intraarticular humerus and shaft of both radius and ulna or either
GROUP3		Intraarticular humerus and both radius and ulna or either

Hand (DASH) score system [11]. The DASH scores were categorized into four categories of excellent (0–5), good (6–15), satisfactory (15–35), and poor (more than 35). The MEPS was used to categorize in four categories of excellent (90–100), good (75–89), fair (60–74), and poor, less than 60 [12].

Statistical Analysis

Data acquired were entered into Microsoft excel sheet and analyzed with Statistical Package for Social sciences (SPSS Inc., Chicago, IL, Version 7.0 for windows 10).

We used descriptive analysis for describing the numerical data in terms of mean and standard deviation or median and interquartile range. We also transformed the numerical data of DASH scores and MEPS. Two categorical variables for comparing the functional outcome of DASH scores and MEPs were used at 6 weeks, 3 months, 6 months, and at final follow-up and used the Chi-square test of association. In the cells where the value was less than 5, we used Fisher's exact test. For comparing the numerical outcome such as pronation, supination, and range of motion, a paired *t* test was used. Similarly, we used the Chi-square test of analysis for finding prognostic factors for various outcomes such as DASH scores, MEPS, union, and nerve injury. For all the tests of association, a *p* value less than 0.05 was considered to be statistically significant.

Results

The incidence was found to be 16.09 cases per 1000 orthopedic injuries over 1 year. Most injuries were caused by road accidents (76.7%) followed by machine-related injuries (13.3%) and rest were caused by fall from a significant height (10%). The majority of injuries belonged to Group 1 (53.3%) followed by Group 2 (33.4%) while there were four cases for Group 3. We observed that most patients were right dominant (53.3%) (Table 1). The majority of cases (86.7%) were managed as single-stage procedures while four cases (13.33%) were managed with two-stage procedures. Age, gender, education, and occupation of patients with floating elbow injuries and its variants were not statistically significant to influence the functional outcome of patients (p value > 0.05). We observed that the groups of injuries, side, dominancy, and mechanism of injury were not statistically significant in predicting the functional outcome of floating elbow injuries; however, intra-articular fracture tends to influence the outcome but was not statistically significant. We found that the open and closed nature of injury and type of surgery (ORIF, External fixator, Intramedullary nail) done to manage the injuries were statistically significant in predicting the final outcome, favoring the ORIF group ($p = 0.013$, $p = 0.005$). Delay in surgery for more than 24 h was statistically significant to predict complications like stiff elbow, decreased ROM of the elbow, wrist, and shoulder, and nerve injury ($p = 0.024$). The results were analyzed with the minimum follow-up of 9 months (range 9–24 months and mean 16 months) (Tables 2, 3).

Table 1 Socio-demographic and injury characteristics of 30 patients

Parameter	Attributes	$N = 30$
Gender	Male	23
	Female	7
Education	Graduate and post-graduate	13
	Twelfth	8
	Till tenth	8
	Illiterate	1
Occupation	Driver, daily wager, factory worker	11
	Students and housewife	10
	Government and private job	7
	Shop keeper	2
Mechanism of injury	Fall from height	3
	Machine injury	4
	Road side accident	23
Group of injury	1a	13
	1b	3
	2a	2
	2b	8
	3	2
Side	Right	16
	Left	14
Dominant hand	Yes	16
	No	14
Type of surgery	Single stage	26
	Multiple stage	4
Open or closed	Open	13
	Closed	17
Duration of surgery	Less than 24 h	17
	More than 24 h	13
Nerve injury preoperative	Yes	9
	No	21

DASH and MEPS Score

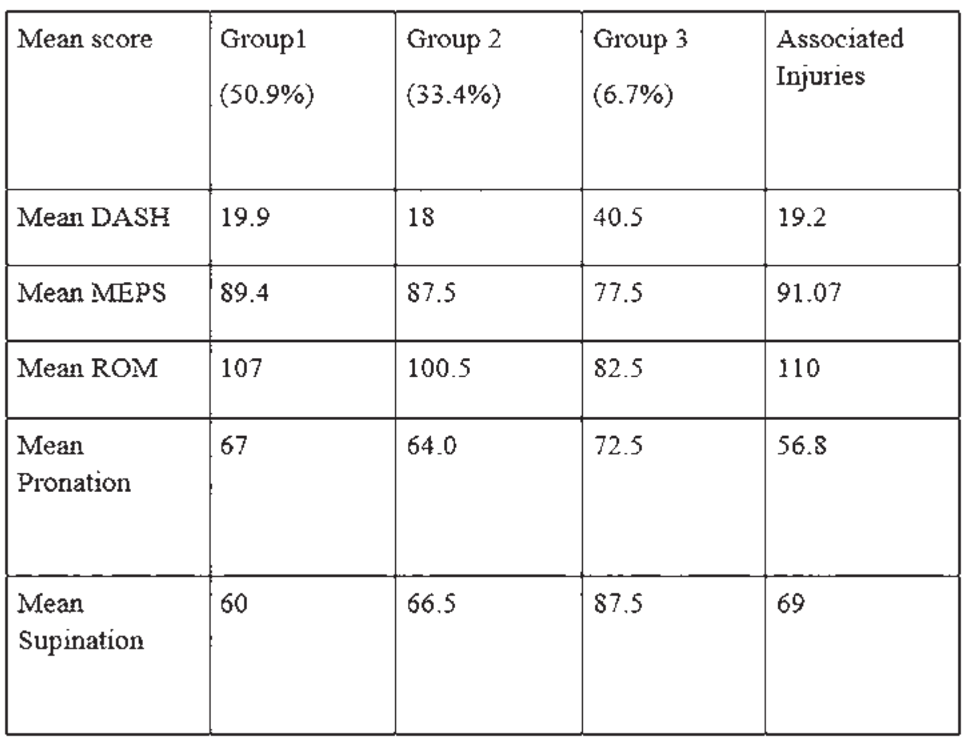
The mean DASH score in group 1, 2, and 3 were 19.9, 18, and 40.15, respectively (Fig. 2). There was statistically significant improvement ($p = 0.000$) in DASH scores at three follow-up periods of 6 weeks, 3 months, and 6 months. The mean MEPS score in groups 1, 2, and 3 were 89.4, 87.5, and 77.5, respectively (Fig. 2). There was a statistically significant improvement in MEPS at 6 months when compared to 3 months ($p = 0.003$).

Table 2 Prognostic factors for DASH and MEPS at 6 months

Parameters	Attributes	DASH at 6 months				p value	MEPS at 6 months				MEPS
		Excellent	Good	Poor	Satisfactory	DASH	Excellent	Fair	Good	Poor	p value
Category of age	18–25 (Gp1-7, Gp2-3, Gp3-1, op-4, closed-7)	1	5	4	2	0.569	6	2	3	1	0.696
	25–35 (Gp1-7, Gp2-5, Gp3-1, op-9, closed-4)	2	3	2	5		7	1	4	0	
	More than 35 (Gp1-4, Gp2-2, op-1, closed-5)	1	3	0	2		5	0	1	0	
Sex	Male (Gp1-16, Gp2-5, Gp3-2, op-13, closed-10)	4	7	5	7	0.491	14	3	6	0	0.238
	Female (Gp1-2, Gp2-5, op-1, closed-6)	0	4	1	2		4	0	2	1	
Category education	12th or above (Gp1-10, Gp2-9, Gp3-2, op-9, closed-12)	4	7	3	7	0.3436	14	1	5	1	0.379
	Less than 12th	0	4	3	2		4	2	3	0	
Occupation	Government and private job	2	0	1	4	0.198	4	0	3	0	0.407
	Driver, daily wager, factory worker	1	4	4	2		6	3	2	0	
	Shop keeper	0	2	0	0		2	0	0	0	
	Students and housewife	1	5	1	3		6	0	3	1	
Categories of injury group	1 (op-6, closed-12)	2	7	4	5	0.782	11	2	5	0	0.445
	2 (op-5, closed-5)	2	4	1	3		7	0	2	1	
	3 (open-2)	0	0	1	1		0	1	1	0	
Articular involvement	Extraarticular (Group 1)	2	7	4	5	0.9376	11	2	5	0	0.662
	Intraarticular(Group 2 and 3)	2	4	2	4		7	1	3	1	
Open or closed	Open (Gp1-6, Gp2-5, Gp3-2)	2	1	5	5	**0.021**	**4**	**3**	**6**	**0**	0.011
	Closed (Gp1-12, Gp2-5)	2	10	1	4		14	0	2	1	
Side	Right (Gp1-12, Gp2-2, Gp3-2, op-7, closed-9)	1	7	5	3	0.146	9	3	3	1	0.223
	Left (Gp1-6, Gp2-8, op-7, closed-7)	3	4	1	6		9	0	5	0	
Dominant hand	Yes	1	7	5	3	0.146	9	3	3	1	0.223
	No	3	4	1	6		9	0	5	0	
Duration between surgery and hospital arrival	Less than 24 h (Gp1-8, Gp2-7, Gp3-2, op-12, closed-4)	3	4	5	5	0.247	8	3	5	1	0.234
	More than 24 h (Gp1-10, Gp2-3, op-1, closed-13)	1	7	1	4		10	0	3	0	
Type of surgery	Single stage (Gp1-16, Gp2-9, Gp3-1, op-9, closed-17)	4	11	3	8	**0.025**	**18**	**2**	**5**	**1**	0.046
	Multiple stage (Gp1-2, Gp2-1, Gp3-1, op-4)	0	0	3	1		0	1	3	0	

Table 3 Associated injury in patients with floating elbow

Associated injury	Yes—14 patients (46.7%) No—16 patients (53.3%)	Number of patients
Associated injury details	Blunt trauma abdomen	1
	Blunt trauma chest	1
	Facio-maxillary injury	1
	Left acetabulum n hip dislocation	1
	Left segmental femur, right proximal tibia fracture closed without neurovascular defect	1
	Left shaft of femur fracture, open knee joint, left Lisfranc injury	1
	Left patella open Grade 2 without neurovascular defect	1
	Open knee joint, left both bone leg fracture open grade 1, right medial malleolus fracture closed without neurovascular defect	1
	Right acetabulum fracture closed without neurovascular defect and blunt trauma abdomen, managed conservative	1
	Right both bone leg fracture	1
	Right mangled lower extremity	1
	Right scapula with acromioclavicular joint disruption	1
	Right sacroiliac joint disruption, bilateral superior pubic rami, inferior pubic rami, left iliac blade fracture, with sacrum fracture closed without neurovascular defect	1
	Right shaft of femur fracture closed without neurovascular defect	1



Mean score	Group1 (50.9%)	Group 2 (33.4%)	Group 3 (6.7%)	Associated Injuries
Mean DASH	19.9	18	40.5	19.2
Mean MEPS	89.4	87.5	77.5	91.07
Mean ROM	107	100.5	82.5	110
Mean Pronation	67	64.0	72.5	56.8
Mean Supination	60	66.5	87.5	69

Fig. 2 Mean outcome scores and mean range of motion in different groups

Pronation, Supination, and Range of Motion

The mean pronation and supination in groups 1, 2, and 3 were 67, 64, 72.5 and 60, 66.5, 87.5, respectively (Fig. 2), while the mean range of motion was 107, 100.5 and 82.5, respectively. It was observed that the mean degree of pronation, supination, and range of motion improved from 6 weeks to 3 months and from 3 to 6 months. The improvement was found significant statistically using a paired *t* test ($p = 0.000$) (Fig. 3).

Fig. 3 Preoperative and postoperative radiographs of a patient with group 3 type of floating elbow injury

The overall mean values of DASH score, MEPS, Range of motion, pronation and supination were 20.6, 88, 103°, 66° and 64°, respectively.

Nerve Injury

Nine patients (30%) with preoperative nerve injury cases were surgically explored and found to have neuropraxia, hence were managed conservatively. There was no statistical difference in the proportion of patients who had nerve injury before or after surgery on the final outcome of these injuries ($p > 0.05$).

Union

Union was achieved in 86.7% of cases and four cases had nonunion; two cases (6.7%) had nonunion of radius and ulna, two cases (6.6%) had nonunion of humerus and radius. It was found that nonunion was observed in cases with open grade 3b and those treated with external fixator with delay in surgery for more than 24 h. All patients underwent re-surgery and union was achieved.

Complications

Nine patients (30%) presented with different complications such as stiff wrist, decreased elbow range of motion, stiff shoulder, postoperative nerve injury, and decreased ROM in the wrist. Associated multisystem injuries and delay in surgery were the factors which were statistically significant for causing these complications ($p = 0.024$).

Discussion

Floating elbow is a rare injury caused by high-energy trauma, it occurs in combination with severe soft tissue damage leading to open fracture and neurovascular injury [4]. Floating elbow injury significantly affects the normal routine activities of the person suffering from it. We searched for the possible prognostic factors that can influence the outcome of floating elbow injuries; we included age, sex, education, occupation, side, dominance, type of surgery, open and closed fracture, type of injury pattern, duration between surgery and hospital arrival, nerve injury, mechanism of injury, as our expected prognostic factors (Table 2).

In previously published data on incidence [13–17], the floating elbow injuries are very rare injuries and thus had a very low incidence. Stoik et al. [18] found an incidence of 1 patient per year in their study; however, in our study, incidence was 16.09 cases per 1000 orthopedic injuries over 1 year. Higher incidence can be attributed to the fact that our institute is a tertiary care center that provides services to a large population and receives a large number of referrals of patients with polytrauma. Jockel et al. [6] observed that the patient's age, arm, dominance, type of surgery, multiple surgeries, and fracture patterns were not statistically significant to influence the functional outcome, and our study also shows similar findings.

Pierce and Hodorski [13], Solomon et al. [4] and Yokoyama et al. [3] reported poorer outcomes in patients with associated radial nerve palsy and Ditsios et al. [19] found that nerve injury leads to poor clinical outcome. However, Jimenez-Diaz et al. [20] concluded that nerve injury is not statistically significant in predicting the functional outcome of these injuries. We observed that nerve injury was not statistically significant to influence the long-term functional outcome, which could be attributed to the fact that all the nerve injuries were neuropraxia in our study, and recovered subsequently without any intervention.

Bisinella and Bellon [21] in their case series found that associated injuries with floating elbow injuries need planning regarding timing of surgical intervention and this can reduce the risk of complication and result in good functional outcome, which was also applicable in our study. We found that patients with multisystem injuries (46.7%) such as polytrauma, blunt trauma abdomen, blunt trauma chest, and head injury (Table 3) suffered complications such as stiffness of elbow, shoulder, and wrist, death due to head injury and amputation due to severe soft tissue injury.

Jimenez-Diaz et al. [20] and Yokoyama et al. [3] found correlation between associated multisystem injuries, open nature and anatomic site and the complications such as infection or nonunion with functional outcome; however, they did not evaluate the relationship of factors such as timing of surgery, open/closed fracture and associated nerve injury on functional outcome. We found that open nature and type of technique used for fixation had a significant influence on final functional outcomes ($p = 0.013$, 0.005, respectively), whereas the timing of surgery affected the outcomes in terms of complications ($p = 0.024$). Stoik et al. [18] found that the conservative method of management of these injuries definitely leads to complete loss of function and thus emphasized on surgical stabilization of these fractures both above and below elbow to improve functional outcome; this finding can also be reiterated with our study.

In our study that there was a significant improvement in DASH scores, MEPS scores, range of motion, and pronation/supination during follow-up from 3 to 6 months ($p < 0.05$). The open fractures with grade 3b and intra-articular fractures which were managed with an external fixator or square nail showed poor DASH score, MEPS score, decreased elbow ROM and nonunion ($p > 0.05$). We observed that educated patients had a tendency towards better functional outcomes as compared to uneducated patients. Five patients who were lost to follow-up, all were from low socioeconomic status and the majority of them were not educated. Although it was not statistically significant ($p > 0.05$), but it is an important factor in developing countries like ours.

Ditsios et al. [19] found intra-articular fractures to have a poorer outcome; we also observed that intra-articular fracture tends to influence the outcome but was not statistically significant in our study. We also observed that Group 1 and 2 types of injuries (Fig. 2) had better functional outcomes as compared to Group 3, although it was not statistically significant.

Strength and Limitations

It is the first prospective study that describes factors influencing the functional outcome of floating elbow injuries and their variations. All cases were operated at the same institute and by the same surgeon and data were collected by a single investigator throughout the period of study to avoid false data and to maintain uniformity. The limitation was the small sample size and relatively shorter duration of follow-up.

Conclusion

The incidence of floating elbow injuries is increasing day by day and frequently associated with polytrauma. The functional outcome of these injuries is not affected by differences in age, gender, education, occupation, side/dominance, and anatomic site of fractures. However, open fracture, type of surgery performed, and delay in surgery have a significant influence on the final outcome. Neuropraxic nerve injuries recover over a period of time and did not influence the final outcome significantly. Timely intervention and a multimodal approach can lead to good results.

Declarations

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval Obtained.

Informed Consent Obtained.

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ORIGINAL ARTICLE

Self-Reported Feelings of Disability Following Lower Extremity Orthopaedic Trauma

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Abstract

Background Nearly 20% of Americans consider themselves disabled. A common cause of disability is unexpected orthopaedic trauma. The purpose of this current study, assessing common lower extremity trauma, is the following: to assess the prevalence of self-reported feelings of disability following these injuries, to determine if self-reported feelings of disability impact functional outcomes, and to understand patient characteristics associated with self-reported feelings of disability.

Methods The functional statuses of patients with tibial plateau fractures and ankle fractures were prospectively assessed. Patient reported feelings of disability (acquired from validated functional outcome surveys), which were compared with overall patient-reported functional outcome and emotional status at each follow-up visit. Additionally, patient demographics were analyzed, to assess associations with feelings of disability.

Results A total of 710 patients were included in our analysis. At short-term follow-up (3 months), a strong positive correlation existed between self-reported feelings of disability and worse functional outcomes (rs = 0.744, $P < 0.001$). At long-term follow-up (12-months), a strong positive correlation existed between self-reported feelings of disability and worse functional outcomes (rs = 0.741, $P < 0.001$). Self-reported feelings of disability were associated with increased age at both short-term ($P = 0.015$) and long-term ($P = 0.003$) follow-ups. At short-term follow-up, 41% of males and 59% of females self-reported feelings of disability ($P < 0.001$) No significant differences existed between genders at long-term follow-up ($P = 0.252$). Self-reported feelings of disability declined at each follow-up visit, from 48.1% at short-term follow-up to 22.1% at long-term follow-up.

Conclusion Self-reported feelings of disability, following lower extremity trauma, had strong positive correlations with worse outcomes. Orthopaedic trauma surgeons should be aware of the percentage of patients who feel disabled following lower extremity fractures, and know that this is associated with sub-optimal outcomes.

Level of Evidence III.

Keywords Orthopedic trauma · Feelings of disability · Orthopedic outcomes · Orthopedic disability

Introduction

Nearly one in every five Americans report having a disability, which contributes to difficulty performing activities of daily living or hinders their livelihood [1]. Resultant disabilities may additionally beget emotional and cognitive impairment [2, 3]. Individuals with disabilities represent the largest minority group in the United States. Patients with disabilities account for "hotspots" in health care, as they visit clinics and hospitals more than others. Hence, every physician will provide care to patients with disabilities during their career [2]. Unfortunately, patients with disabilities have been demonstrated to experience numerous disparities in healthcare, predominantly in the fields of preventative medicine [2]. The

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literature has demonstrated that these disparities are often the result of decreased accessibility to healthcare, financial barriers, and sub-optimal health literacy [2].

Orthopaedic injuries are a common reason for hospitalization following trauma, and they are a frequent cause of disability [4]. Nearly half of all Americans will sustain a fracture by the time they are sixty-five years of age [5]. These musculoskeletal ailments are associated with tremendous financial and social costs [6, 7]. Almost half of patients with fractures of the lower extremity were found to have residual disability at one-year follow-up [8]. Furthermore, a quarter of patients who sustain lower extremity injuries, are not able to return to work at one-year post-injury [9].

Although these studies provide awareness to the prevalence of disability following lower extremity fractures, there is a paucity of large prospective studies that assess how feelings of disability impact functional outcomes following orthopaedic trauma. The purpose of this current study, assessing common lower extremity trauma (tibial plateau and ankle fractures), is three-fold. (1) To assess the prevalence of self-reported feelings of disability following these injuries, (2) To determine if self-reported feelings of disability impact functional outcomes, following these injuries, (3) To understand if patient demographics are associated with self-reported feelings of disability, following these injuries.

Materials and Methods

An analysis was performed from two prospectively collected Institutional Review Board (IRB) approved databases of lower extremity fractures of the tibial plateau and ankle. Informed consent was obtained to include patients, and track their outcomes, in these databases. Outcomes in patients with acute tibial plateau fractures and acute ankle fractures were assessed using the validated Short Musculoskeletal Function Assessment (SMFA) survey. Questionnaires were collected by trained researchers at 3-month, 6-month, and long-term (12-month or greater) follow-up.

All questionnaires were obtained from interviewing consecutive patients seen at one of two outpatient settings at our academic center. Consecutive patients were prospectively followed, over a 6-year period, from October 2000 to January 2007 for acute ankle fractures. Consecutive patients were prospectively followed, over an 11-year period, from March 2006 to March 2016 for acute tibial plateau fractures. These time periods of prospective data collection were for two different IRB approved databases. Patients were excluded from inclusion in these prospective databases if they were under the age of 18. Patients were excluded from data analysis if they did not answer the question to assess feelings of disability at the given time-point.

Feelings of disability were evaluated utilizing the SMFA survey question of "How often do you feel disabled?", in which patients chose one of five options "1 = None of the time, 2 = A little of the time, 3 = Some of the time, 4 = Most of the time, 5 = All the time." Patients who responded to this question with one of the following answers, "3 = Some of the time, 4 = Most of the time, 5 = All the time," were considered to have feelings of disability. This classifications of self-reported feelings of disability were calculated as a dichotomous variable, to allow for reporting the prevalence, and longitudinal changes, of patients who experienced moderate to severe feelings of disability following their injury. All other analyses considered the full range of responses to the questions assessing feelings of disability, 1–5, as ordinal values.

Statistical analysis was performed using a Spearman's rho test to assess correlations between self-reported feelings of disability and overall function. Functional outcomes were assessed utilizing patient's total SMFA score and SMFA sub-categories (function, bothersome nature of injury, daily activities, emotional status and mobility). Statistical significance was considered when $P < 0.05$.

Results

A total of 710 patients were included in our analysis. 435 patients sustained ankle fractures and 275 patients sustained tibial plateau fractures.

At short-term follow-up (3-months), a strong positive correlation existed between self-reported feelings of disability and worse functional outcomes (rs = 0.744, $P < 0.001$). At 3-month follow-up, strong positive correlations existed between self-reported feelings of disability and worse scores in the following SMFA categories: Function (rs = 0.718, $P < 0.001$), bothersome nature of the injury (rs = 0.703, $P < 0.001$), daily activities (rs = 0.670, $P < 0.001$), and emotional status (rs = 0.714, $P < 0.001$). A weak positive correlation existed between self-reported feelings of disability and decreased mobility (rs = 0.196, $P < 0.001$). This is demonstrated in Table 1.

At long-term follow-up (12 months), a strong positive correlation existed between self-reported feelings of disability and worse functional outcomes (rs = 0.741, $P < 0.001$). At long-term follow-up, strong positive correlations existed between self-reported feelings of disability and worse scores in the following SMFA categories: Function (rs = 0.723, $P < 0.001$), bothersome nature of the injury (rs = 0.723, $P < 0.001$), daily activities (rs = 0.732, $P < 0.001$), emotional status (rs = 0.731, $P < 0.001$) and mobility (rs = 0.692, $P < 0.001$). This is demonstrated in Table 2.

Self-reported feelings of disability were associated with increased age at both short-term ($P = 0.015$) and long-term

Table 1 Positive correlations between self-reported feelings of disability and worse functional outcomes at short-term (3 months) follow-up

SMFA Category	Spearman's rho	*P* value
Total	0.744	< 0.001
Function	0.718	< 0.001
Bothersome nature of injury	0.703	< 0.001
Daily activities	0.670	< 0.001
Emotional status	0.714	< 0.001
Mobility	0.196	< 0.001

Table 2 Positive correlations between self-reported feelings of disability and worse functional outcomes at long-term (12 months) follow-up

SMFA category	Spearman's rho	*P* value
Total	0.741	< 0.001
Function	0.723	< 0.001
Bothersome nature of injury	0.723	< 0.001
Daily activities	0.732	< 0.001
Emotional status	0.731	< 0.001
Mobility	0.692	< 0.001

($P = 0.003$) follow-up [Table 3]. At short-term follow-up, 41% of males and 59% of females self-reported feelings of disability ($P < 0.001$). At long-term follow-up, 21% of males and 26% of females self-reported feelings of disability ($P = 0.252$).

Self-reported feelings of disability declined at each follow-up visit (Fig. 1).

Discussion

In this study, self-reported feelings of disability were strongly correlated with worse functional outcomes following lower extremity orthopaedic trauma. Previous studies have demonstrated that psychosocial factors, such as catastrophic thinking, anxiety, or mental illness, may explain much of the inter-patient variability of disability that exists following orthopaedic pathologies [10–12]. Yet, to our knowledge, this is the first study to correlate the degree of patient-perceived disability with prospective functional outcomes following lower extremity orthopaedic trauma.

Recent reports have validated a need for the adaptation of evidence-based bio-psychosocial models of care in orthopedics, to more comprehensively treat patients, while concurrently reducing the wide variability of inter-patient disability [13]. Formulating a better understanding of both the causes and effects of patient-reported feelings of disability is an important undertaking that will further facilitate this adaptation.

A recent study from Lindenhovius reported the relationship between patient-reported disability measures and objective physical impairment following elbow trauma. However, much of the total patient-reported disability remains unexplained and poorly related to objective impairment or injury severity [14]. These findings are similar to a study from Doornberg et al. which reported that only 17% of the variation in measured disability following elbow trauma was a result of objective impairment [15].

Related studies have demonstrated that psychosocial factors are important long-term predictors of disability following orthopaedic pathology [10, 11, 16]. In particular, a patient's perception of pain, pain interference, or mental illness has been described as strong predictors of measured disability [15, 17]. This is in agreement with the results of our study, which demonstrate worse emotional status among patients who report feelings of disability. A recent review from Hadjistavropolus et al. discusses this further, specifically describing the influence of health related anxiety on both disability and the development of chronic pain [18]. Vranceanu et al. better defined this relationship in their report on patients with upper extremity pain, in which a cognitive-behavioral model of health related anxiety was utilized, to assess the relationship between increased health concerns and perceived disability. Their study reports a strong, positive relationship between health concerns and perceived disability. The study likewise demonstrates that this perceived disability was also correlated with somatic symptoms and idiopathic, well-defined pain [13].

The concept that patient perceptions are associated with patient outcomes in orthopedics is expanded upon by the correlation between self-reported feelings of disability and decreased functional outcomes, as demonstrated in our

Table 3 Differences in mean age between patients exist, between those who have self-reported feelings of disability following lower extremity trauma, and those who did not

Short term follow-up	Self-reported feelings of disability	No self-reported feelings of disability
	43.8 years old	47.2 years old
Long-term follow-up	Self-reported feelings of disability	No self-reported feelings of disability
	45.5 years old	50.4 years old

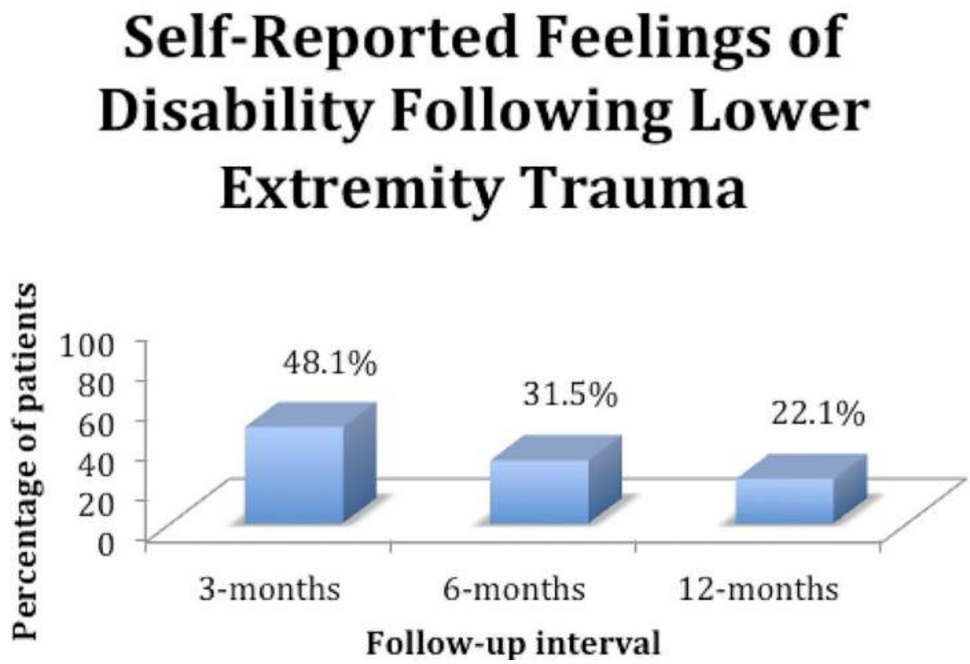

Fig. 1 Self-reported feelings of disability, following lower extremity trauma, decreased at each additional follow-up visit

present study. Our results may also suggest using patient perceptions of disability as risk factors for poor outcomes. This has been described in other areas of medicine. De Heer et al. demonstrated that poor perceptions of health are risk factors for depression and worsened outcomes in patients who suffer from Fibromyalgia [19]. Additionally, our study corroborates the necessity of bio-psychosocial models of care in orthopaedic surgery, and further suggests the interrelatedness of psychological, social, and biological factors regarding outcomes in orthopedics, particularly lower extremity trauma.

This study is limited by the inherent weaknesses of our outcome measure, the Short Musculoskeletal Function Assessment. In such an assessment, it is difficult to gain a completely objective measure of functional status, as the information is self-reported. Therefore, the presence of anxiety or negativity may have contributed to a portion of the relationship between feelings of disability and worse outcomes. However, we feel the SMFA is a well-defined and tested measure, and these weaknesses should not deter the importance and clinical impact of this study.

Conclusion

Self-reported feelings of disability, following lower extremity trauma, had strong positive correlations with worse outcomes, at both short-term and long-term follow-up. However, the patients who felt disabled at the 3-month time point had worse emotional status. Patients who felt disabled were of older age. At long-term follow-up, self-reported feelings of disability significantly decreased. Orthopaedic trauma surgeons should be aware of the percentage of patients who feel disabled following lower extremity fractures, and know that this is associated with sub-optimal outcomes.

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Declarations

Conflict of interest David Kugelman declares he has no conflict of interest. Jack Haglin declares he has no conflict of interest. Ariana Lott declares she has no conflict of interest. Sanjit Konda declares he has no conflict of interest. Kenneth Egol declares he has no conflict of interest.

Ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent Informed consent was obtained from all patients for being included in the study.

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ORIGINAL ARTICLE

Proximal Femoral Plate, Intramedullary Nail Fixation Versus Hip Arthroplasty for Unstable Intertrochanteric Femoral Fracture in the Elderly: A Meta-analysis

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Abstract

Introduction Multiple operative modalities are available for management of unstable intertrochanteric femoral fractures. This meta-analysis was conducted to find out if there is superiority of surgical fixation by proximal femoral plate or surgical fixation by intramedullary nail over hip arthroplasty for management of unstable intertrochanteric femoral fractures in the elderly.

Methods A search for relevant studies that published from January 2000 to November 2018 through the electronic literature database of Cochrane library, Medline, Trip Database and Wiley online library.

Results A total of 19 studies including 14 prospective RCTs, and five retrospective studies. This meta-analysis showed that nail group had shorter operative time than plate group ($P<0.0001$), and less blood loss than the plate and arthroplasty groups ($P<0.0001$), cut-out was higher in nail group than the plate group ($P<0.0001$), mortality rate was higher in hip arthroplasty compared to other groups ($P<0.0001$), Harris hip score within 6 months of the operation was higher in the arthroplasty group compared with the nail and plate groups, while within 1 year of the operation, nail group had higher Harris hip score than arthroplasty group ($P<0.0001$).

Conclusions This meta-analysis suggested that the intramedullary nail fixation method is a preferred method for management of unstable intertrochanteric femoral fractures in the elderly over hip arthroplasty and proximal femoral plate fixation.

Keywords Intertrochanteric · Extracapsular hip fractures · Intramedullary fixation · Proximal femoral plate · Hip arthroplasty

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Introduction

The average lifespan worldwide is increasing, which results in growth of the elderly population and subsequently increase in the incidence of osteoporotic hip fractures. The worldwide incidence of hip fracture was 1.6 million in the year 2000; and the number is expected to reach 6 million in the year 2050 [1, 2]. Intertrochanteric femoral fractures comprise nearly 45% of all hip fractures and out of these, 50–60% are classified as unstable. Multiple operative modalities are available for management of unstable intertrochanteric femoral fractures. However, there is no clear evidence from clinical research to indicate if hip arthroplasty is more superior to surgical fixation and vice versa [1–5]. Therefore, this meta-analysis was performed to find out if there is superiority of surgical fixation by proximal femoral plate or surgical fixation by intramedullary nail over hip arthroplasty and vice versa by comparing the advantages and disadvantages of the devices including patient's morbidity and mortality.

Materials and Methods

Search Strategy

A search for relevant studies that published from January 2000 to November 2018 through the electronic literature database of Cochrane library, Medline, Trip Database, Wiley online library using the following keywords: Intertrochanteric OR Pertrochanteric OR trochanteric, extracapsular hip fractures OR intramedullary fixation OR Proximal femoral plate OR cephalomedullary nail OR hip arthroplasty OR endoprosthesis; Comprehensive meta-analysis program software was used for our meta-analysis.

Inclusion and Exclusion Criteria

We identified literature that met the following inclusion criteria: (1) patients older than 60 years, (2) unstable intertrochanteric femoral fracture, (3) the articles restricted to English language, (4) studies that were designed as interventional studies (Randomized clinical trials or non-randomized clinical trials), and (5) each study has to include at least 20 cases either managed by surgical fixation or hip arthroplasty and a mean follow-up period of 2 years minimum.

While, the exclusion criteria were: (1) stable intertrochanteric femoral fracture, (2) patients had a metastasis or myeloma, infection, or congenital deformity, (3) patients with neurological diseases as Cerebral palsy, Parkinson's disease, etc. (4) type of literature as a "review" and "talk," "letters," "commentary," and "case report"; cadaver or model studies., and (5) data duplicated or overlapped.

Selection of Literature

The *PRISMA* flow diagram was used to select the included studies. All the titles and abstracts of the relevant studies were first categorized, and then the full-text articles that met the eligibility criteria were read and selected for inclusion (Fig. 1).

Quality Assessment of Included Studies

The Cochrane tool was used to assess the following items: randomization, allocation concealment, blinding of participants, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other bias, for each individual item, while assessment of the included non-RCTs was done according to the Newcastle–Ottawa scale (Tables 1, 2).

Statistical Analysis

Weighted mean differences (WMDs) or odds ratios (ORs) corresponding 95% confidence interval (CI) were estimated and pooled across studies to assess the discrepancy between different methods with a value of $P<0.05$ as statistically significant. Heterogeneity was assessed using the I^2 value and Chi-square test, a random effect model was used.

Results

Included Studies

A total of 1970 potentially relevant articles were identified from the databases.

At first, 87 studies were included, 16 of them are excluded due to duplication, Following closer examination of the remaining 71 studies through reading the full text of each and risk of bias assessment process, further 52 studies are excluded with reasons as they did not fulfill the study's inclusion criteria (Fig. 1).

Clinical Outcomes

According to: there have been many parameters we have worked in the study as mentioned below: Type of intervention, Operative time, Blood loss, Blood transfusion, Hospital stay, Implant related complication, Reoperation, Mortality assessment and Harris hip score.

Type of Intervention

A total of 1764 patients from 19 studies were included.

The majority was managed by intramedullary nail (954 cases) followed by proximal femoral plate (407 cases) and hip arthroplasty (403 cases) for unstable intertrochanteric hip fractures, respectively. This means that up to 54% of cases were managed by intramedullary nails, while about 46% distributed nearly equally between proximal femoral plate and hip arthroplasty.

According to Operative Time

In studies comparing different types of intervention, we found that cases managed by nail shows less operative time than plate [7, 13, 14, 21] ($Chi^2=2.310$, $P<0.0001$, $I^2=94.674$, Supplementary Fig. 2), while systematic reviews of Individual studies [8, 11, 12, 15, 18, 21, 23] found cases managed

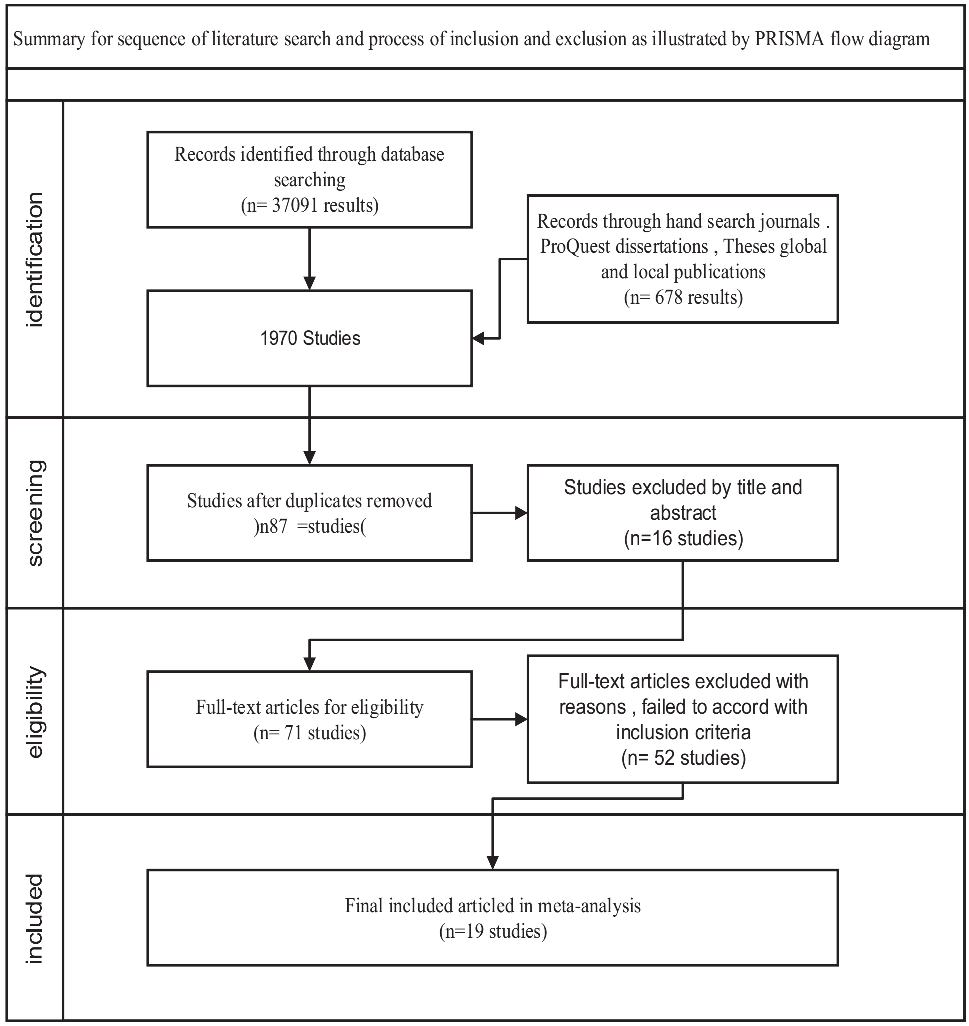

Fig. 1 Preferred reporting items for systematic reviews and meta-analyses (*PRISMA*) flow diagram of study selection

Table 1 Risk of bias assessment of the RCTs

Study	Randomization	Allocation concealment	Blinding of participants	Incomplete outcome data	Selective outcome reporting
Boldin [6]	Low risk	Low risk	Low risk	Unclear risk	Low risk
Miedel [7]	Low risk	Low risk	Low risk	Low risk	Low risk
Grimsrud [8]	Low risk	Low risk	Low risk	Low risk	Low risk
Bonnevialle [9]	High risk	Low risk	Low risk	Low risk	Low risk
Richard Borger [10]	Low risk	Low risk	Low risk	Low risk	Unclear risk
LeeYoung-Kyun [11]	Low risk	Low risk	Low risk	Unclear risk	high risk
Zha [12]	Low risk	Low risk	Low risk	Low risk	Low risk
Tao [13]	Low risk	Low risk	Low risk	Low risk	Low risk
Guo [14]	Low risk	Low risk	Low risk	Low risk	Low risk
Nishikant [15]	Low risk	Low risk	Low risk	Low risk	Low risk
Özkayın [16]	Low risk	Low risk	Low risk	Low risk	Low risk
Keizo Wada [17]	Low risk	Low risk	Low risk	Low risk	Low risk
Malkesh [18]	Low risk	Low risk	Low risk	Low risk	Low risk
Jolly [19]	Low risk	Low risk	Low risk	Low risk	Low risk

Table 2 Risk of bias was assessed with use of the Newcastle–Ottawa Scale

Study	Exposed cohort	Non exposed cohort	Ascertainment of exposure	Outcome of interest	Comparability	Assessment of outcome	Length of follow-up	Adequacy of follow-up	Total score
Herman [20]	*	*	*	*	–	*	*	*	7
Ming Hui Li Lei [21]	*	*	*	*	–	*	*	*	7
Zhenhai [22]	*	*	*	*	*	*	*	*	8
Temiz A [23]	*	*	*	*	*	*	*	*	8
Güven M [24]	*	*	*	*	–	*	*	*	7

"*"Means a score of 1; "**"means a score of 2; the total score of this scale is 9

A higher overall, score corresponds to a lower risk of bias; a total score of 5 or less indicates a high risk of bias

by nail showed less operative time than plate and hip arthroplasty, respectively.

According to Intraoperative Blood Loss

There was a significant difference in results of meta-analysis according to blood loss between individual studies that managed by either: the plate or the nail group [7, 13, 14, 22], (Supplementary Fig. 3), while it was found that cases managed by intramedullary nail group showed less blood loss than both plate and hip arthroplasty groups with a significant difference ($P < 0.0001$, $I^2 = 99.493$).

According to Blood Transfusion

Meta-analysis of studies according to blood transfusion could not be assessed because of the smaller-sized results of the studies [7, 9], while systematic review of individual studies that were managed by either: plate, nail or hip arthroplasty according to blood transfusion showed insignificant difference.

According to Hospital Stay

The pooled results indicated that there was insignificant difference in duration of hospital stay between the plate and nail group [13, 14] ($Chi^2 = 0.335$, $P = 0.063$, $I^2 = 71.026$, Supplementary Fig. 4), and there was insignificant difference in results of meta-analysis according to hospital stay between individual studies that are managed by either: plate or nails [18, 23], ($Chi^2 = 9.961$, $P = 0.060$, $I^2 = 97.034$).

According to Implant-Related Complications

A. Superficial infection

Meta-analysis of studies found that there was insignificant difference in superficial infection between the plate and nail groups [7, 14] ($Chi^2 = 0.000$, $P = 0.976$, $I^2 = 0.000$, Supplementary Fig. 5), while meta-analysis of studies found that there was significant difference in superficial infection between the nail and hip arthroplasty groups [16] ($P < 0.0001$, $I^2 = 31.138$, Supplementary Fig. 6) and systematic review of individual studies found that cases managed by hip arthroplasty had more superficial infection than cases managed by the plate and nail groups [6, 8, 10–12, 15, 17, 18, 20, 21, 23].

B. Deep infection

Meta-analysis of study [16] studies that were managed by nail versus hip arthroplasty according to deep infection showed insignificant difference, (Supplementary Fig. 7), while systematic reviews of studies [6, 8, 15–18, 20, 21] according to deep infection in cases with unstable intertrochanteric femoral fracture in the elderly either managed by plate, nail or hip arthroplasty showed insignificant difference.

C. Cut-out complication

The pooled results showed higher cut-out complication in cases managed by nail than cases managed by plate with significant difference [6, 10–12, 15, 18, 20, 21, 23] according to cut-out complication: ($Chi^2 = 2.649$, $P < 0.0001$, $I^2 = 86.881$, Supplementary Fig. 8).

D. Implant failure

Meta-analysis of studies and also systematic reviews of individual studies [6, 8, 10–12, 15, 17, 18, 20, 21, 23] according to implant failure in cases either managed by either plate, nail or hip arthroplasty showed insignificant difference ($P = 0.015$, $I^2 = 57.901$).

E. Deep venous thrombosis

Meta-analysis of studies and also systematic reviews of individual studies [6, 8, 10–12, 15, 17, 18, 20, 21, 23] according to DVT in cases with unstable intertrochanteric femoral fracture in the elderly either plate, nail or hip arthroplasty showed insignificant difference (Supplementary Figs. 9 and 10).

According to the Need for Re-operation

Meta-analysis of studies [7] indicated that there was insignificant difference in the need for re-operation between plate versus nail ($Chi^2 = 0.000$, $P = 0.555$, $I^2 = 0.000$, Supplementary Fig. 11).While systematic reviews of individual studies [6, 8, 10–12, 15, 17, 23] showed that the need for re-operation was higher in the plate and nail groups than the hip arthroplasty group.

According to Mortality Assessment

Meta-analysis of study [7] indicated that there was insignificant difference in mortality assessment between different groups: ($Chi^2 = 0.152$, $P = 0.056$, $I^2 = 56.577$ Supplementary Fig. 12). While, systematic reviews [6–8, 17] showed high mortality rate in cases underwent hip arthroplasty within 1 year compared to other groups.

According to Harris Hip Score for Follow-up

The pooled results indicated that there was insignificant difference in *HHS* for follow-up between cases managed by plate group versus the nail group [13, 14, 16] ($Chi^2 = 0.000$, $P = 0.668$, $I^2 = 0.000$, Supplementary Fig. 13), while systematic review of individual studies [18, 21, 23] results 6 months postoperatively showed that the *HHS* was higher in the hip arthroplasty group in comparison with the nail and the plate groups, while 1 year postoperative, it was found that nail group had significantly higher *HHS* compared with the hip arthroplasty group.

Discussion

This meta-analysis was conducted to find out if there is superiority of surgical fixation by proximal femoral plate or by intramedullary nail over hip arthroplasty for management of unstable intertrochanteric femoral fractures in the elderly from the current literature to provide guidance on the appropriate clinical choice to accommodate individual patients. In this meta-analysis, it was found that intramedullary fixation could achieve significantly shorter operative time, less intraoperative blood loss, also higher post-operative functional hip scores which achieve the long-term operative purposes including restoring the limb functions and early mobilization, and decreasing the re-operation rate in comparison with proximal femoral plate and hip arthroplasty for management of unstable intertrochanteric femoral fractures in the elderly. Wu-Bin Shu et al. [25]concluded that GN has the least total incidence of complications for treating unstable intertrochanteric fractures among the four interventions.

These results were almost consistent with our meta-analysis results. Most of our included studies in this meta-analysis were RCTs (fourteen RCTS with 1217 participants), which, therefore, overcomes the shortcomings of recall or selection bias in non-randomized studies. The methodological quality of included retrospective studies was high; (a total of two studies scored 8 stars, while three studies scored 7 stars) according to the NOS.

However, there was heterogeneity in this meta-analysis results which can be explained by different implant devices of internal medullary nails, surgeon expertise, surgical technique and post-operative rehabilitation.

So after evaluation of all data and reviewing previous systematic reviews that compared different intramedullary nail fixation, proximal femoral plate and hip arthroplasty with exclusion of stable intertrochanteric fractures, we can recommend intramedullary nail fixation for the treatment of unstable femoral intertrochanteric fractures in the elderly, with some modifications and precautions according to type of fracture, quality of bone and the associated medical conditions.

There were several strengths in this network meta-analysis:

1. The meta-analysis has included prospective randomized clinical trials with large sample size which increases the statistical power.
2. A random effect model was used to avoid heterogeneous results.
3. We compared treatment strategies indirectly, when no head-to-head trial existed, more precise efficacy estimates were based on direct and indirect comparisons with various interventions.
4. The use of the 95% confidence intervals of inconsistency factor values reached zero, demonstrating no substantial inconsistency.

But, undoubtedly, this study had some limitations:

1. Some of our included articles have not always reported some items which were needed for comparison between different types of interventions or they are reported in various ways (e.g., number and percentage, mean, median and SD, etc.)

2. The qualities of the studies were quite variable. Some studies were of unclear bias as to randomization sequence generation; some had weak blinding, or imperfect allocation concealment; therefore, selection bias or confounding factors might be present, influencing our results.
3. Some factors that may affect the post-operative functional outcome were not reported as post-operative physiotherapy and rehabilitation.

Summary and Conclusion

Intertrochanteric femoral fracture is a devastating skeletal injury which is common in elderly osteoporotic patients and it greatly affects the patient lifestyle, physical and psychological conditions. Proximal femoral plate, intramedullary nail and hip arthroplasty are all used for the management of unstable intertrochanteric femoral fractures in the elderly.

In this study, it was concluded that the intramedullary nail fixation is a preferred method for management of unstable intertrochanteric femoral fractures in the elderly over hip arthroplasty and proximal femoral plate fixation as it has shorter operative time and less blood loss, Also, the intramedullary nail fixation shows higher post-operative functional hip scores which achieves the long-term operative purposes include restoring the limb functions and early mobilization and decreasing the re-operation rate.

According to the adverse effects, this study showed that hip arthroplasty group has a higher mortality rate, more blood loss, more superficial infection and longer operation time than the intramedullary nail and proximal femoral plate, while the need for re-operation was higher in proximal femoral plate and intramedullary nail than the hip arthroplasty group.

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Authors' contributions It has been a teamwork; each one has his specific role: MSEW (Orthopedic surgery resident—Faculty of Medicine, Tanta University, Egypt) and Assist. Prof. Dr. MAER (Assistant Professor of orthopedic surgery—Faculty of Medicine, Tanta University, Egypt) were responsible for data collection for the study including reading full-text articles and exclusion of articles that did not met the inclusion criteria. Assist. Prof. Dr. AMS (Assistant Professor of orthopedic surgery—Faculty of Medicine, Tanta University, Egypt) was responsible for data extraction and writing the original draft. Prof. Dr. LMAEY (Professor of orthopedic surgery—Faculty of Medicine, Tanta University, Egypt), was responsible for research activity planning and execution in addition to writing review and editing. Prof. Dr. IK (Professor of Public Health & Community Medicine—Faculty of Medicine, Tanta University, Egypt) was responsible for providing the statistical analysis for this study.

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Availability of Data and Materials Electronic search was search was done, so data are available.

Declarations

Conflict of Interest The authors had no conflicts of interest to declare in relation to this article.

Ethical Approval This article does not contain any studies with human participants performed by any of the authors; thus, no ethical approval is required.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Consent to Publish Formal written consent to publish before publication of the work has been provided.

Informed Consent For this type of study, informed consent is not required.

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CASE REPORT

Bilateral Radial Head Fracture Secondary to Weighted Push-Up Exercise: Case Report and Review of Literature of a Rare Injury

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Abstract

A 33-year-old male presented with bilateral radial head fractures after weighted prone push-up exercise. The patient had Mason type I and II on right and left sides, respectively. He was managed conservatively with limited immobilisation and early range of motion exercises. The fracture healed and patient had no complaints at the last follow-up of 13 months. Bilateral radial head fracture is rare with push-up exercise, and can be successfully treated conservatively with immobilisation and early rehabilitation. Although push-up exercises are an excellent workout with known benefits, unusual modifications of standard techniques should be avoided.

Keywords Radial head fracture · Push up injuries · Conservative · Elbow forces · Home fitness

Introduction

Radial head fractures are common, constituting approximately one-third of all elbow fractures [1]. It is usually associated with severe trauma, direct injury or fall on outstretched hand [1, 2]. Patients usually present with pain and swelling of the lateral aspect of elbow with painful rotation of the forearm. Undisplaced fractures are managed with sling and early mobilisation, the treatment of displaced fractures is predicated on the extent of displacement and the size of fragments [3, 4]. Bilateral radial head fracture is rare [4] and only few cases have been reported in literature [4–7]. Various injuries due to push-up exercises have been reported in literature [8, 9], but bilateral radial head due push-up exercises has not been reported.

We present the case of a 33-year-old healthy male who sustained a bilateral radial head fracture while doing weighted push-ups that was treated conservatively. To our knowledge, the present report is the first case report of an unusual mechanism of injury in the English language literature. The purpose of this case report is to report an unusual aetiology of bilateral radial head fracture and raise awareness about injuries related to nonstandard modification of prone push-up techniques.

Case Report

An otherwise healthy moderately built 33-year-old male presented to the Orthopaedic outpatient department with complaints of painful movements in both elbows. Blood investigations in recent past were not suggestive of any metabolic bone disease nor there was any history of prolonged drug intake. The patient gave an history of doing weighted push-ups and experienced acute pain in both the elbows since then. Patient had made his 3-year

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Fig. 1 Anteroposterior (**a**) and lateral (**b**) radiograph of right elbow showing undisplaced radial head fracture

Fig. 2 Anteroposterior (**a**) and lateral (**b**) radiograph of left elbow showing minimally displaced radial head fracture

8-month-old child (15 kg) to sit on his upper back with both legs hanging on either side of the trunk and had performed push-ups with forearm in full pronation. He had sustained injury after 2 repetitions of the exercise. On orthopaedic evaluation, he had tenderness on both the radial heads with restriction of supination and pronation bilaterally. Flexion at elbows was terminally painful, while shoulder movements were painless. There was no neurovascular deficit. Plain radiographs of elbows showed fractures of the both the radial heads. The fracture was classified as Mason type I on right side (Fig. 1) and type 2 on the left side (Fig. 2). The patient was counselled for conservative management and was given oral analgesics along with bilateral above elbow plaster of paris slab for 1 week on the right side and 2 weeks on left side. Following the removal of slab, the patient was started on active physiotherapy for both the elbows and 16-week radiograph showed bilateral complete union of both the

Fig. 3 Left elbow radiograph at 16-week follow-up showing united radial head fracture

Fig. 4 Right elbow radiograph at 16-week follow-up showing united radial head fracture

fractures (Figs. 3, 4). At 13-month follow-up, the patient had normal range of movements in both elbows with no signs of instability.

Discussion

Fractures of the radial head are the most common fractures in the elbow [1]. The usual mechanism of radial head fracture is axial loading of radius on capitellum in a semi-flexed pronated forearm. With the forearm in pronation, the anterolateral margin of the radial head comes into contact with the capitellum which is susceptible to a shearing type of injury on axial loading [4]. Other mechanism of injuries includes direct injury over the lateral aspect of elbow, and fall on abducted arm with elbow in flexion. The degree of comminution of the fracture is related to the energy of the fall. Back in 1954 Mason classified the radial head fracture in 3 types [10]. Type I as undisplaced marginal fracture. Type II as displaced marginal fracture and type III is a comminuted fracture. Bilateral radial head fracture is uncommon

Table 1 List of previously published cases with bilateral radial head fractures

Author	Year	Number of patients	Age/sex	Mode of injury	Management
Hodge [4]	1999	2	27/M 33/F	Fall from bicycle Fall onto the floor	Arm sling pouch Analgesics and physiotherapy
Deshmukh et al. [6]	2003	1	19/F	Kick to the elbow	Aspiration under sedation, rehabilitation
Zakir Shariff et al. [5]	2005	1	43/F	Trivial trauma	Arm sling pouch
Ng et al. [7]	2007	1	56/F	Fall on outstretched hand	Collar and cuff
Verma et al. [11]	2009	1	18/M	Fall on elbow	Radial head excision
Gawande et al. [12]	2017	1	28/M	Roadside accident	Above elbow slab
Our Study	2020	1	33/M	Push-up exercise	Above elbow slab and rehabilitation

and few case reports with bilateral radial head have been published with different mechanisms of injury. The earliest report was published 2 decades ago and only 5 cases were reported since then (Table 1) [5–7, 11, 12]. Hodge [4] reported two cases of nondisplaced bilateral radial head or neck fractures resulting from falls on outstretched hands. In our case, the patient initially engaged in prone bodyweight push-ups which was later replaced by weighted push-ups (14.7 kg) on his back so as to increase the intensity of workout. To our knowledge, there have been no prior reports of push-up-induced bilateral radial head fracture.

The management of radial head fractures depends on the type of the fracture and associated injuries of elbow. Mason type I fractures is usually treated with a sling for few days and active mobilisation as early as possible [2] while treatment of Mason type II Fractures is debatable [13]. Few studies have reported favourable outcome with conservative treatment of Mason type II fractures [14, 15]. Delay in restoration of early active movement leads to a delay in the recovery of function. Several studies of radial head fractures have shown that the shortest period of immobilisation had the best patient-reported outcome measure scores (PROMs) at follow-up [16, 17].

Home fitness has been a way of living for decades and different forms of upper and lower body exercises can be done at home without an equipment. Push-ups, bench pressing, and power lifting are common exercises for strengthening the upper extremity. Estimated injury rates in powerlifting and weightlifting are low compared to other sports. Despite the excessive amount of training, in comparison to contact sports, bodybuilding deals with relatively slow, defined, and controlled movements [18]. Acute injuries commonly occurring during weight training include sprains, ligament ruptures, tendon avulsions, and compartment syndromes [19]. Elbow injuries in elite bodybuilders is usually due to improper form or inadequate warm up and are usually mild like muscle sprain, lateral epicondylitis or bursitis, however, few cases of elbow dislocations, instability has also been reported. Other factors that have been suggested as risk factors for injuries are heavy loads in extreme joint positions [19]. Mixed martial arts can combine into one sport many martial arts forms, including wrestling, boxing, judo, and jujitsu. Elbow injury rates among wrestlers have been reported to account for up to 28% of all injuries sustained [20, 21]. Matthew et al. in survey of upper extremity injuries among martial arts participants found that the most commonly injured area of the upper extremity was the hand (53%) followed by the shoulder/upper arm (27%) and elbow (19%) [22]. Elbow injuries such as triceps tendon rupture [23], elbow dislocation, ulnar collateral ligament (UCL) [21] injury has been well reported in literature. Younger wrestlers appear to be susceptible to various types of avulsion fractures about the elbow, including the olecranon and the medial humeral epicondyle [20]. The push-up is an free body exercise with excellent cardiovascular benefits [24] that engages several muscle groups including the biceps, triceps, pectoralis, muscles of hip, leg and postural muscles depending upon the variation performed. It is usually an essential part of fitness programs for health-conscious people and athletes [25], however, because of its significant demands on the body, it should not be done without knowledge of potential benefits and risks. Smith et al. studied forces across the wrist joint in eight cadavers and found that during a push-up movement wrist joints are subjected to large axial compressive forces along with radially directed forces [26]. Morrey et al. studied the transmission of axial force across the radiohumeral joint during simulated active motion of the elbow and concluded that the greatest axial force transmission occurs between 0 and 30 degrees of flexion, which decreases with increase in flexion. The authors also stated that force transmission was greater in pronated forearm as compared to forearm in supination [27]. A systematic review of Kinetic analysis of push-up exercises revealed that for the standard push-up, the values of the Peak Force for both arms ranged from 41 to 98% bodyweight [28].

We analysed the forces exerted on the upper extremity with wide base hand position push-up exercise. The joint forces exerted on the upper extremity during the push-up

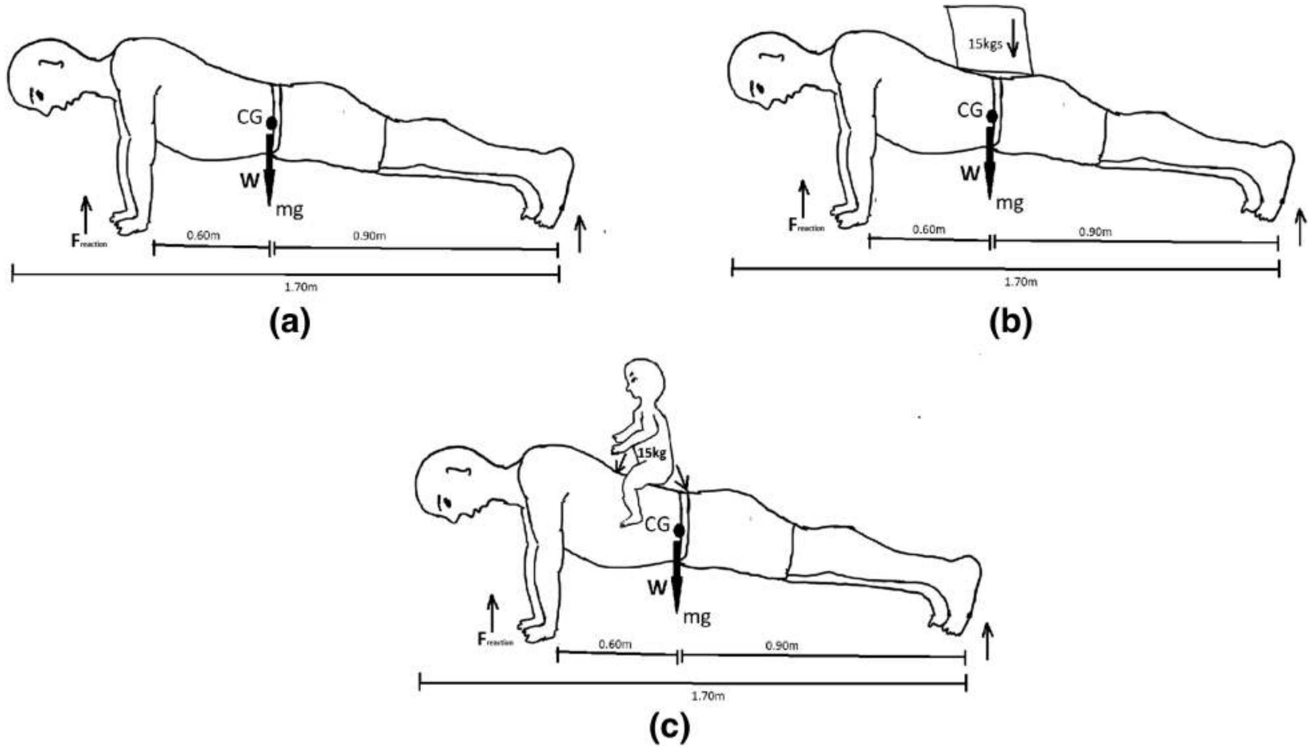

Fig. 5 **a** Free body diagram of showing forces acting through upper limbs during push-up in 70-kg male with height of 170 cm. **b** Free body diagram of showing forces acting through upper limbs during push-up with 15 kg static weight in 70-kg male with height of 170 cm. **c** Free body diagram of showing forces acting through upper limbs during push-up with child on the back (unstable 15 kg weight) in 70-kg male with height of 170 cm

exercise in 70 kg male with height of 170 cm was found to be 412 N (Fig. 5a). The forces differ during acceleration and deceleration phase; however, we have calculated the force in one single position. When a person does push-ups with weight of 15 kg on his back (static position), the force is increased to 500.3 N (Fig. 5b), however, with an unstable weight on back (child) the forces exerted might not be evenly distributed which makes a person susceptible to injury (Fig. 5c). The probable mechanism on injury in our case was axial loading of radial head in pronated forearm. The weight of the child and siting on one side of the back added to the uneven loading of the elbows thereby explaining different grades of injury in both the elbows.

The injuries associated with push-ups are widespread and not limited to elbow and wrist, but also involves shoulder joint, foot and back. Different variations of push-ups such as wall push-ups, knee push-ups, knuckle push-ups, single arm push-ups, and weighted vest push-ups can be done to increase the intensity of the workout and recruitment of different muscles [29]. However, with the increase in intensity of the workout, there is a sustainable increase in the risk of injuries. Common factors for injuries are pre-existing disorder of wrist, elbow or shoulder, velocity of exercise [25], improper posture, inadequate training, over enthusiastic training, and inadequate warm up.

Table 2 List of previously reported injuries due to push-up exercise

Author	Year	Age, sex	Injury	Push-up variation	Management
Mikawa et al. [8]	1994	52, M	Quadriplegia	Standard prone push-up	Operative
Busche et al. [9]	2003	19, M	Stress fracture of the hamate body and fourth metacarpal base	Military style push-ups	Conservative
Meena et al. [30]	2014	24, M	Stress fracture of ulna	Standard prone push-up	Conservative
Our study	2020	33, M	Bilateral radial head fracture	Weighted prone push-up	Conservative

After an extensive literature search, we came across only few reported articles with injuries associated with push-up exercise. The injuries reported were not limited to muscle sprains and ligaments injuries but fractures and catastrophic spinal injuries causing quadriplegia have also been reported (Table 2) [8, 9, 30].

Although injuries with standard prone push-ups are relatively rare, overenthusiastic modifications to increase the intensity might cause serious injuries and hence is not recommended. It is imperative to have an adequate knowledge of different variations of push-up to optimise the workout intensity without compromising proper form and risking injury.

Declarations

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed Consent For this type of study, informed consent is not required

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CORRECTION

Correction to: Bilateral Radial Head Fracture Secondary to Weighted Push-Up Exercise: Case Report and Review of Literature of a Rare Injury

Subodh Kumar Pathak[1] · Abhijeet Ashok Salunke[2] · Jasneet Singh Chawla[1] · Aryan Sharma[1] · Harish V. K. Ratna[1] · Rakesh Kumar Gautam[1]

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The original version of this article unfortunately contained a mistake. The corresponding author was incorrectly assigned. The correct corresponding author is Subodh Kumar Pathak.

The original article has been corrected.

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CASE REPORT

Neglected Broken Femoral Intramedullary Nail Resulting in an Urethrocutaneous Fistula

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Abstract

A femur fracture is one of the most commonly encountered fractures by orthopaedicians worldwide. Being one of the longest and strongest bones in the body, it is one of the principal load-bearing bones of the lower extremity. Various modalities of fixation have been tried and tested for femur fracture but the most accepted fixation modality for diaphyseal femur fracture worldwide is the interlocking intramedullary nailing. However, intramedullary nailing is not free of any complications. Complications such as infection, non-union, malunion, limb length discrepancy due to wrong size nail, screw or nail breakage, and injury to neurovascular structures while passing guidewire or drilling for the interlocking bolt are commonly reported. We report a case of a patient who presented with a neglected broken femoral nail which resulted in an urethrocutaneous fistula. As per our literature review, this complication has never been reported before.

Keywords Broken femoral nail · Implant breakage · Urethrocutaneous fistula

Introduction

Intramedullary interlocking nailing has been the gold standard treatment for diaphyseal fractures of the femur. The prime advantage being, it can provide rotational and axial stability, especially when the fracture pattern has comminution and involves the diaphyseal bone [1]. In spite of such sophisticated implants, failure of the implant continues to be prevalent.The implant breakage may be a nail breakage or bolt breakage, leading to both axial and rotational instabilities at the fracture site. This instability may cause pain, swelling, deformity, inability to bear weight and also at times the implant may penetrate out of the skin [2]. Broken nails or screws can irritate the surrounding soft tissue which may lead to devastating consequences if left unattended. Here, we report an interesting case of neglected broken femoral nail in an elderly male which led to an urethrocutaneous fistula.

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Case Report

Sixty-nine-year-old patient presented with pain and deformity of left thigh for 3 years. He also complained of a wound over the outer aspect of the lower third of the left thigh, which was discharging urine for the last 3 months but had dried up in the last week. He had sustained a left femur shaft fracture 20 years back which had been treated surgically by interlocking intramedullary nail. He had sustained a repeat trauma 3 years back, breaking his left femur shaft again along with the nail. But he had refused to take any kind of treatment for that and continued to mobilize with walking aids after 2 months of bed rest. He had noticed deformity in the left thigh after the second trauma along with the progressive shortening of the left lower limb. He had been having mild pain in the left thigh and groin for the last 3 years, which had increased in severity in the last 3 months. Pain in the groin particularly got aggravated while passing urine and partially relieved by taking analgesics.

On inspection, his left lower limb was significantly shortened with deformity in the left thigh (Fig. 1). There was a single sinus 0.5 mm × 0.5 mm with crustations over the lateral aspect of the lower third of the left thigh with no active discharge (Fig. 2). There was minimal warmth surrounding the sinus and no tenderness. On palpation, there was gross abnormal mobility at the mid-thigh level associated with

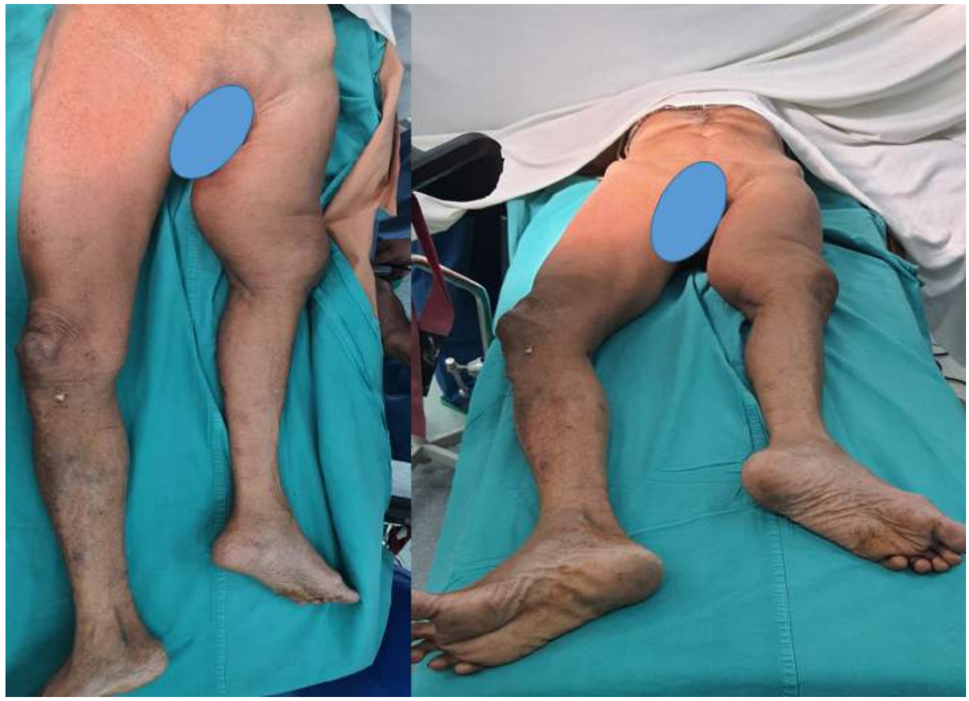

Fig. 1 Clinical photograph showing significant shortening of the left lower limb with the gross deformity at the thigh

Fig. 2 Clinical photograph showing a sinus with crustations over the lateral aspect of the lower third of left thigh with no active discharge (yellow pointer)

pain. The broken intramedullary nail could be palpated in the left groin region in a subcutaneous location (Fig. 3). The passive movements in the left hip were painful and severely restricted and the affected lower limb was shortened by 17 cm. There were no distal neurovascular deficits.

Plain radiographs of the left thigh showed gap non-union of the left femur shaft with broken interlocking intramedullary nail in-situ (Fig. 4). The distal segment of the broken nail had migrated to the perineal area. Arterial Doppler studies showed patent vessels with good flow in both lower limbs. Ascending cystourethrogram showed the urethra was patent with no dye leakage but the broken nail end was in close proximity of the bulbar urethra (Fig. 5).

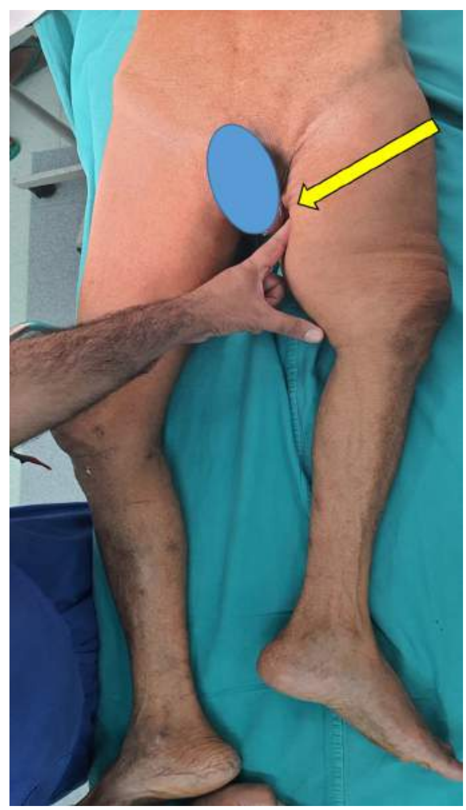

Fig. 3 Clinical photograph showing intramedullary nail being palpable in left groin region in the subcutaneous plane (yellow pointer)

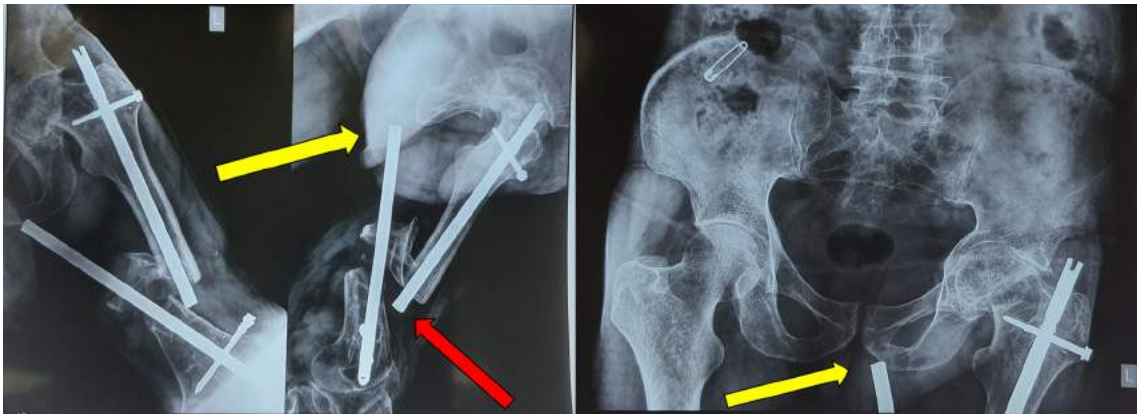

Fig. 4 Plain radiographs of left thigh showing gap non-union of the left femur with broken interlocking intramedullary nail in situ (red pointer). The proximal tip of the distal segment of the broken nail is seen pointing towards the perineum (yellow pointer)

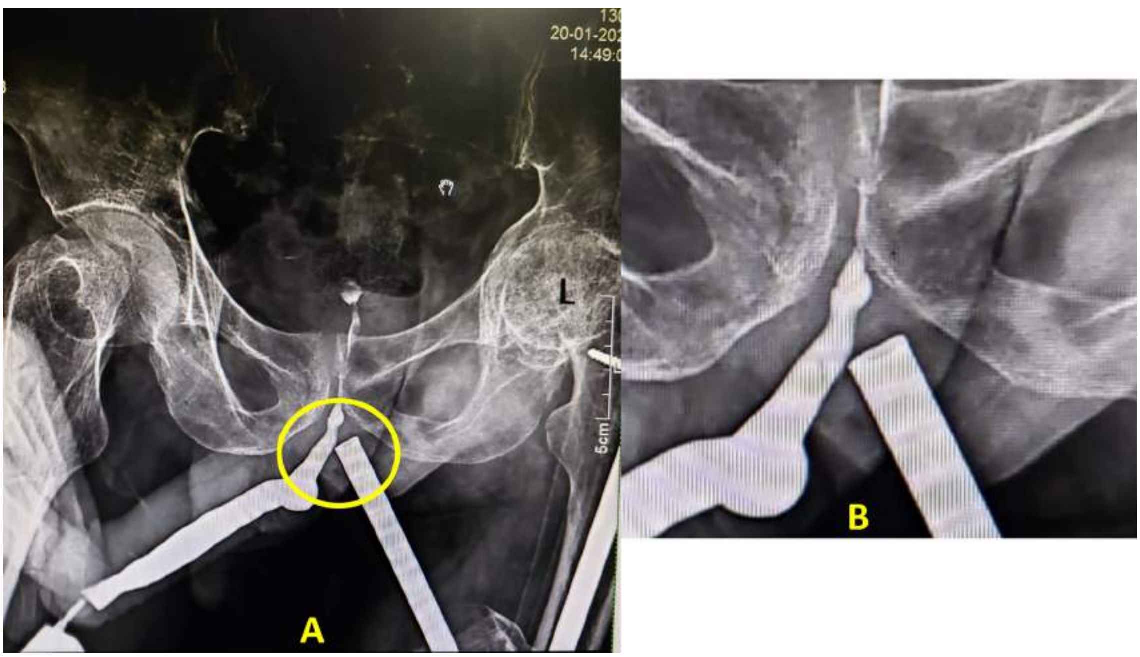

Fig. 5 **A** Ascending cystourethrogram showing patent urethra with no dye leakage but broken nail end was in close proximity of the urethra (yellow ring). **B** Enlarged picture showing the proximity of the nail to the bulbar urethra

The patient was explained about the need for broken implant removal and staged limb reconstruction. He was not willing for any of the reconstructive procedures and wanted only the removal of the broken implant. Accordingly, the consequences were explained and informed consent was taken for surgical treatment from the patient and his attendants.

Surgery was done under spinal anesthesia. First, a cystoscopy was done which showed a fistulous opening with a flimsy cover in the bulbar urethra (Fig. 6). Then, the proximal segment of the broken femoral nail was removed through an incision over the lateral aspect of the left hip joint with the help of a universal conical bolt and extractor. The removal of the distal segment of the nail posed a challenge. Even though it could be palpated in the subcutaneous location in the medial aspect of the upper third of the thigh, its broken tip had migrated into the perineum. To avoid iatrogenic injury to the urethra and other structures in the perineum, the distal segment had to be removed through the left knee with the help of a broken nail extractor (Figs. 7 and 8). Repeat cystoscopy after implant removal showed no additional injuries in the urethra.

The post-operative period was uneventful and the patient was given a thigh brace with a pelvic belt for

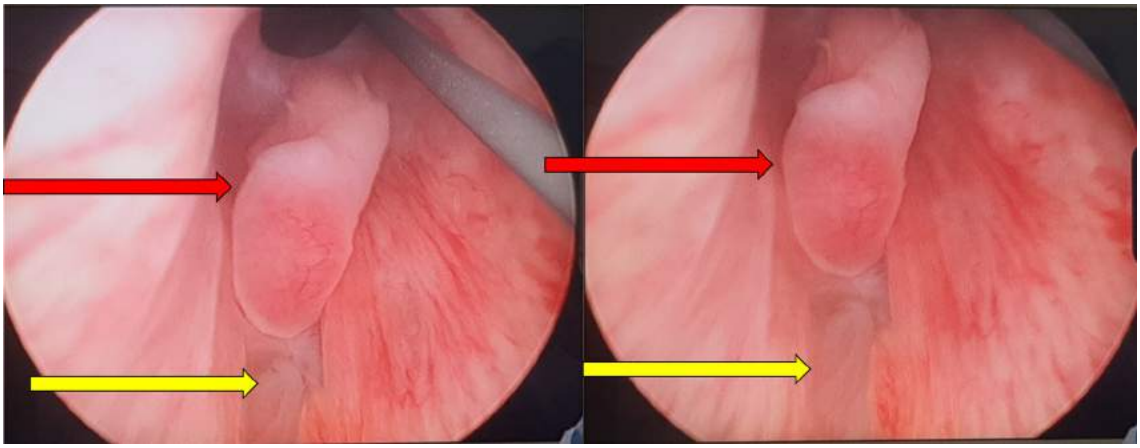

Fig. 6 Cystoscopy showing fistulous opening with flimsy cover in the bulbar urethra (yellow pointer). Eroded and raised flap of urethral mucosa due to fistula (red pointer)

Fig. 7 Broken implant post removal

non-weight-bearing mobilization. He was kept on an indwelling urinary catheter for 4 weeks.

At 6-week post-operative follow-up, he was passing urine without discomfort and was mobilizing with weight bearing as tolerated with thigh brace and walker stand. The sinus in the lateral aspect of the lower third of the thigh had completely dried out.

Discussion

Intramedullary interlocking nailing has been the gold standard procedure for diaphyseal fracture of the long bone. With the advent of interlocking systems, rotational and axial stability is also taken care of even in comminuted

Fig. 8 Immediate post-operative radiographs

fractures [1]. Despite these advantages, intramedullary nailing is associated with complications such as infection, non-union, malunion, limb length discrepancy, knee flexion restriction, locking screw prominence, neurovascular injury during drilling for interlocking bolts, and implant breakage [2]. Implant breakage may be either due to a breakage of the locking bolts or a break in the nail itself [1].

The incidence of broken intramedullary nails varies between 1 and 3.3% worldwide [2]. Breakage of intramedullary nail can cause complications like the migration of broken implants, skin penetration, pain, instability and inability to bear weight. Implant removal of such broken nails also may be very challenging at times and needs good planning and adequate instrumentation in the successful removal of such broken components [1–6].

Here, we present our case report wherein the neglected broken implant resulted in an urethrocutaneous fistula. Repeat trauma must have led to the breakage of the nail at the fracture site resulting in the migration of the distal aspect of the nail into the perineum resulting in an urethrocutaneous fistula. After proper counseling and convincing the patient and relatives, we ended up removing the broken implants. If left untreated, the nail would have caused unimaginable complications. As per our literature search, no such case has been ever reported. Through this case report, we want to highlight how a neglected broken implant can cause catastrophic complications if left untreated. Unusual complications are sometimes likely in the settings of neglected trauma and broken implants and one must be alert and tailor treatment appropriately.

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Declarations

Conflict of Interest There are no conflicts of interest.

Ethical Approval The institutional ethical committee clearance has been taken.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed Consent Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article along with their surgical consent.

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