ISSN 2218-5836 (online)

World Journal of *Orthopedics*

World J Orthop 2021 August 18; 12(8): 515-619

Published by Baishideng Publishing Group Inc

World Journal of Orthopedics

Contents

Monthly Volume 12 Number 8 August 18, 2021

World Journal of Orthopedics

Monthly Volume 12 Number 8 August 18, 2021

Contents

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
ISSN 2218-5836 (online)

LAUNCH DATE
November 18, 2010

FREQUENCY
Monthly

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EDITORIAL BOARD MEMBERS
http://www.wjgnet.com/2218-5836/editorialboard.htm

PUBLICATION DATE
August 18, 2021

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World Journal of Orthopedics

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World J Orthop 2021 August 18; 12(8): 515-533

DOI: 10.5312/wjo.v12.i8.515

ISSN 2218-5836 (online)

REVIEW

International recognition of the Ilizarov bone reconstruction techniques: Current practice and research (dedicated to 100th birthday of G. A. Ilizarov)

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Author contributions: Malkova TA contributed to the acquisition of data; both authors Malkova TA and Borzunov DY contributed to the conception and design, analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript.

Conflict-of-interest statement: The authors declare no conflicts of interest for this review.

Manuscript source: Invited manuscript

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Abstract

The Ilizarov method is one of the current methods used in bone reconstruction. It originated in the middle of the past century and comprises a number of bone reconstruction techniques executed with a ring external fixator developed by Ilizarov GA. Its main merits are viable new bone formation through distraction osteogenesis, high union rates and functional use of the limb throughout the course of treatment. The study of the phenomenon of distraction osteogenesis induced by tension stress with the Ilizarov apparatus was the impetus for advancement in bone reconstruction surgery. Since then, the original method has been used along with a number of its modifications developed due to emergence of new fixation devices and techniques of their application such as hexapod external fixators and motorized intramedullary lengthening nails. They gave rise to a relatively new orthopedic subspecialty termed "limb lengthening and reconstruction surgery". Based on a comprehensive literature search, we summarized the recent clinical practice and research in bone reconstruction by the Ilizarov method with a special focus on its modification and recognition by the world orthopedic community. The international influence of the Ilizarov method was reviewed in regard to the origin country of the authors and journal's rating. The Ilizarov method and other techniques based on distraction osteogenesis have been used in many countries and on all populated continents. It proves its international significance and confirms the greatest contribution of Ilizarov GA to bone reconstruction surgery.

Key Words: Ilizarov method; Ilizarov apparatus; Distraction osteogenesis; Bone lengthening; Bone defect; Bone transport; Arthrodesis

Specialty type: Orthopedics

Country/Territory of origin: Russia

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: February 15, 2021
Peer-review started: February 15, 2021
First decision: April 6, 2021
Revised: April 8, 2021
Accepted: July 9, 2021
Article in press: July 9, 2021
Published online: August 18, 2021

P-Reviewer: Yusufu A
S-Editor: Gao CC
L-Editor: Filipodia
P-Editor: Xing YX

Core Tip: The Ilizarov method of bone reconstruction involves bone repair and new bone formation. It is based on the biological phenomenon of distraction osteogenesis that is used for bone lengthening and deformity correction. The Ilizarov bone transport is a salvage procedure for a number of conditions, including large bone defects and infection. The method gave an impetus to new developments in bone reconstruction surgery based on the regeneration potential of bone tissue. Acceleration of distraction regenerate consolidation is one of the objectives of the current research in new bone formation.

Citation: Malkova TA, Borzunov DY. International recognition of the Ilizarov bone reconstruction techniques: Current practice and research (dedicated to 100th birthday of G. A. Ilizarov). *World J Orthop* 2021; 12(8): 515-533
URL: https://www.wjgnet.com/2218-5836/full/v12/i8/515.htm
DOI: https://dx.doi.org/10.5312/wjo.v12.i8.515

INTRODUCTION

Reconstructive surgery is performed to recover body parts that are affected aesthetically or functionally in congenital defects, developmental abnormalities or trauma. Bone reconstruction is the procedure of repair, rebuilding, and reshaping of skeleton bones. The goal of bone reconstruction surgery is reparation and creation of vital bone tissue with a variety of treatment methods available. It involves the management of bone injuries and their sequelae such as nonunion, post-traumatic bone defects and bone infection as well as bone deformities and shortening of the extremities due to acquired conditions or congenital malformations. It aims to correct bone loss, length and axis, reshape a limb segment and change its malposition so that to restore or improve its anatomy and functions.

The Ilizarov method is one of the current methods used in bone reconstruction. It originated in the middle of the past century and comprises a number of bone reconstruction techniques performed with a ring external fixator developed by Ilizarov GA (1921-1992) in 1951 in the former Soviet Union[1]. Professor Ilizarov GA (Figure 1) and his team were searching for solutions to develop external fixation (EF) techniques to treat the pathology of long and short bones of both upper and lower limbs, cancellous bones of the skull, pelvis and spine, and joint disorders at one of the largest orthopedic centers for limb reconstruction founded in Kurgan (Russia) in 1971[1-4]. Bone repair and reconstruction with this method are realized by means of applying compression or distraction forces to bone fragments for bone consolidation, axial alignment or new bone formation through the phenomenon of distraction osteogenesis induced by tension stress with the Ilizarov apparatus based on external supports and transosseously drilled wires that, driven with threaded units, are able to produce multiplanar actions on bone fragments. The scientific activity of the Kurgan institute for traumatology and orthopedics promoted basic research on the investigation of bone and soft-tissue regeneration[1-4]. The fundamental and clinical studies on the principles of bone regeneration and reconstruction using the Ilizarov tension-stress effect were disclosed in the author's monograph and several publications that appeared in the English language at the end of the last century[2-4]. They have been considered as major publications of the author and still are his most read works that have been cited more than 1500 times. The Ilizarov bone compression-distraction method, implemented with the author's apparatus, has been called the classical Ilizarov method[1].

The Ilizarov method techniques became known to the world orthopedic community and started to be used in several European countries in the 1980s. Since then, the original method has been used along with a number of its modifications and developments due to emergence of new fixation devices and techniques of their application[1,5,6]. The geography of their application has expanded much while the advancements in bone reconstruction that followed are of international significance and gave rise to a relatively new orthopedic subspecialty which has been termed limb lengthening and reconstruction surgery (LLRS)[7,8]. The purpose of this update was to

Figure 1 Ilizarov GA at the beginning of his career in Kurgan (1960). Photo courtesy of the Ilizarov Center Museum.

summarize the clinical practice and research in bone reconstruction with the Ilizarov and LLRS techniques published in the last 5 years with a special focus on their modification, advance, and recognition by the world orthopedic community.

BONE FIXATION DEVICES

Internal or external bone fixators are mechanical means in bone reconstruction ensuring the stability of a fractured or osteotomized bone, bone compression or distraction, and guided fragment transport. The Ilizarov system that comprises circular external fixator modules and techniques of their application for specific clinical situations[4] has experienced many modifications over the last 50 years[9,10]. Development and progress in bone fixation devices have been greatly influenced by the Ilizarov's "revolutionary entrance" to the world of orthopedics and aimed at constant improvement of clinical outcomes and patients' comfort. External fixators (the Ilizarov apparatus, hybrid and hexapod external fixators, the Orthofix limb reconstruction system, the Taylor Spatial Frame) are the main devices in bone reconstruction surgery that involves new bone formation and correction[5,6,10]. The conventional circular external fixator has been enhanced with innovative configurations, pin and ring modifications, wire and half-pin coatings that can potentially decrease infection rates in thick soft-tissue limb segments while parts fabricated from carbon fibers make the whole circular frame weight lower[5,9]. Monolateral rail external systems have been used for a better comfort of patients undergoing a bone lengthening procedure in the femur[6]. Computerized circular fixators and motorized intramedullary lengthening nails which ensure distraction osteogenesis have been called the major orthopedic advances in the techniques of limb lengthening[5]. However, they are either dependent on specialized computer software and computed tomography (CT) data or costly for the health systems and therefore cannot be used on a large scale. New systems have been designed based on a commercially available motorized lengthening nail for an all-internal segmental bone transport and optional lengthening but their application has been still under investigation[11]. Motorized internal lengthening plates for lengthening in the situations in which intramedullary nailing is contraindicated have been recently under development and might be a major advancement in the field of limb lengthening[12].

Nevertheless, despite the emergence of innovative devices, the Ilizarov-type external fixators remain affordable and preferred devices for management of a great variety of orthopedic conditions due to good clinical results achieved by their application, fast bone tissue formation during callus distraction, much less shear forces compared to unilateral external or hexapod fixators, versatility and lower costs[6]. Moreover, their manufacture has been organized by international and national companies in many countries of the world.

CURRENT CLINICAL PRACTICE AND RESEARCH IN THE ILIZAROV TECHNIQUES OF BONE RECONSTRUCTION

Our review is based on a comprehensive literature search for clinical studies and research on the current use of the Ilizarov techniques for bone reconstruction or their modifications in PubMed, Scopus and Web of Science databases written in the English language and published in the period from 2016 to 2020 with a special emphasis on the international representation of their authors and journals of their publication. The studies available from the journals included into the international indexing systems above mentioned were grouped according to their targeted applications, as described by Ilizarov GA[1,4]. The international influence of the Ilizarov method on the current state of bone reconstruction was reviewed in regard to the origin country of the authors and the impact factor that measures journal's citations, and therefore shows journal's significance for the world orthopedic audience.

Fracture repair

The use of EF in the management of fractures is an old concept. Ilizarov GA and his Kurgan team attempted to design a set of the external apparatus parts that could be assembled into frames for definitive treatment of bone injuries and on any bone segment, including hand and foot bones[4]. However, the evolution of fixation means and of the Ilizarov techniques over the years has specified the fracture types for which the Ilizarov external frames are more efficient. First of all, those are complex open and closed comminuted fractures which are not amenable to open reduction and internal fixation or cast immobilization[13,14]. Indications include pediatric juxta-articular distal radial, distal femoral, distal humeral and distal tibial fractures that are comminuted, complicated, and/or open[15]. The basic principles of the Ilizarov fixation for fracture repair in children avoid additional injury to the growth plate with K-wires, enable careful and accurate reduction without interfragmentary compression, ensure anatomic alignment and fracture stability, preserve periosteal blood supply and allow for joint motion and early weight-bearing. Management of complex pediatric tibial fractures (open injuries, with bone loss or soft-tissue compromise) with the Ilizarov fixator was found safe, effective and reliable with good functional results and health-related quality of life during treatment[16]. Numerous published reports regarding complex trauma reflect the utilization of the Ilizarov techniques in adults, especially for para-articular injuries[17-24]. The Ilizarov bone transport for isolated and *comminuted tibial* fractures with bone defects or tibial deformities was found effective after studying its long-term outcomes and complications at one center for more than 30 years[25]. The Ilizarov ring fixator was recommended as an effective treatment modality for open comminuted distal femur fractures and resulted in high union rate, adequate alignment and satisfactory functional outcomes[17]. It can be reliably used and showed good clinical and quality-of-life results in adult trauma for tibia plateau and pilon fractures[18-22]. Clinical and radiographic outcomes of the Ilizarov technique for high-energy pilon and severe tibial plateau fractures (Schatzker IV-VI) were accompanied by minimal complications or impaired functions. Definitive fixation with circular external fixator in the patients with multiple traumatic injuries was effective in a comparative study evaluating its outcomes *vs* plating for complex Schatzker VI tibial plateau fractures with better union rates, lower infection and compromised soft tissues problems despite some walking impairments detected[18]. There was no difference regarding the rate of deep infection, reoperations, range of knee motion and concerns about physical satisfaction between the two groups treated for proximal tibial fractures with the Ilizarov frame or locking plates[22]. Neglected tibial pilon fractures treated with the Ilizarov frame healed without deep infection and ankle arthrodesis was avoided in most cases[21]. The use of EF for treating displaced intra-articular calcaneal fractures was an alternative to plating and screw fixation with good results achieved by clinicians in most cases due to early mobilization of the peritalar joints and early post-operative loading[23,24]. Long-term functional outcomes of definitive treatment utilizing bone transport for exposed comminuted tibial fractures with bone defects were in line with the literature[25].

The Ilizarov fixator was used in elderly patients for tibia plateau fractures, pilon fractures, ankle fusions, non-unions, deformity correction and miscellaneous trauma [26]. It was concluded that there was no difference between the subgroups of diseases concerning the physical and mental health. First reports on Ilizarov EF for periprosthetic femur and tibial fractures after total knee arthroplasty (TKA) have appeared and have been judged as a feasible and low invasive treatment option providing stable fixation, early post-operative mobilization and no major complications what is

especially important in elderly individuals after TKA[27]. Microvascular fibular grafting was combined with the Ilizarov circular fixation for large acute bone defects in severe trauma with acute bone loss[28]. And finally, placement of the Ilizarov external frame has been much used as a temporary bone fixation means in polytrauma cases and acute compartment syndrome due to high-energy trauma in the lower limbs [29]. The authors of the studies point to the advantages of the Ilizarov fracture stabilization such as maintaining the frame till union, early mobilization, restoration of the normal lower extremity alignment, versatility, and improved union rate in patients with multiple traumatic injuries, including exposed fractures associated with soft tissue trauma.

Long-bone nonunion and defects, including infected ones

The management of bone defects and nonunion continues to be a subject of great interest in the international orthopedic literature[30,31]. A contemporary surgeon has a number of options with proven clinical evidence for management of bone defects and nonunion. Depending on the anatomical location and the size of the defect, current treatment techniques range from acute shortening to vascularized bone grafts, the Ilizarov bone transport and the Masquelet induced membrane technique[31-33]. As shown by several comparative studies, these treatment options have their advantages and limitations. However, the Ilizarov bone transport has been the most frequent practice in nonunion and defect management, especially in infected tibia[34,35]. Current clinical investigations focus on the need for complete eradication of infection through radical debridement[34-39]. Deep femoral infection resulting from intramedullary fixation of closed femoral fractures was resolved with staged treatment that included radical debridement and continuous canal irrigation, followed by monolateral bifocal bone transport[36]. The technique of an L-shaped partial corticotomy with preservation of intact and uninvolved posterior tibial bone was proposed that reduced circular fixator duration in the cases of focal tibial osteomyelitis and bone deficit of 8 cm after debridement[37]. Extensive debridement of all the devitalized tissues and bone transport was a reliable solution in the treatment of gunshot bone defects of the tibia[38]. On the contrary, limited debridement was enough to control infection and achieve good results without radical resection in managing chronic osteomyelitis in pediatric cases[40]. Both bone transport and soft-tissue flaps were used concurrently for management of post-traumatic composite bone and soft tissue defects[41]. EF techniques were found to play a key role in the management of nonunion after Monteggia injuries[42,43]. Lengthening using external fixators was possible in bone resection defects due to tumors[44,45].

Much research has been done in finding solutions for filling critical-sized bone defects in order to promote faster new bone formation utilizing distraction osteogenesis[30,31]. There is a variety of more or less biologic alternatives for the reconstruction of defects, but still distraction osteogenesis undoubtedly has the highest potential for remodeling[31]. One of them is trifocal treatment (two lengthening sites) that shortens EF duration[38]. It was associated with better results compared with bifocal treatment (one lengthening site) for defects of > 8 cm, despite a longer operative time in the trifocal group. Several mechanical solutions utilizing compression and distraction were proposed for failed distraction osteogenesis in large bone defects[46]. One more technique is ipsilateral fibula expansion that is an option of radial instead of longitudinal distraction osteogenesis. Gradual fibular transfer with the Ilizarov external fixator was used in post-traumatic and post-infection large tibial bone defects[47,48]. Although the induced membrane technique has gained much popularity in bone defect treatment, the Ilizarov bone transport remains the main tool in the situations with bone deformity and limb length discrepancy[31]. Its main merits are viable new bone formation to bridge the defect, high union rates and functional use of the limb throughout the course of its many-months treatment, preventing disuse osteoporosis[33-35,49].

Long-bone lengthening and deformity correction

Most modifications of the classical Ilizarov method refer to limb lengthening and deformity correction. First, it was the Taylor Spatial frame supplied with computer guidance for long-bone lengthening and deformity correction[5,6,50]. Then, EF was supplemented by internal fixation with a nail. The combined modifications used currently are lengthening over nail and lengthening and then nailing techniques[6]. One more combined technology is the use of flexible intramedullary HA-coated wires along with the Ilizarov apparatus[51]. These techniques apply external fixators in the lengthening procedure and intramedullary nails in the regenerate consolidation phase to protect the regenerate. However, the comparative studies evaluating the efficacy of

bone formation and prevalence of complications show that they are superior to the conventional method only in regard to the EF index and decrease in the total time of being with the external fixator on[52]. The most recent developments are motorized implantable lengthening nails that provide reasonable lengthening magnitudes[6,53-55]. Despite the complications reported in small series of patients, the new technology of motorized intramedullary nails (MIMN) has simplified upper limb lengthening surgery and made lower limb lengthening more comfortable for patients[53]. Monolateral EF lengthening was compared with MIMN lengthening in children with congenital femoral deficiency and similar lengthening parameters[54]. The MIMN group had lower complication rates and better range of motion at the end of distraction and at consolidation. MIMN technology yields better results for range of motion, which is one of the benefits to patient's quality of life. Improved patient comfort and psychological tolerance, faster recovery of activities, low infection rates and absence of fractures in the regenerated bone are the merits of MIMN against the limitations, such as maximum distraction of 5 cm and the fact that it cannot be used if the growth plates are still open. The PRECICE nail was found to carefully manage the rate of distraction to prevent complications in bone consolidation but the remote controller and the cost were found its weak points[6,55]. Moreover, it was reported that reamed intramedullary nailing showed an adverse effect on bone regeneration during the distraction phase in tibial lengthening[56].

Limb deformity and shortening remains a main issue of bone reconstruction in pediatric orthopedics and its correction is a necessity for a variety of rare congenital conditions[57-61]. EF systems are preferred by the surgeons in pediatric cases[57-59]. Ilizarov two-ring tibial lengthening was found effective in maintaining segmental alignment, efficient in callus production and relatively comfortable for pediatric patients with few significant complications[58]. Monolateral external systems for femoral lengthening were used children and adolescents[59]. Despite the popularity of guided growth systems, the EF role in pediatric deformity correction is significant and can be played by different external devices that allow multiplanar corrections[62]. Nevertheless, Ollier's disease, fibrous dysplasia, osteogenesis imperfecta and other metabolic diseases are still great challenges for orthopedic surgeons[63-66]. Titanium or hydroxyapatite-coated elastic nails in combination with an external fixator may be a way out in limb lengthening and deformity correction of abnormal bone in children [61,65]. These thin HA-coated implants show osteoactive properties and do not migrate as reported by long-term follow-ups. Upon external frame removal after completion of correction, they remain in situ for reinforcement of the abnormal bone in patients with metabolic bone disorders and skeletal dysplasia. Correction through combined bony realignment and lateral collateral ligament tightening in achondroplasia was reported with good or excellent subjective outcomes[66].

Very good results were achieved in humeral lengthening with the Ilizarov techniques. Although the motorized nails were also attempted for this purpose, more magnitude was achieved with EF[67-69]. A series of extensive lengthening in patients with achondroplasia and hypochondroplasia was compared showing complications by bone segment, and between the techniques of simultaneous bilateral lengthening and crossed lengthening[70]. Humeral lengthening in that series was associated with significantly fewer complications and quicker healing than lower-extremity lengthening. The crossed lengthening technique in the lower extremity had a greater incidence of malalignment and leg-length discrepancy compared with the transverse technique. This experience may be useful for limb lengthening done for esthetic purposes[6,71,72]. Recently, limb lengthening for esthetic purposes in patients with constitutional short stature performed either with the Ilizarov-type fixator in the tibia or MIMN in the tibia and femur has become very popular. It was shown to be safe and was judged beneficial to the patients in regard to their social capabilities and self-confidence. Yet, patients should be well informed about the complications and risks of the esthetic lengthening surgery[72].

The basic osteotomy techniques were discussed in regard to bone formation and the study stressed the importance of the procedure for qualitative distraction osteogenesis [73]. The regular 1-mm rate of daily lengthening, confirmed in the historical experiments by the Ilizarov's team[4], should be followed with any fixator or adjusted down if problems appear in order to have stable bone regeneration[48]. The regenerate condition and consolidation is of primary concern to allow full weight-bearing[74]. Current research in limb lengthening has been based on the experiments which are aimed at distraction osteogenesis acceleration and faster regenerate maturation that take many months to complete efficient bone formation. The protocol of injecting bone marrow aspirate concentrate in multiple areas of poor regenerate was used to correct delayed union in achondroplasia during distraction osteogenesis, but the study evokes

concerns of bias in confirming its role for faster healing[75]. Several studies used pharmacological agents to improve regenerate formation. Teriparatide, the bioactive component of parathyroid hormone, was delivered by daily subcutaneous injections after bone-transport docking[76,77]. It was stated that teriparatide treatment during the consolidation phase of distraction osteogenesis doubled the mineralization rate of the regenerate when compared to no treatment. The experiment on a canine model attempted automated high-frequency distraction with a daily 3-mm rate and confirmed that the bone had the potential for regeneration under the conditions described but there were concerns about the response of soft tissues and joints[78]. Histological differences were observed in bone and muscle tissue when Ilizarov fixation was supplemented by intramedullary HA-coated thin nails compared with no intramedullary stabilization in that experiment. Only few recent studies were found on the effect of mechanical forces and some agents to accelerate or improve bone regeneration[76-79]. Thus, the problem still remains on the agenda of future research. There has been an increasing interest in technologically based surgical strategies for limb deformity correction and lengthening[80]. Nevertheless, the recent advances in an increased use of computers and mobile devices along with the application of dynamic hexapod EFs and MIMN are still based on the principles described by Ilizarov GA and Paley D.

Rare conditions

Although there is a lot of investigation on the management of congenital pseudarthrosis of the tibia (CPT) and an extreme interest to the Masquelet technique attempted recently for this rare pathology, the appropriate solutions have not been found yet[81-86]. Latest reports support a combined basis in CPT management for both the biological and mechanical components of the conditions, utilizing the Ilizarov EF and intramedullary rod stabilization along with a corticocancellous bone autograft. It could ensure a statistically significant reduction in the number of refractures compared with standalone fixation methods. A multicenter study of the influencing factors in the management of Crawford-type IV CPT with follow-ups till skeletal maturity showed that the use of the Ilizarov technique, transfixing the ankle and subtalar joints, use of a cortical graft and not operating on the fibula were associated with better outcomes than combining intramedullary nailing with the Ilizarov technique and the use of bone morphogenetic protein[85]. The induced membrane technique combined with the Ilizarov bone transport has been tried to improve the outcomes of CPT management and demonstrated promising results in regard to avoid refractures[86]. It also included morphological investigation of the human induced membrane and its potential for osteogenesis. Injections of bone marrow aspirate concentrate in the pseudarthrosis site after focus removal in combination with circular EF achieved faster bone healing compared with EF only, and the lower refracture rate but a longer follow-up would be required to determine if the results of this adjuvant therapy will hold up over time[87]. It was revealed that additive rhBMP-2 might shorten the time to initial healing of pseudarthroses but not guarantee bony union[81]. Severe cases of proximal tibial dysplasia associated with CPT were treated using lengthening either with a transphyseal distraction or an osteotomy directly next to the physis[88]. It found that lengthening through the physis had a lower healing index (faster healing) than after metaphyseal corticotomy but should be best done near maturity. Reconstruction with several procedures along with EF ended in limb salvage in tibial hemimelia[89,90]. Lengthening and deformity correction with the Ilizarov principles were reported for multiple hereditary exostoses of the forearm, radial deformity, radial clubhand, ulnar longitudinal deficiency[91-94]. A large series of children with hereditary exostoses was reported who were treated by either unilateral or circular EF for lengthening[91]. A technique of bifocal distal radial osteotomy for acute angular correction distally and lengthening with EF more proximally was described for patients with distal radial deformity and concurrent shortening[92].

Foot bone malformation and deformities

The Ilizarov techniques of gradual correction in multicomponent foot deformities and gradual soft tissue distraction with open releases and/or bony procedures can achieve a pain-free and plantigrade foot[95-99]. Placement of the Ilizarov-type frame on the foot and its adjustments require both an experienced surgeon and a motivated patient but the techniques achieve the goals both in bone reconstruction and functionality of the foot. In complex cases, distraction osteogenesis should be reserved as a salvage solution and should be performed at specialized centers. The techniques for foot pathology are implemented with a number of frame modifications, including hexapod external fixators[99]. The techniques may be regarded as salvage procedures in

neglected adult clubfoot, challenging ulcerations, ankle joint arthrodesis for treating Charcot neuroarthropathy despite the complications[96,100-103]. Thus, a hybrid technique of circular EF and an intramedullary nail coated with antibiotic cement salvaged lower limbs in most patients and achieved a functional and clinically stable foot in infected neuropathic ankles[104]. Infected ankles were also salvaged with the Ilizarov method[104-106]. Reconstruction of the hind foot and ankle with concurrent lengthening through a distal tibial corticotomy utilizing the Ilizarov frame was found comparable to other treatment alternatives[107]. Modifications were proposed for rare congenital malformations of the foot, including brachymetatarsia and cleft foot[108-110]. Different foot and ankle frame assemblies were grouped into a few standard hexapod configurations and foot treatment strategies were demonstrated[111].

Hand malformation and deformities

The Ilizarov-type external mini-fixator and some other small external fixators were specially developed for hand bone injuries, lengthening, congenital malformation and deformities[112-115]. They confirm the success of the ideas of Ilizarov GA in utilizing distraction osteogenesis and soft tissue traction in the management of hand pathology [4].

Joint disorders

Ilizarov's ideas also contributed to joint reconstruction surgery[4,116]. Reconstruction techniques continue to find applications in the management of complex pediatric hip pathology. Recently, good results have been reported using EF systems for correction of proximal femoral deformities secondary to slipped capital femoral epiphysis, Perthes' disease in children, coxa vara, sequelae of pediatric hip septic coxitis, and ischemic deformities of the hip[116-121]. A safe and effective technique of a low-profile Ilizarov external fixator was applied for developmental coxa vara following an acute, opened wedge subtrochanteric valgus-flexion-derotation femoral osteotomy using a percutaneous multiple hole drilling for treating multiplanar proximal femoral deformities in children[117]. Proximal femoral and triple pelvic osteotomies and the Ilizarov frame module were successfully used for treatment of adolescent developmental hip dysplasia[119]. Pertrochanteric osteotomy and femoral neck lengthening by distraction were efficient in treatment of proximal hip ischemic deformities in children [120]. Management of a chronic, traumatic posterior hip dislocation in an 8-year-old boy by open reduction, grafting, femoral shortening, and stabilization with articulated iliofemoral EF was described[121].

Joint distraction with EF frames is not a frequent procedure but the published studies report on clinical improvements in adult patients with knee osteoarthritis [122]. Despite the short follow-ups, small sample sizes and high frequency of pin tract infection reported which is of concern, since most patients will further require joint replacement, the technique might allow delaying joint replacement surgery for several years[123]. Ankle arthrodiastasis was also shown as an option for patients with end-stage primary or post-traumatic ankle osteoarthritis[124]. The authors believe that distraction within the joint optimizes the intraarticular environment for equilibration of hydrostatic pressure, promoting subchondral morphoangiogenesis, and decreases subchondral sclerosis, thereby mitigating pain. The process allows for joint salvage as an alternative to arthrodesis or ankle implant arthroplasty. The authors see joint distraction to be a useful approach to the management of ankle pain secondary to loss of functional joint surface.

Unfortunately, arthrodesis is still a salvage surgical procedure for knee and ankle joints in cases of infected total arthroplasty, tumor, failed arthroplasty or posttraumatic complication. Arthrodesis of the knee with the Ilizarov external fixator has been found successful in achieving quality of fusion and recovery of the limb supporting function [125,126]. Effective ankle arthrodesis using either external or internal fixation was reported but better outcomes were achieved in the EF group[127]. The technique of tibiotalocalcaneal arthrodesis in patients with and without diabetes, closed arthrodesis in infected neuropathic ankles and infected ankle fractures with segmental bone-loss using Ilizarov concepts were assessed as salvage procedures[107,128,129]. An interesting study on the use of shoulder arthrodesis for septic arthritis of the shoulder due to proximal humerus osteomyelitis was presented[130].

Other pathology

We should finally mention flat bone reconstruction based on the Ilizarov principles. The apparatus for transpedicular EF in spinal pathology was first experimented on animals under the supervision of Ilizarov GA and later developed by his followers at the Ilizarov Center in Kurgan[131]. It could provide gradual controlled correction for

high-grade kyphoscoliosis in adolescents and transition to internal fixation following its removal with preserved correction at long term. The Ilizarov's experimental team also investigated gradual expansion of skull bones and surrounding soft tissues. It was applied for traumatic skull defects and brain vascularity stimulation after brain stroke but the techniques remained on the stage of uncompleted clinical trials. On the contrary, the role and significance of craniomaxillofacial distraction procedures have been much discussed in the specialized literature and has been found applicable in craniofacial deficiency or dentofacial anomalies that are corrected with distraction procedures and special devices[132,133]. Another Ilizarov's idea of stimulating the vascularity in chronic ischemic diseases in the lower extremities has been revived and its modification has been called tibial transverse distraction[134,135].

THE INTERNATIONAL IMPACT OF THE ILIZAROV METHOD ON THE EVOLUTION OF BONE RECONSTRUCTION SURGERY

The laws of compression-distraction osteogenesis due to tension-stress effect were discovered by Professor Ilizarov GA and his team of scientists more than 60 years ago and the techniques were termed "transosseous osteosynthesis"[1-4]. Our literature review shows that they have been still largely implemented with the external apparatus that bears his name. The versatility of the assemblies constructed from the Ilizarov apparatus set of parts resulted in a great variety of possible applications in bone reconstruction surgery that are fracture repair, bone nonunion, mal-union, bone defects, limb length discrepancy, long-bone deformity, hip disorders, knee arthrodesis, ankle arthrodesis, foot deformities, foot bone lengthening, anomalies and fractures of the hand. It is the main tool in the management of complex intraarticular fractures, bone transport and bone infection in the tibia, foot deformities and ankle arthrodesis. No other system of external bone fixation is able to produce so many options and variants used for bone recovery. The biological phenomenon of distraction osteogenesis developed by Ilizarov GA may be considered one of the greatest achievements in bone reconstruction surgery.

Our goal was to present to your attention the studies on the current international practice and research in bone reconstruction that have been based on the Ilizarov's ideas. The search for literature in the international databases has revealed a huge amount of practical studies that encapsulate a broad spectrum of pathologies treated with interventions or devices developed within the LLRS subspecialty due to the impact of the Ilizarov method. The original Ilizarov techniques of bone reconstruction and their modifications or innovations have been investigated at a variety of institutions across the world but the main centers of clinical research and practice are located in the United States, United Kingdom, China, Russia, Italy, Egypt, and India [136,137]. It is well seen from Table 1 that presents the number of authors per country that published their studies in the period under investigation (data from PubMed platform of the National Library of Medicine, United States) (Table 1).

The impact of the Ilizarov method on bone reconstruction surgery is of great international value. Interestingly, but the shortcomings of the Ilizarov method which are mainly related the ring fixator such as transfixation of muscles and other soft tissues with wires and half-pins, pain, pin-tract infection, and psychosocial limitations imposed on the patient due to prolonged use of the Ilizarov circular fixator have led to vigorous research and development of new devices able to decrease or avoid them. However, the principles of new bone tissue formation discovered by Ilizarov GA have been recognized as universal. Ilizarov-minded surgeons continue to use this method due to its efficacy proven by more than a half-century practice. LLRS has been regarded as an orthopedic subspecialty that emerged due to the advancements in bone reconstruction after the introduction of the Ilizarov method[138]. National limb lengthening and reconstruction societies, though under various names, have been active worldwide. The first one was the Association for the Study and Application of the Ilizarov Methods (ASAMI) that appeared in Italy and was the one that played the major role in the popularization of the Ilizarov techniques. Its activities were broadened by the International ASAMI and the International LLRS which hold biannual meetings around the world. Such meetings and courses were held in Milan, Baltimore, Cairo, Lima, St. Petersburg, Barcelona, Bombay, San Paolo, Miami, Liverpool, Dhaka, Sydney, and other cities. The nearest meeting has been scheduled to be held in Mexico in 2022. There is a LLRS specialty day at the annual meeting of the American Academy of Orthopaedic Surgeons at which bone reconstruction surgeons from around the world present their studies and hold workshops. The *Journal of Bone*

Table 1 Number of authors per country that published their studies on bone reconstruction with the Ilizarov techniques or their modifications (PubMed search results for 2016-2020)

#	Country	Number of authors	%	#	Country	Number of authors	%
1	China	105	19.1	26	Spain	4	0.7
2	Russian Federation	52	9.5	27	Nigeria	4	0.7
3	United States	43	7.8	28	Belgium	3	0.5
4	United Kingdom	40	7.3	29	Canada	3	0.5
5	India	39	7.1	30	Indonesia	3	0.5
6	Egypt	39	7.1	31	Serbia	3	0.5
7	Japan	22	4.0	32	Singapore	3	0.5
8	Poland	21	3.8	33	Cameroon	3	0.5
9	Pakistan	18	3.3	34	Iran	2	0.4
10	Turkey	16	2.9	35	Netherlands	2	0.4
11	Italy	15	2.7	36	Finland	1	0.2
12	Germany	12	2.2	37	Iraq	1	0.2
13	Bangladesh	10	1.8	38	Ireland	1	0.2
14	Switzerland	9	1.6	39	Israel	1	0.2
15	Thailand	8	1.5	40	Kuwait	1	0.2
16	Australia	7	1.3	41	Mexico	1	0.2
17	Greece	7	1.3	42	Morocco	1	0.2
18	Tunisia	7	1.3	43	Philippines	1	0.2
19	France	6	1.1	44	Puerto Rico	1	0.2
20	South Korea	6	1.1	45	Saudi Arabia	1	0.2
21	Austria	5	0.9	46	Sudan	1	0.2
22	Brazil	5	0.9	47	Portugal	1	0.2
23	Denmark	5	0.9	48	Argentina	1	0.2
24	Malaysia	5	0.9	49	Lebanon	1	0.2
25	South Africa	4	0.7		Total of authors	550	100

and Joint Surgery of the Association of Bone and Joint Surgeons publishes annual guest editorials on the topic of new studies in limb lengthening and deformity correction [136].

Our survey which is based on the data from the international databases for the latest 5-year period has revealed that more than 150 journals dedicated their space to the topic under our discussion. These journals published more than 750 articles on the Ilizarov techniques of bone reconstruction and their modifications submitted by the authors from 50 countries. SCImago metrics on ratings of the journals in the field of Orthopedics&Sports Medicine based on Scopus® database shows that numerous studies have been published in the journals of high citation level and international value (Table 2). The high-rated journals, popular among orthopedic surgeons, such as *Injury*, *Bone and Joint Journal*, *Journal of Paediatric Orthopaedics*, *International Orthopaedics*, *Journal of Foot and Ankle Surgery* have published the biggest number of the articles (Table 2). Table 2 also lists the countries of the authors that published their clinical and basic research on the Ilizarov techniques, their modifications and related fields of study. The most read and cited orthopedic journals also appear to have a wide authors' representation from around the world.

Authors from the countries with large population such as China, the United States, India and Russia came first in the line. China was formally introduced with the Ilizarov method in 1990 but has become the leader in the last 10 years. The interest to the original method evoked new ideas and applications, including continuous basic research on the biological mechanisms of distraction osteogenesis and its translation to

Table 2 Publication of studies on the Ilizarov techniques or their modifications in the international journals of high scientific impact and specialized limb lengthening and reconstruction surgery journals in 2016-2020 (SCImago metrics and Scopus database)

#	Journal title	Society, institution or publishing company	SJR 2019	Number of articles	Origin country of the authors of the studies
Quartile Q1					
1	*Injury*	British Trauma Society, Australasian Trauma Society, Saudi Orthopaedic Association in Trauma	0.904	40	Australia, Austria, China, Egypt, Germany, India, Italy, Japan, Malaysia, Poland, French Republic, Serbia, South Africa, Spain, Switzerland, Turkey, United Kingdom, United States
2	*Bone and Joint Journal*	British Editorial Society of Bone and Joint Surgery, United Kingdom	2.375	14	Australia, Austria, China, Egypt, Germany, India, Italy, Kuwait, Pakistan, Russia, South Korea, Switzerland, United Kingdom
3	*International Orthopaedics*	International Society of Orthopaedic Surgery and Traumatology (SICOT)	1.533	14	Austria, China, Egypt, Ireland, Japan, Russia
4	*Journal of Orthopaedic Trauma*	Orthopaedic Trauma Association, AO Trauma North America, Belgian Orthopaedic Trauma Association, *etc.*	1.023	9	Egypt, Japan, Switzerland, United Kingdom, United States
5	*Archives of Orthopaedic and Trauma Surgery*	Springer Verlag, Germany	1.152	8	Belgium, Egypt, Italy, Netherlands, Poland, Russia, Serbia, South Africa, Switzerland, United Kingdom
6	*Journal of Pediatric Orthopaedics*	Pediatric Orthopaedic Society of North America (POSNA)	1.19	7	Egypt, India, Iran, Republic of Korea, United Kingdom, United States
7	*Clinical Orthopaedics and Related Research*	Association of Bone and Joint Surgeons	1.487	5	Australia, China, United Kingdom
8	*Knee*	British Association for Surgery of the Knee, the Australian Knee Society, and the German Knee Society	1.083	4	China, Greece, Italy, Turkey
9	*Scientific reports*	Universities and research institutions, United Kingdom	1.341	4	China, Poland
10	*HSS Journal*	Hospital for Special Surgery, United States	0.76	3	Israel, Italy, Russia, United States
11	*Orthopaedics and Traumatology: Surgery and Research*	French Society for Orthopaedic Surgery and Traumatology (SoFCOT)	0.949	3	Egypt, France, United Kingdom
Quartile Q2					
12	*Journal of Orthopaedic Translation*	Chinese Speaking Orthopaedic Society (CSOS) and the International Chinese Musculoskeletal Research Society (ICMRS)	0.73	16	China, Hong Kong, United Kingdom
13	*BMC Musculoskeletal Disorders*	BioMedCentral, part of Springer Nature	0.76	12	China, Japan, Mexico, Poland
14	*Journal of Pediatric Orthopaedics Part B*	International Federation of Paediatric Orthopaedic Societies (IFPOS)	0.411	12	China, Egypt, India, Poland, French Republic, Spain, United Kingdom, United States
15	*Journal of Foot and Ankle Surgery*	American College of Foot and Ankle Surgeons	0.619	11	China, Egypt, Greece, Japan, French Republic, United Kingdom, United States
16	*Medicine (United States)*	Medicine®, universities and research institutions in the United States	0.639	8	China, Japan, Poland, United States
17	*Journal of Orthopaedic Surgery and Research*	BioMedCentral, part of Springer Nature	0.669	7	China, Denmark, Germany, Poland, United Kingdom, United States
18	*Journal of Orthopaedic Science*	Japanese Orthopaedic Association	0.56	6	China, Japan, South Korea, United Kingdom
19	*Journal of Children's Orthopaedics*	European Paediatric Orthopaedic Society (EPOS)	0.597	5	Egypt, France, Italy, Russia, Switzerland
20	*Acta Orthopaedica et Traumatologica Turcica*	Turk Ortopedi ve Travmatoloji Dernegi	0.442	4	China, Russia, Turkey
21	*European Journal of Orthopaedic Surgery and Traumatology*	Springer-Verlag France SAS, part of Springer Nature	0.681	4	Egypt, Greece, Italy, Serbia, United Kingdom, United States
22	*Orthopaedic Surgery*	Chinese Orthopaedic Association and John Wiley and Sons Australia, Ltd.	0.618	4	China, Thailand

23	*World Journal of Orthopaedics*	Baishideng Publishing Group	0.798	4	Egypt, Russia
24	*Foot and Ankle Surgery*	European Foot and Ankle Society	0.716	3	China, Egypt
Quartile Q3					
25	[1]*Strategies in Trauma and Limb Reconstruction*	British Limb Reconstruction Society	0.481	30	Australia, Denmark , Egypt, India, Italy, Pakistan, Russia, Singapore, Turkey, United Kingdom, United States
26	*Indian Journal of Orthopaedics*	Indian Orthopaedic Association (IOA)	0.39	10	Greece, India, Italy, Russia
27	*Journal of Clinical Orthopaedics and Trauma*	Delhi Orthopaedic Association	0.469	10	India, Italy, Russia, Thailand
28	*Journal of Orthopaedics*	Prof. PK Surendran Memorial Educational Foundation and Indo Korean Orthopaedic Foundation	0.2	10	China, India, Indonesia, Japan, Russia, Turkey, United Kingdom, United States
29	*Ortopedia Traumatologia Rehabilitacja*	Foundation of Medical Education, Poland	0.195	6	India, Italy, Poland
30	*Revista Brasileira de Ortopedia*	Brazilian Society of Orthopedics and Traumatology	0.437	6	Brazil, China, India, Russia
31	*Chinese Journal of Traumatology*	Daping Hospital and the Research Institute of Surgery of the Third Military Medical University	0.385	5	Brazil, India, Russia, Singapore
32	*Clinics in Podiatric Medicine and Surgery*	Clinics series, ELSEVIER	0.326	5	United States
33	*Acta Orthopaedica Belgica*	The Belgian Orthopaedic Trauma Association	0.31	4	Egypt, India, Russia, United States
34	*Malaysian Orthopaedic Journal*	Malaysian Orthopaedic Association and ASEAN Orthopaedic Association	0.25	4	India, Pakistan
Quartile Q4					
35	[1]*Genij Ortopedii*	Association of Study and Application of Methods of Ilizarov (Russia)	0.151	109	Bangladesh, France, India, Russia, Switzerland, United States, Uzbekistan
36	*Trauma Case Reports*	Affiliated to *Injury* Journal	0.15	4	Japan
37	*Mymensingh Medical Journal*	Bangladesh Academy of Sciences	0.159	3	Bangladesh
38	[2]*Journal of Limb Lengthening and Reconstruction*	Association of Study and Application of Methods of Ilizarov and the International Limb Lengthening and Reconstruction Society	-	80	India, United States, United Kingdom, Portugal, Brazil, Japan, Egypt, Canada, South Africa, Saudi Arabia, Malaysia, Russia, Italy, Germany, Lebanon, Greece, Israel, Argentina, Australia

[1]Specialized limb lengthening and reconstruction surgery (LLRS) journals.
[2]Specialized LLRS journals not included in Scopus. SJR: Scientific Journal Ranking (SCImago Journal and Country Rank).

the clinical practice[137]. One of the newest editions is the *Journal of Orthopaedic Translation* of the Chinese Speaking Orthopaedic Society (CSOS) and the International Chinese Musculoskeletal Research Society (ICMRS) which main goal is to publish papers that "identify and fill scientific knowledge gaps at the junction of basic research and clinical application (from bench to bedside) or community application (from bench to community)". It published 16 articles on the application of the techniques based on the Ilizarov method and basic research in a special issue (November 2020), titled *Ilizarov Techniques in China for 30 years: From Research to Clinical Translation* that focuses on shortening of treatment duration by stimulating distraction histogenesis [135,137].

There are three specialized journals that are meant by their founders to be dedicated to LLRS. *Strategies in Trauma and Limb Reconstruction* of the British Limb Reconstruction Society has been adopted as the English language journal on this subspecialty by several ASAMI and LLRS societies (Brazil, Egypt, Japan, LLRS North America, LLRS South Africa, LLRS Nordic, ASAMI Philippines, Pakistan, Malaysia, South Korea, CEFM China)[1,66,73]. *Journal of Limb Lengthening & Reconstruction*, the official publication for the International ASAMI and ILLRS, is a platform for exchanging the opinions on the topics of bone and joint reconstruction that has issued six volumes since its initiation but unfortunately still lacks indexing by the interna-

tional databases of Scopus, Web of Science and the PubMed platform[8,74]. The *Genius of Orthopaedics (Genij Ortopedii)* issued at the Ilizarov National Medical Research Center for Traumatology and Orthopedics (former Russian Ilizarov Scientific Center for Restorative Traumatology and Orthopedics) by ASAMI Russia has been included in the Scopus database and provides a free on-line access to its volumes both in Russian and English[86]. These journals show the evolution and the main tendencies in LLSR in the post-Ilizarov era reflected in clinical and basic research.

It is no doubt that the use of the Ilizarov method has been discussed in general medical and orthopedic journals that are issued in national languages or are read at national level. Those journals may not be included into the famous databases and are not so much known to the international orthopedic community but could testify on the geography of the Ilizarov method distribution across the continents[139]. The studies written by the authors from Cameroon and Nigeria on Ilizarov limb reconstruction in Africa conclude that the use of the Ilizarov method has been sparsely reported on the continent but should be "popularized in the countries with limited resources because it would be an attractive alternative to the amputations that are sometimes performed" [140,141].

Although the Ilizarov method requires a lot of training and expertise to perform it successfully, a great number of surgeons throughout the world have mastered its principles and basic techniques to improve or save their patients' lives. The three databases that we have reviewed include the studies of the authors practicing in 50 developed and developing nations from all the populated continents. We have undertaken a lot of effort to fulfill the noble goal of this investigation but acknowledge that our data are far from complete but they prove that the Ilizarov's ideas of bone reconstruction have been shared in clinical practice and followed across the world.

CONCLUSION

The Ilizarov's principles of bone reconstruction have stood the test of time and have been internationally recognized. It has been confirmed by numerous studies published in honored international and national journals. The Ilizarov method and other techniques based on distraction osteogenesis have been used in a great number of countries and all continents. These facts prove its international significance and confirm the greatest contribution of Ilizarov GA to bone reconstruction surgery. Undoubtedly, the great heritage he has left to the world should be emphasized once again in 2021, the year when his 100th birthday is marked.

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World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2021 August 18; 12(8): 534-547

DOI: 10.5312/wjo.v12.i8.534

ISSN 2218-5836 (online)

MINIREVIEWS

Calcar-guided short-stem total hip arthroplasty: Will it be the future standard? Review and perspectives

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Author contributions: Kutzner KP conducted the review and wrote the manuscript.

Conflict-of-interest statement: The author is a medical advisor for Mathys Ltd., Bettlach, Switzerland. No further conflicts of interest have been declared.

Manuscript source: Invited manuscript

Specialty type: Orthopedics

Country/Territory of origin: Germany

Peer-review report's scientific quality classification

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Abstract

Short stems in total hip arthroplasty (THA) are becoming increasingly popular. In Germany, already 10.4% of all primary THAs are performed using a cementless short stem. The concept of modern, calcar-guided, short stems aims for an individualized reconstruction of the hip anatomy by following the calcar of the femoral neck, a bone- and soft-tissue-sparing implantation technique, and physiological loading. The stem design uses either metaphyseal fixation alone or additional diaphyseal anchoring, depending on the stem alignment and indication. These individualized anchorage types increase the potential indications for the safe use of a short stem. The design features may account for potential advantages of current short stem implants compared with earlier short-stem designs, particularly in cases of reduced bone quality or osteonecrosis of the femoral head and femoral neck fractures. The implantation technique, however, requires distinct knowledge regarding the characteristics of varus and valgus positioning, with the potential for clinical consequences. A learning curve for surgeons new to this technique must be taken into account. Cortical contact with the distal lateral cortex appears to be crucial to provide sufficient primary stability, and the use of intraoperative imaging to identify "undersizing" is highly recommended. Current results of several national registries indicate that calcar-guided short stems are among the most successful implants in terms of mid-term survivorship. However, long-term data remain scarce. This review introduces the characteristics of calcar-guided short-stem THA and summarizes the current evidence.

Key Words: Total hip arthroplasty; Short stem; Calcar-guided; Classification; Indications;

Grade A (Excellent): A
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: February 14, 2021
Peer-review started: February 14, 2021
First decision: May 3, 2021
Revised: May 10, 2021
Accepted: July 20, 2021
Article in press: July 20, 2021
Published online: August 18, 2021

P-Reviewer: Fujino T
S-Editor: Wang JL
L-Editor: A
P-Editor: Xing YX

Anchorage; Optimys

Core Tip: Modern calcar-guided short stems offer numerous advantages compared with conventional total hip arthroplasty (THA). The broad potential to reconstruct the individual hip geometry, the reduced proximal bone remodeling, and the simplified soft-tissue-sparing implantation represent true accomplishments in THA. Mid-term data indicates encouraging outcomes and excellent implant survival. If long-term data confirm these promising results, chances are good that calcar-guided short stems will become the future standard in THA.

Citation: Kutzner KP. Calcar-guided short-stem total hip arthroplasty: Will it be the future standard? Review and perspectives. *World J Orthop* 2021; 12(8): 534-547
URL: https://www.wjgnet.com/2218-5836/full/v12/i8/534.htm
DOI: https://dx.doi.org/10.5312/wjo.v12.i8.534

INTRODUCTION

Total hip arthroplasty (THA) is considered one of the most successful procedures developed during the last century, with excellent long-term results. Worldwide, increasingly younger and more active patients with osteoarthritis are being treated, demanding increasing levels of postoperative clinical function and the ability to engage in physical activity[1]. In Europe, over 20% of all patients treated with THA are under the age of 60 years[2]. The demand for surgical procedures and implants that allow for an active, high-quality, daily life continues to grow. Minimally invasive techniques are on the rise, allowing for the performance of muscle- and soft-tissue-sparing implantations. In contemporary THA, in addition to choosing the right approach, the choice of implant can potentially determine the postoperative outcome. Selecting an adequate femoral implant strongly contributes to the optimal use of minimally invasive techniques[3].

To date, four types of femoral implants are available for THA: hip resurfacing, conventional straight stems, anatomical shortened conventional stems, and short stems.

Hip resurfacing has been introduced as a bone-sparing alternative to conventional THA, associated with a reduced risk of dislocation, easy replication of hip biomechanics, and easier revision, if necessary[4]. However, problems with femoral head necrosis and osteolysis caused by wear and metallosis caused by metal-on-metal bearing couples have resulted in a strong decline in the implantation numbers. The unrestricted use of this technique cannot currently be recommended[5].

Although excellent long-term survival rates have been reported with the use of conventional femoral stems in THA, proximal stress shielding and thigh pain often occur after THA[6-8]. In younger patients, who will likely require eventual revision surgery, the conservation of proximal bone mass and extended service life are preferable for femoral implants. Additionally, minimally invasive techniques may be adversely affected using conventional stems[3].

Short stems have become increasingly popular in recent years. Short-stem THA aims to preserve bone, prevent stress shielding, and provide favorable conditions for revision without altering the basic concepts of conventional THA. Most short-stem designs focus on metaphyseal fixation. Short femoral stems were previously developed decades ago to ensure a bone- and soft-tissue-sparing implantation approach; however, in recent years, numerous innovations and modifications have emerged on the market[9]. However, some short-stem designs have already been withdrawn from the market for a variety of reasons. In Europe, the concept of short-stem THA has become increasingly important, and implantation numbers increase yearly. For example, in Germany, 10.4% of all primary THA procedures are performed using a cementless short stem[10]. However, a large variety of short stem models are available, which differ in both design and function[11].

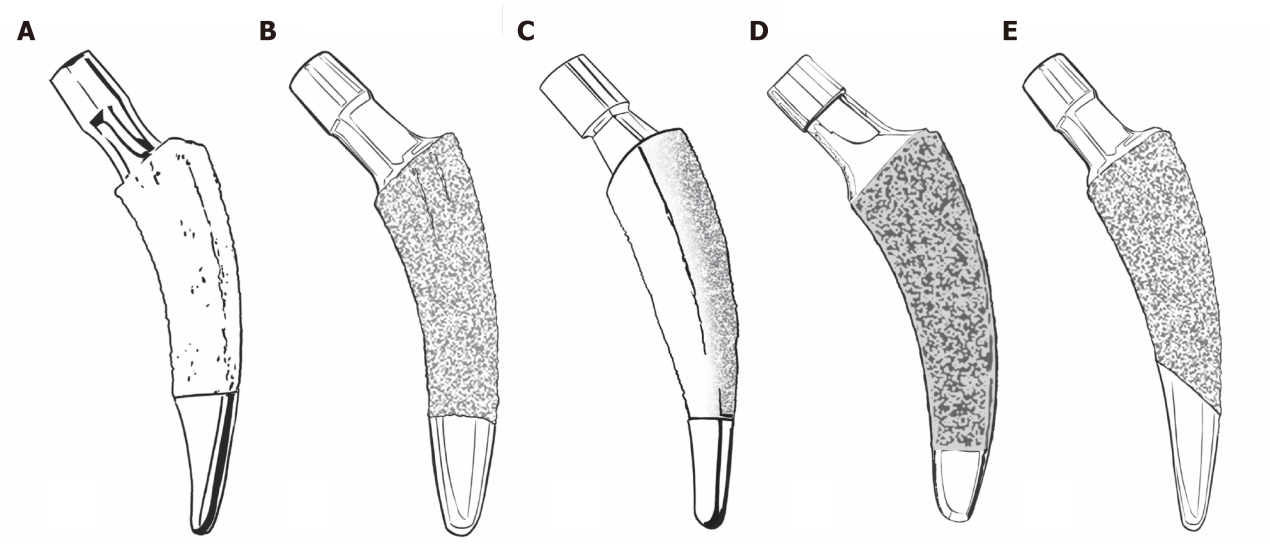

Figure 1 Common new-generation calcar-guided short stems. A: Nanos stem (Smith&Nephew, Marl, Germany; on the market since 2004); B: MiniHip stem (Corin, Cirencester, UK; on the market since 2007); C: ColloMIS stem (Lima Corporate, Villanova di San Daniele del Friuli, Italy; on the market since 2009); D: optimys stem (Mathys Ltd., Bettlach, Switzerland; on the market since 2013); E: A2 stem (Artiqo, Luedinghausen, Germany; on the market since 2016).

For most new-generation short-stem designs, short- and mid-term results have been reported[12-15]. At present, however, little data is available regarding long-term outcomes[16]. A major concern in reducing length and diaphyseal fixation of the femoral component is the concomitant reduction of implant stability and the increase of interface micromotion. By interfering with osteointegration, the long-term risk of implant loosening might increase as well[17,18]. Also, positive effects on bone remodeling and stress shielding in the long term have yet to be demonstrated for many short-stem designs[19].

The concept of modern calcar-guided short stems in THA aims for the precise reconstruction of the individual, anatomic hip geometry, using a bone- and soft-tissue sparing implantation technique associated with a physiological loading in the meta-diaphysis to conserve proximal bone stock over the long term. This new-generation short stem design allows for the reconstruction of the individual patient's anatomy by following the calcar of the femoral neck[20]. Meta-diaphyseal anchoring is applied, consisting of either pronounced metaphyseal anchorage alone or with additional diaphyseal anchorage, depending on the stem alignment and indication[15,21]. The classification of this stem design therefore is challenging; however, in Europe, the term "calcar-guided" has become established in recent years[22] (Figure 1).

CLASSIFICATION

An early classification system for short stems in THA was proposed by Jerosch[23] and adjusted by Falez *et al*[11]. This system is based on the corresponding level of the femoral neck resection, differentiating between neck-retaining, partially neck-retaining, and neck-resecting short stems. Distinctions in terms of biomechanics and implantation techniques are also considered. Another recent classification system, described by Khanuja *et al*[24], was introduced in 2014. This system categorizes all short-stem designs into four groups, in addition to subgroups. The group of partially neck-retaining stems defined by Jerosch comprises the group of calcar-loading stems defined by Khanuja *et al*[24] (Group 2). A subclassification method was added, dividing calcar-loading stems into trapezoidal, rounded, threaded, and thrust-plate designs. Modern calcar-guided short stems are almost exclusively classified as trapezoidal, rounded, calcar-loading stems according to the system defined by Khanuja *et al*[24] (Groups 2A and B). The newest generation of contemporary short stems consists almost exclusively of calcar-guided and calcar-loading short stems, such as the Nanos stem (Smith&Nephew, Marl, Germany), the MiniHip stem (Corin, Cirencester, UK), the ColloMIS stem (Lima Corporate, Villanova di San Daniele del Friuli, Italy), the optimys stem (Mathys Ltd., Bettlach, Switzerland), and the A2 stem (Artiqo, Luedinghausen, Germany) (Figure 1). All of these stem designs can be anchored either by metaphyseal anchorage alone or with the addition of diaphyseal

anchorage, depending on an individualized positioning. Thus, classification depends not only on the design features but also on the positioning.

To account for differences in the individualized positioning and anchorage of calcar-guided short stems, a second subclassification method is suggested, distinguishing metaphyseal anchorage [for example Group 2B(M)] from meta-diaphyseal anchorage [Group 2B(MD)], for all stems summarized in Group 2B (Figure 2A and B).

RECONSTRUCTION OF THE ANATOMY

The design of modern calcar-guided short stems features a characteristically rounded shape that can be adapted to the medial anatomical calcar curve (Figure 3). The positioning is performed according to the individual anatomy along the calcar curve [20]. It is dependent on the resection level of the femoral neck. This feature differentiates this design from other conventional stems and many other short-stem designs. Calcar-guided short stems can follow a valgus anatomy into a valgus position or a varus anatomy into a varus position. The positioning must be accomplished by the surgeon, through the intraoperative selection of an individualized, adjusted level of resection, according to the preoperative plan (Figure 4A and B). A high resection of the femoral neck leads to a varus position, with a corresponding high offset, whereas a low resection results in a valgus alignment and a corresponding low offset[20]. It has been demonstrated that the individual anatomy of the proximal femur can, therefore, be reconstructed across a broad bandwidth and offset, allowing leg length to be restored[25-27]. Kutzner *et al*[21] introduced a classification divided into Groups A–E, in which Groups A and B represented varus anatomies, Groups C represented a neutral hip, and Groups D and E represented valgus anatomies, based on the caput collum diaphysis (CCD) angle. A stem design with an anatomical calcar fit has been reported to be advantageous for preventing unwanted valgization[28]. Additionally, in the second plane, the natural anterior tilt of the femoral neck can only be preserved by a short femoral implant, without needing the application of high antetorsion, facilitating the restoration of both lateral and anterior offset[29] (Figure 5).

SPARING THE BONE AND SOFT TISSUE

Due to the short and rounded design, the insertion of the instruments and the implantation itself is performed using a 'round-the-corner' technique, which spares the greater trochanter region[30]. This conveniently avoids the potential fracturing of the trochanter and also reduces the damage to muscle and soft tissues that insert at the piriformis fossa and the greater trochanter, such as the crucial gluteal muscles. Compared with the implantation of conventional implant designs, more proximal femur bone mass can be preserved during short stem implantation surgery[31]. Minimally invasive approaches, without transection or damage to the muscles, are clearly facilitated by the use of this technique (Figure 6). Recent studies have indicated that calcar-guided short stems are advantageous compared with conventional stem designs in terms of intraoperative blood loss and the rates of blood transfusion[32]. In general, the design features of calcar-guided short stems are particularly suitable for minimally invasive approaches[30].

ANCHORAGE

The primary concept of short stems focuses on anchoring in the metaphysis. Most short-stem designs use three-point anchoring to achieve a stable primary fixation (Figure 7A–C). The first short-stem design to pursue this philosophy was the Mayo stem (Zimmer Biomet, Warsaw, Indiana, USA), which was introduced in 1985 and is no longer available on the market (Figure 7A). The pronounced metaphyseal anchorage aimed to achieve the physiological loading of the proximal femoral bone. The minimization of stress shielding is preferable[21,33]. The preservation of bone stock is considered to be beneficial in case future revision surgery is necessary[31]. A popular and widespread representative of the metaphyseal anchoring philosophy is the Metha stem (Aesculap, Tuttlingen, Germany) (Figure 7B). The design features of this stem in the distal part do not easily accommodate an additional diaphyseal anchorage, which is almost impossible to attain during surgery, even in neutral or

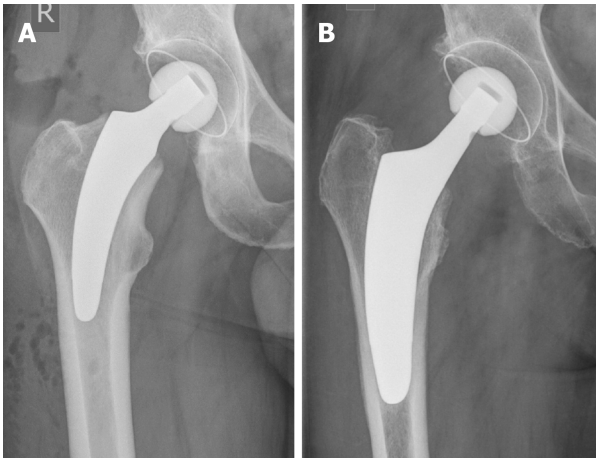

Figure 2 Introduction of a subclassification to account for the individualized positioning of group 2A and 2B stems, according to Khanuja *et al*[24]. A: Metaphyseal anchorage [for example group 2B(M)]; classical three-point anchoring; B: Meta-diaphyseal anchorage [group 2B(MD)]; additional fit-and-fill in the proximal diaphysis. Citation: Khanuja HS, Banerjee S, Jain D, Pivec R, Mont MA. Short bone-conserving stems in cementless hip arthroplasty. *J Bone Joint Surg Am* 2014; 96: 1742-1752.

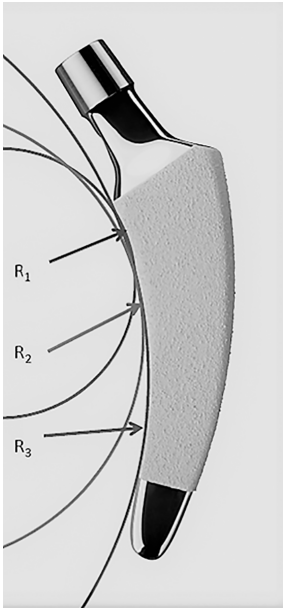

Figure 3 The design of modern calcar-guided short stems, with a rounded shape, is adapted to the medial anatomical calcar curve. In the case of the optimys stem (Mathys Ltd., Bettlach, Switzerland), three different radii were used to design the curve (R1-3). (Copyright Mathys Ltd., Bettlach, Switzerland).

valgus anatomies (Figure 8A). Therefore, a strictly non-compromised proximal bone stock and sufficient bone quality are mandatory prerequisites for the safe implantation of this stem[14]. Similarly, the Nanos stem, an early representative of calcar-guided short stems, features narrowing in the distal section of the stem, primarily intended to allow proximal fixation, at the same time limiting the option of additional diaphyseal anchorage (Figure 8B).

In new-generation, calcar-guided, short-stem THA, in addition to individualized positioning, the anchoring type can be individualized. When using the optimys stem in a varus position, a classical three-point anchoring approach should be attempted (Figure 2A). In the neutral and valgus position, an additional diaphyseal anchorage is possible (Figure 2B). In varus hips, the high level of the osteotomy proximal wedging combined with the three-point anchoring approach is typically sufficient, whereas in valgus hips, due to the low resection level, the stems may require an additional diaphyseal anchorage to achieve primary stability[34] (Figure 8C). Changing the type of anchorage through the addition of a diaphyseal anchorage will potentially result in negative effects on proximal bone remodeling and stress shielding compared with

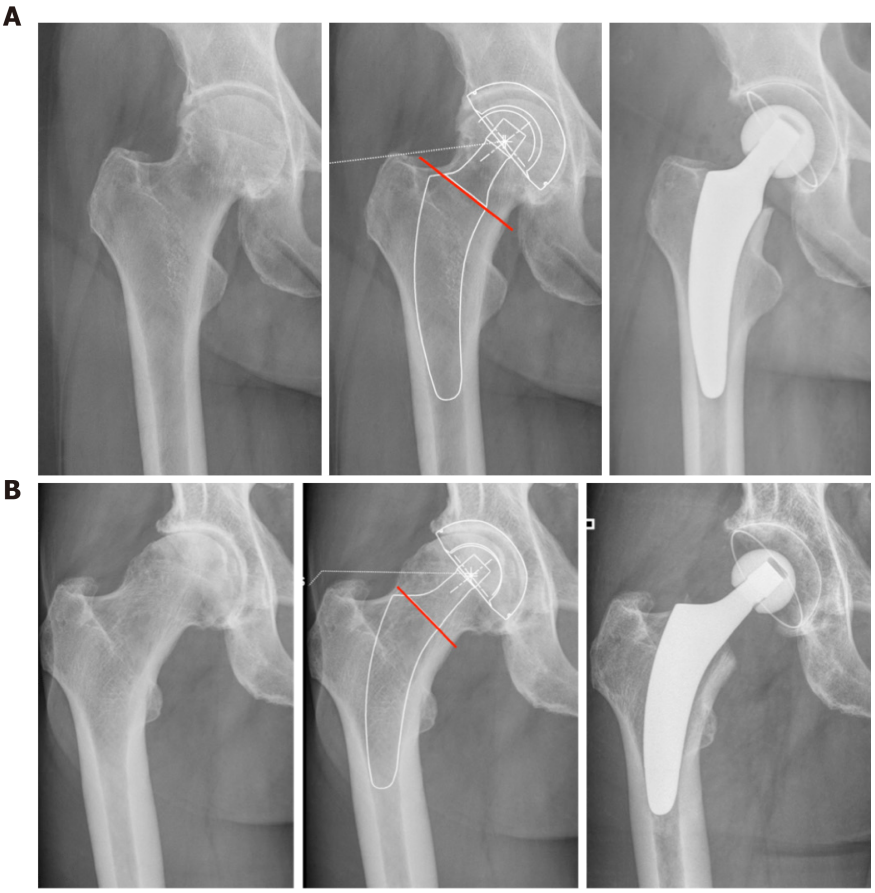

Figure 4 Individualized levels of resection, according to preoperative planning. A: Valgus anatomy; B: Varus anatomy.

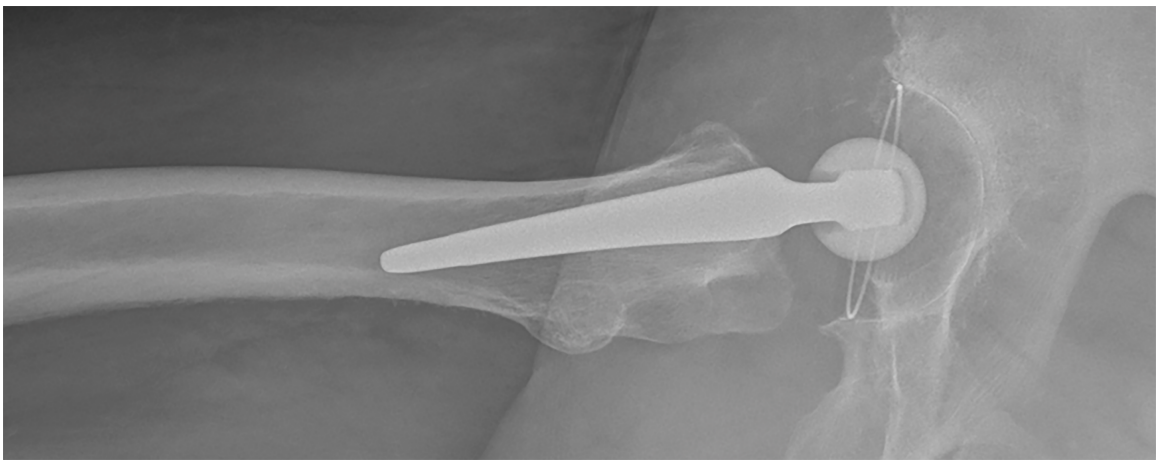

Figure 5 The natural anterior tilt of the femoral neck (in the second plane) can only be reconstructed using a short stem.

metaphyseal anchorage alone[21,34]. However, the option of additional individualized anchorage types increases the potential indications for the safe use of a short stem. The design features of calcar-guided short stems, including the ability to apply individualized meta-diaphyseal anchorages, may account for advantages of this stem type compared with earlier short-stem designs in terms of indications for use, including reduced quality of bone, osteonecrosis of the femoral head (ONFH), and femoral neck fractures[35-37].

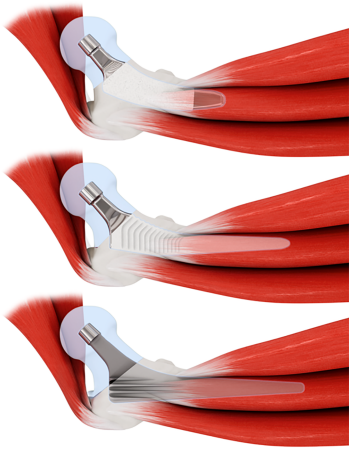

Figure 6 Using rounded short stems (top), minimally invasive approaches, without requiring transection or damage to the muscles, are facilitated compared with conventional stems (middle and bottom). Copyright Mathys Ltd., Bettlach, Switzerland.

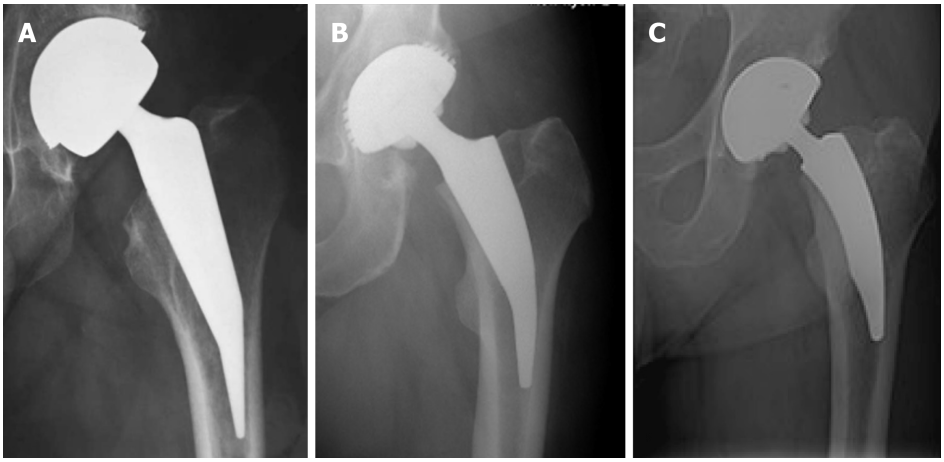

Figure 7 Metaphyseal anchoring using three-point fixation. A: Mayo stem (Zimmer Biomet, Warsaw, Indiana, USA); B: Metha stem (Aesculap, Tuttlingen, Germany); C: Nanos stem (Smith&Nephew, Marl, Germany).

BONE REMODELING

Due to distinct differences in the manifestation of bone remodeling, Yan *et al*[19] concluded in a recent review analysis that short stems should not be treated as one single implant group because periprosthetic bone loss is highly dependent on each particular stem design. The Metha stem has been associated with bone loss in the calcar region, whereas the Nanos stem presented bone resorption primarily in the greater trochanteric region, and these differences may be due to differences in the stem designs. Compared with conventional stems, such as the CLS stem (Zimmer Biomet, Warsaw, Indiana, USA) and the Bicontact stem (Aesculap, Tuttlingen, Germany), the study by Yan *et al*[19] also indicated that most short stems were associated with an overall lower rate of bone remodeling. A recent dual-energy X-ray absorptiometry study reported by Hochreiter *et al*[38] evaluated bone remodeling around the calcar-guided optimys stem. Bone mineral density increased primarily in the lateral region (Gruen zones 2 and 3) and the distal-medial region (Gruen zone 5), suggesting lateral loading. Thus, stress-shielding was limited, and periprosthetic bone loss was minimized when using this stem design.

Typical signs of diaphyseal stress, such as cortical hypertrophy, are commonly observed during the use of several conventional stem designs, frequently resulting in thigh pain. Cortical hypertrophy was commonly observed with the Fitmore stem (Zimmer Biomet, Warsaw, Indiana, USA)[39], whereas a low rate of distal bone remodeling associated with cortical hypertrophy has been reported for the calcar-guided optimys stem[33]. Almost all new-generation short stems present with a polished tip to reduce peak stresses and to prevent distal ingrowth (Figure 1).

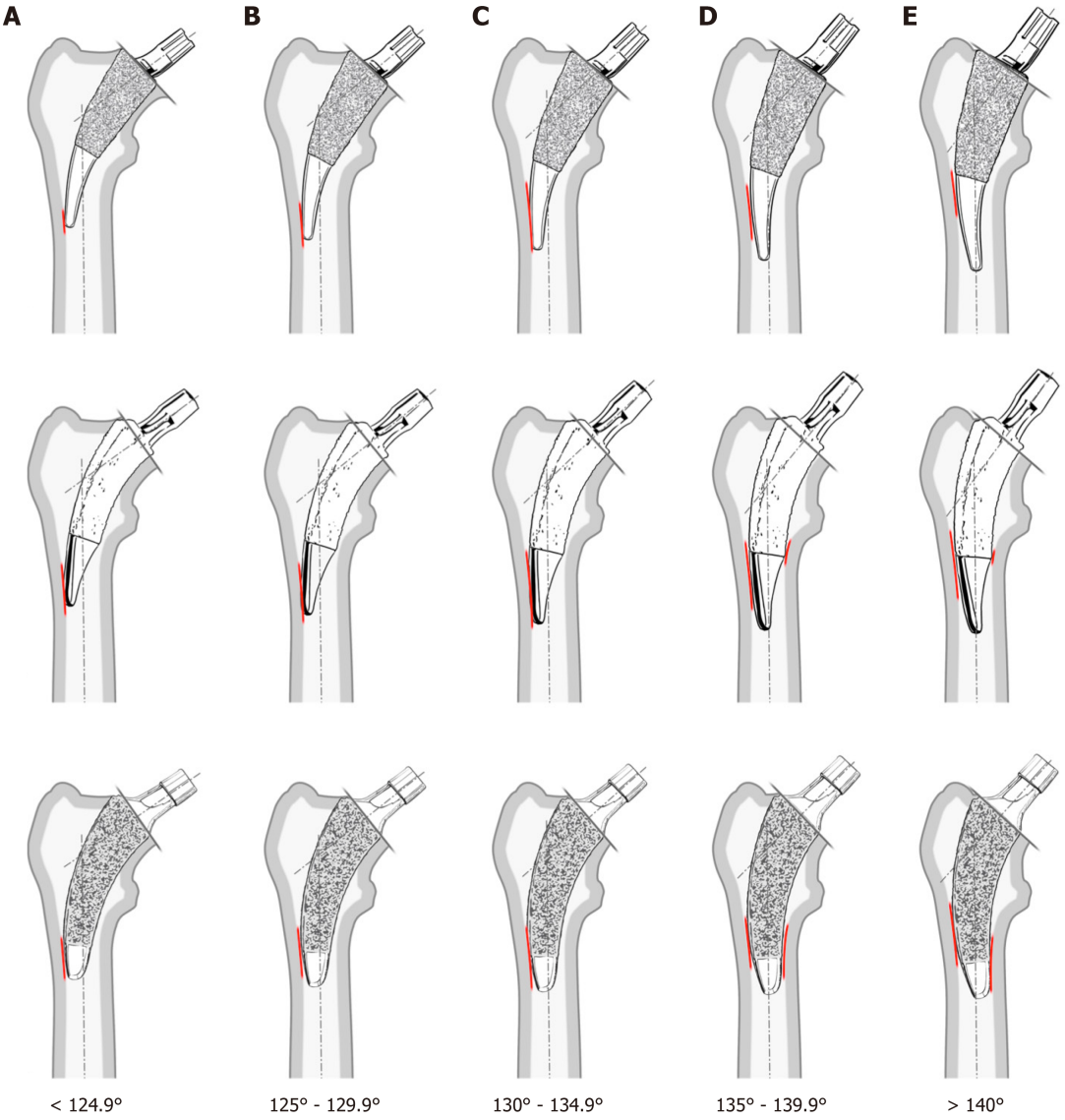

Figure 8 Characteristics of various short stem designs at different CCD angles, according to the classification of Groups A–E established by Kutzner *et al*[22,35]. A: Metha stem (Aesculap, Tuttlingen, Germany); additional diaphyseal anchorage is almost impossible to attain; B: Nanos stem (Smith&Nephew, Marl, Germany); narrowing in the distal part limits the option of additional diaphyseal anchorage; C: Optimys stem (Mathys Ltd., Bettlach, Switzerland); in neutral and valgus positions, an additional diaphyseal anchorage is possible, when intended. (Copyright Mathys Ltd., Bettlach, Switzerland).

MIGRATION AND SECONDARY STABILITY

The reduction in the length and diaphyseal fixation of the femoral component in short-stem THA may cause some concerns. A concomitant reduction of implant stability and an increase in interface micromotion might interfere with osteointegration, increasing the risk of aseptic loosening[17], which is likely to have crucial effects on long-term outcomes and revision rates. Whether this new group of stems will perform as well as conventional stems, which have a 25-year survival rate of 60%, cannot yet be predicted [40]. Studies investigating the migration patterns of modern short stems using EBRA-FCA (Ein-Bild-Roentgen-Analyse; femoral component analysis) have suggested an initial, pronounced settlement into the metaphyseal bone upon the initiation of full weight-bearing, followed by a subsequent stabilization[41-46]. In a recent investigation, most of the investigated stems showed delayed settlement during the first 2 years after surgery, suggesting that these new-generation stems are likely to display different migration patterns from conventional stems[34]. Male patients and heavy-weight patients have been shown to be at higher risk of subsidence, as are stems with valgus alignment[41]. Recent studies using radiostereometric analyses (RSA) have confirmed these findings. De Waard *et al*[47] reported the occurrence of secondary stabilization after initial migration using the optimys stem, suggesting a low risk of long-term aseptic loosening. Similarly, the mid-term results reported by the

prospective RSA study performed by Floerkemeier *et al*[48] using the Metha stem showed no correlation between a greater initial migration and inferior clinical outcomes and no increased risk of aseptic loosening.

A securely achieved cortical contact with the distal lateral cortex appears to be crucial to provide sufficient primary stability[49] (Figure 8). A missing cortical contact has previously been defined as "undersizing"[49]. The use of intraoperative imaging to identify the potential "undersizing" of calcar-guided short stems is highly recommended, especially with regard to individualized positioning[20,50]. If the cortical contact is not securely achieved with the trial components, the stem should be upsized. At the mid-term, no clinically negative consequences were obvious in terms of implant survival[15,34]. Long-term results should, however, be obtained to further determine the impacts of early migration on secondary stability and short stem survival.

INDICATIONS

Short stems have been developed for use in young and active patients. To date, this group of patients continues to be primarily treated with short-stem THA. The most frequent indications for short-term THA are primary and secondary osteoarthritis; however, indications have constantly been expanded during recent years. To date, little clear evidence is available regarding the indications and contraindications of short stem use due to the limited availability of data.

Several short stems have been reported to be suitable for use in patients with developmental dysplasia of the hip joint[15,51-53]. While investigating the calcar-guided short stem MiniHip, Buttaro *et al*[54] found a survival rate of 100% at 5 years, using revision for aseptic loosening as the end point. They concluded that this stem design was well suitable for patients with hip dysplasia, producing only a few intraoperative technical problems.

Undoubtedly, the quality of the femoral bone stock plays a crucial role in the safe use of calcar-guided short stems. A recent multicenter investigation found a significantly increased periprosthetic fracture rate in patients with Dorr type C femora compared with those with Dorr type A and B femora[35]. Thus, the indication for use should be limited to Dorr type A and B. However, as the rates of stem revision did not differ significantly between younger and older patients; therefore, advanced age alone is not necessarily a contraindication for the use of calcar-guided short-stem THA, although longer follow-up has yet to be obtained[35].

The opportunity to intentionally choose an additional fit-and-fill in the proximal diaphysis associated with some calcar-guided short-stem designs potentially accounts for advantages compared with other short stems, particularly in terms of the broad range of indications associated with the use of these short stems. In addition to the classical short-stem philosophy of metaphyseal anchorage (Figure 9A), the same patient can also be treated by adding a fit-and-fill in the proximal diaphysis, if desired, such as in cases of reduced bone quality (Figure 9B). Generally, in these cases, the stem requires some degree of upsizing.

The indication of ONFH in short-stem THA is controversial. The potentially reduced bone quality and the osteonecrotic area beyond the femoral head may also affect the femoral neck and the metaphyseal bone, and metaphyseal anchoring designs may be associated with poor primary stability and impaired osteointegration, which can jeopardize implant survival. For example, Schnurr *et al*[55] compared the use of the Metha stem in patients with ONFH with its use in patients with primary osteoarthritis over a 10-year period. They found that the aseptic loosening rate was significantly elevated among patients with ONFH. Recently, Afghanyar *et al*[36] reported a survival rate of 100% at the mid-term for the calcar-guided optimys stem in patients with ONFH. The findings strongly support the safe use of calcar-guided short stems for the treatment of patients with ONFH (Figure 10), providing sufficient primary stability and successful osteointegration. Further data on different calcar-guided short stems have confirmed these findings[56,57].

To date, little evidence regarding the use of short cementless femoral components in cases of femoral neck fractures is available. However, Schneider *et al*[37] reported promising results using a calcar-guided short stem in patients with a femoral neck fracture who were active, characterized by Dorr type A or B femora, and provide an intact cortical ring of the femoral neck (Figure 11). A total of 16% of patients who required treatment due to femoral neck fracture were found to be eligible for this stem design, and a low complication rate was reported. However, the study has not come to

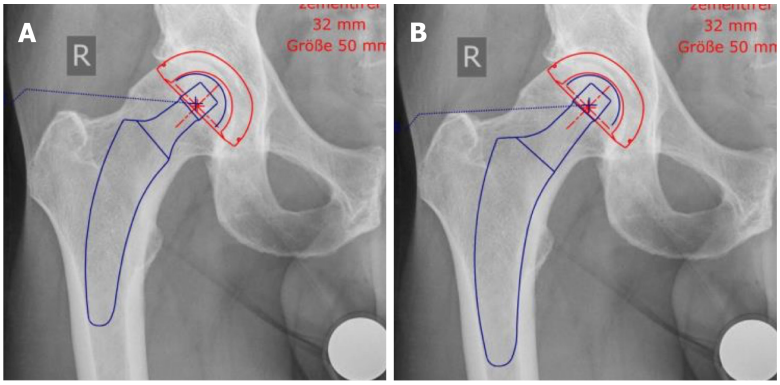

Figure 9 The same patient can be planned and treated by the application of metaphyseal anchorage or the addition of a fit-and-fill in the proximal diaphysis by valgization and upsizing, depending on the indication and bone quality. A: Metaphyseal anchorage; B: Additional fit-and-fill in the proximal diaphysis.

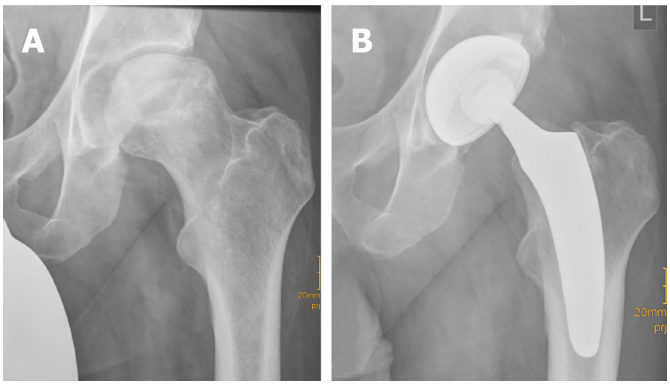

Figure 10 Calcar-guided short stem total hip arthroplasty in a case of osteonecrosis of the femoral head. A: Preoperative; B: Postoperative.

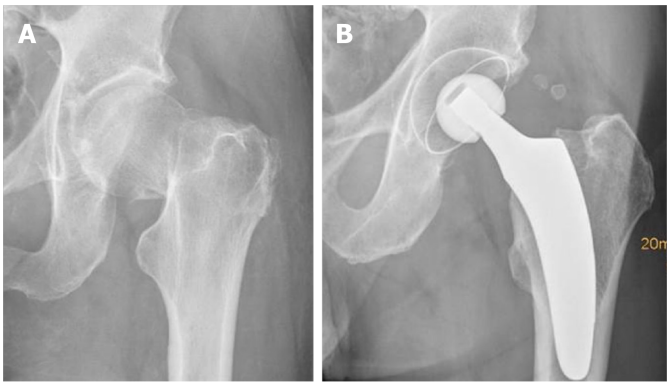

Figure 11 Calcar-guided short stem total hip arthroplasty in a case of a femoral neck fracture. A: Preoperative; B: Postoperative.

an end yet. Two additional studies are available in the literature that investigated shorter stem designs in patients with femoral neck fractures, which reported encouraging outcomes; however, both stem designs were classified as shortened conventional stems (Group 4) based on the system established by Khanuja *et al*[58,59].

Cemented short-stem THA may represent a potential alternative for patients with poor bone quality and osteoporosis, such as Dorr type C femora. To date, however, no new-generation short stem THA with cemented fixation are available on the market. Using prototypes of the optimys stem fabricated using polished steel (Figure 12), a recent *in vitro* biomechanical study demonstrated that the concept of a line-to-line cementation technique could be further pursued for the development of a cemented short stem in THA[60]. This finding was confirmed in a validated, computed tomography-based, finite element analysis performed by Azari *et al*[61] that quantified

Figure 12 Prototype of a cemented calcar-guided short stem made out of polished steel (optimys stem, Mathys Ltd., Bettlach, Switzerland). Copyright Mathys Ltd., Bettlach, Switzerland.

the mechanical performance of this short stem design. The results suggested that cemented short stems are a promising alternative for use in osteoporotic bone and may, therefore, further expand the range of indications in the future.

REGISTRY DATA

In recent years, short stems have increasingly been involved in national arthroplasty registries. The results of several national registries indicate that calcar-guided short stems are among the most successful implants in terms of early-stage survivorship. For example, in the German national joint registry, calcar-guided short stems, such as the optimys stem, the Nanos stem, the A2 stem, and the MiniHip stem, have been associated with excellent implant survival[10]. These results are strongly supported by findings from the Australian and the Swiss national registries, which provided similar results for these implant designs[62,63]. However, only mid-term registry data are currently available.

CONCLUSION

Modern calcar-guided short-stem THA offers numerous advantages compared with conventional THA. The broad potential to reconstruct the individual anatomical hip geometry, the reduction in proximal bone remodeling, and the simplified soft-tissue-sparing implantation represent true accomplishments. In Europe and globally, this group of implants is likely to become increasingly popular. Although this group of implants is still young, a large body of evidence has been obtained. The short- and mid-term outcomes are encouraging, although long-term results remain scarce.

If the long-term results confirm the promising early data, the option to anchor the femoral implant individually and the associated broad range of indications are likely to strongly favor calcar-guided stem designs as the future standard in THA. However, standard procedures, in general, should be easy to implement, reproducible, and practicable for every surgeon, regardless of technical expertise or surgical experience. The individualized implantation technique, however, requires distinct knowledge of the characteristics associated with varus and valgus positioning and the consequences of different types of anchoring, resulting in a significant learning curve for surgeons new to this technique, which must be considered. Contraindications to the use of these implants should be respected. Thus, improving education and collecting further clinical evidence will be crucial determinants of the future of calcar-guided short-stem THA.

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World Journal of Orthopedics

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World J Orthop 2021 August 18; 12(8): 548-554

DOI: 10.5312/wjo.v12.i8.548

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Basic Study

Fibula pro-tibia *vs* standard locking plate fixation in an ankle fracture saw bone model

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Author contributions: Okoro T contributed study design, performance of biomechanical testing, analysis of results, drafting and proof reading of manuscript; Teoh KH contributed study design, analysis of results, drafting and proof-reading of manuscript; Tanaka H contributed study design, supervision of study, analysis of results, drafting and proof reading of manuscript.

Supported by Research Grant Provided by AOUK.

Institutional review board statement: This was a biomechanical study and did not involve human and the use of animals.

Conflict-of-interest statement: The authors have no conflict of interest to declare.

Data sharing statement: No additional data are available.

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Abstract

BACKGROUND

Locking plate fixation in osteoporotic ankle fractures may fail due to cut-out or metalwork failure. Fibula pro-tibia fixation was a technique prior to the advent of locking plates that was used to enhance stability in ankle fractures by achieving tri or tetra-cortical fixation. With locking plates, the strength of this fixation construct can be further enhanced. There is lack of evidence currently on the merits of tibia-pro-fibula augmented locking plate fixation of unstable ankle fractures.

AIM

To assess if there is increased strength to failure, in an ankle fracture saw bone model, with a fibula pro-tibia construct when compared with standard locking plate fixation.

METHODS

Ten osteoporotic saw bones with simulated supination external rotation injuries were used. Five saw bones were fixed with standard locking plates whilst the other 5 saw bones were fixed with locking plates in a fibula pro-tibia construct. The fibula pro-tibia construct involved fixation with 3 consecutive locking screws applied across 3 cortices proximally from the level of the syndesmosis. All fixations were tested in axial external rotation to failure on an electromagnetic test frame (MTS 858 Mini-Bionix test machine, MTS Corp, Eden Praire, MN, United States). Torque at 30 degrees external rotation, failure torque, and external rotation angle at failure were compared between both groups and statistically analyzed.

Manuscript source: Invited manuscript

Specialty type: Orthopedics

Country/Territory of origin: United Kingdom

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Received: February 9, 2021
Peer-review started: February 9, 2021
First decision: June 25, 2021
Revised: July 2, 2021
Accepted: August 2, 2021
Article in press: August 2, 2021
Published online: August 18, 2021

P-Reviewer: Liu J
S-Editor: Gao CC
L-Editor: A
P-Editor: Xing YX

RESULTS

The fibula pro-tibia construct demonstrated a statistically higher torque at 30 degrees external rotation (4.421 ± 0.796 N/m *vs* 1.451 ± 0.467 N/m; *t*-test P = 0.000), as well as maximum torque at failure (5.079 ± 0.694N/m *vs* 2.299 ± 0.931 N/m; *t*-test P = 0.001) compared to the standard locking plate construct. The fibula pro-tibia construct also had a lower external rotation angle at failure (54.7 ± 14.5 *vs* 67.7 ± 22.9).

CONCLUSION

The fibula pro-tibia locking plate construct demonstrates biomechanical superiority to standard locking plates in fixation of unstable ankle fractures in this saw bone model. There is merit in the use of this construct in patients with unstable osteoporotic ankle fractures as it may aid improved clinical outcomes.

Key Words: Unstable ankle fractures; Pro-tibia fixation; Improved stability; Simulated biomechanical analysis; Osteoporotic fractures; Ankle injuries

Core Tip: Locking plate fixation in osteoporotic ankle fractures may fail due to cut-out or metalwork failure. This study compared a fibula pro-tibia construct to standard locking plate fixation in an ankle fracture saw bone model. The fibula pro-tibia construct demonstrated biomechanical superiority and there is merit to consideration of its use in patients with unstable osteoporotic ankle fractures.

Citation: Okoro T, Teoh KH, Tanaka H. Fibula pro-tibia *vs* standard locking plate fixation in an ankle fracture saw bone model. *World J Orthop* 2021; 12(8): 548-554
URL: https://www.wjgnet.com/2218-5836/full/v12/i8/548.htm
DOI: https://dx.doi.org/10.5312/wjo.v12.i8.548

INTRODUCTION

In osteoporotic bone, there is unsatisfactory fixation strength with uni-cortical cancellous fixation for distal fibula fractures[1,2], which can lead to loss of fixation as well as delayed or non-union[3]. The ways to try to obviate these risks include the use of locking, posterior plating, or non-locking constructs with adjunct fixation. One such example of the latter is the use of tri- or tetra-cortical fixation with fibula pro-tibia (syndesmotic) screws[1]. In comparison to the same construct without additional screws, fibula pro-tibia fixation has demonstrated a 9% increase in torque to failure, 24% increase ability to withstand external rotation, and a 34% increase in energy before failure of the construct[4]. This technique adds little operative time, is inexpensive, and is a technically straightforward method to increase the stability of the construct[4].

In unstable bi-malleolar ankle fractures, the talus remains attached to the lateral malleous[5]. Reducing the medial malleolus alone may prevent anatomical repositioning of the talus, as in some cases the lateral malleolus cannot be accurately reduced when it impinges on the proximal fibular fragment. Repositioning of the talus can be achieved by forcibly internally rotating the ankle in such cases, but this stretches the fibular collateral ligament. When external immobilization is discontinued, the lateral ligaments remain in a stretched position and slight to moderate talar instability, which predisposes to development of late degenerative arthritis, may be the result[5].

The lateral malleolus appears therefore to be the key to the anatomical reduction of displaced bi-malleolar fractures, and restoring the integrity of the lateral malleolus restores the integrity of the ankle[5].

Being able to maintain the integrity of the lateral malleolar fixation in osteoporotic bone in therefore important. This study aims to biomechanically assess whether there is an increased strength to failure with a fibula pro-tibia construct when compared with standard locking plate fixation for ankle fractures in an ankle fracture saw bone model.

MATERIALS AND METHODS

Materials

Ten osteoporotic saw bones (Pacific Research Laboratories Inc., Vashon, WA, United States) with simulated supination external rotation injuries were used in this study.

Fracture simulation

A lateral malleolar ankle fracture was simulated with an osteotomy at the lateral malleolus (oblique orientation, starting medially at the level of the tibial plafond), and extending distally and laterally at a 45° angle[4]. Figure 1 illustrates the simulated lateral malleolar fracture.

Fracture fixation

Five of the lateral malleolar osteotomies were fixed in a standard fashion using a fibular locking plate (Stryker Variax locking plate; Stryker, Mahwah, NJ, United States; Figure 2A) whilst fibula pro-tibia fixation was utilized in the other 5 models [fibular locking plate (Stryker Variax locking plate; Mahwah, NJ, United States)] with tri-cortical fixation. Tri-cortical fibula pro-tibia fixation entailed the use of 3 consecutive fully threaded cortical 3.5mm locking screws placed proximal to the lateral malleolar osteotomy at the level of the tibio-fibular syndesmosis (Figure 2B).

Biomechanical testing

Each model was then subjected to biomechanical analysis after being mounted on a resin and tested on an electromagnetic test frame (MTS 858 Mini-Bionix test machine, MTS Corp, Eden Praire, MN, United States), Figure 3, with measurement of torque (N/m) at 30 degrees external rotation, maximum failure torque (N/m) and external rotation angle (°) at failure.

Statistical analysis

The student's *t*-test was used to analyze differences between both groups with a P value < 0.05 taken as statistically significant.

RESULTS

Fibula pro-tibia vs standard locking plates (torque assessment)

The mean torque for the fibula pro-tibia constructs at 30° external rotation was 4.421 ± 0.796 N/m, which was significantly higher than that obtained for the standard locking plate fixation constructs 1.451 ± 0.467 N/m (*t* test $P = 0.000$). This difference was also noted in the maximum torque to failure (tibia-pro-fibula 5.079 ± 0.694 N/m *vs* standard locking plate fixation 2.298 ± 0.931 N/m; *t* test $P = 0.001$).

The torque values of each construct for the above parameters are detailed in Tables 1 and 2.

Fibula pro-tibia vs standard locking plates (angle to failure)

There was a lower mean external rotation angle to failure for the fibula pro-tibia construct (54.7° ± 14.5°) compared to standard locking plate fixation 67.7° ± 22.9°, but this was not statistically significant; *t* test $P = 0.313$.

DISCUSSION

Open reduction and internal fixation for an unstable ankle fracture in young patients is relatively predictable with excellent outcomes[6]. However the management of ankle fractures in the elderly remains less predictable, secondary to the various comorbidities associated with elderly patients such as osteoporosis, diabetes, cardiovascular, and peripheral vascular disease[3].

A recent trial demonstrated superiority of tibio-talo-calcaneal (TTC) nailing over standard locking plate fixation in the elderly in terms of having a low risk of complications, an earlier return to previous level of mobility, and the allowance of an immediate return to full weight bearing[6]. A limitation to the use of the TTC nail in routine practice is the risk of proximal peri-prosthetic fractures, as well as the need for the availability of a senior trauma surgeon or foot and ankle specialist to obtain

Table 1 Torque (N/m) recorded for fibula pro-tibia and standard locking plate constructs (torque at 30 degrees external rotation)

Construct	Fixation type	Torque (N/m)
1	Fibula pro-tibia	3.723
2	Fibula pro-tibia	5.692
3	Fibula pro-tibia	4.695
4	Fibula pro-tibia	4.043
5	Fibula pro-tibia	3.954
6	Standard locking plate	0.829
7	Standard locking plate	1.709
8	Standard locking plate	1.539
9	Standard locking plate	1.155
10	Standard locking plate	2.022

Table 2 Torque (N/m) recorded for fibula pro-tibia and standard locking plate constructs (maximum torque at failure)

Construct	Fixation type	Maximum torque at failure (N/m)
1	Fibula pro-tibia	4.270
2	Fibula pro-tibia	5.970
3	Fibula pro-tibia	5.176
4	Fibula pro-tibia	5.468
5	Fibula pro-tibia	4.513
6	Standard locking plate	1.187
7	Standard locking plate	2.869
8	Standard locking plate	1.519
9	Standard locking plate	2.497
10	Standard locking plate	3.422

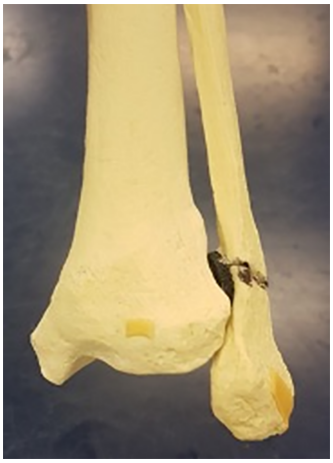

Figure 1 Simulated lateral malleolar sawbone ankle fracture.

optimal outcomes[7].

This study demonstrates that the fibula pro-tibia locking plate construct has biomechanical superiority to standard locking plates in a saw-bone model. There is increased torque at 30 degrees external rotation as well as a higher torque at maximum failure of the construct. The reduced maximal external rotation angle at failure of the

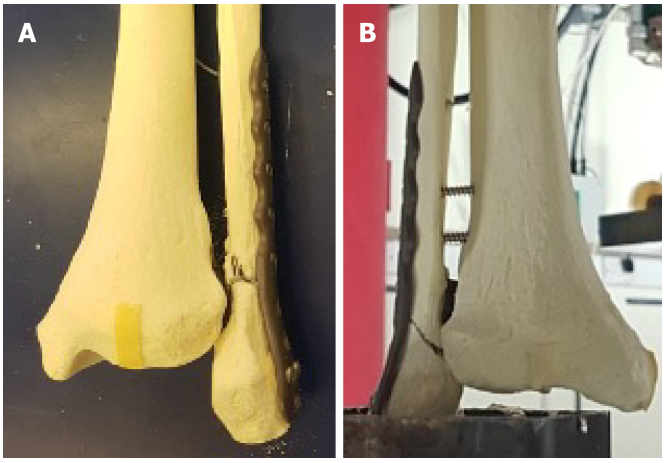

Figure 2 Sawbone lateral malleolar fixation construct. A: Sawbone lateral malleolar fracture treated with standard locking plate; B: Sawbone lateral malleolar fracture treated with locking plate in fibula pro-tibia configuration.

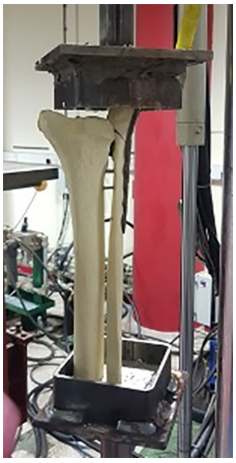

Figure 3 Fibula pro-tibia construct of ankle fracture sawbone model mounted on the electromagnetic test frame (MTS 858 Mini-Bionix test machine, MTS Corp, Eden Praire, MN, United States).

construct is most likely due to the increased rigidity of the fixation, which is potentially beneficial for osteoporotic bone.

A limitation of this study is that it was performed on sawbones not cadaveric bone. Such data may therefore not be readily transferable to a clinical scenario, as we have performed an isolated analysis of a lateral malleolar fracture. The data we have shown however gives an objective assessment of the difference in biomechanical properties between the two constructs. Another limitation of the study is that we have not used a model that accounts for a bi-malleolar fracture pattern. The lateral malleolus is key to the anatomical reduction of displaced bi-malleolar fractures, and restoring the integrity of the lateral malleolus restores the integrity of the ankle[5]. The use of fibula pro-tibia fixation in this study demonstrates that there is up to approximately 3 times the level of torque achieved at 30 degrees external rotation and twice the failure torque in comparison to standard locking plate fixation. Initiating use of the adjunctive technique whilst performing such fixation is inexpensive, adds little operative time, and is not technically demanding. We propose the 3, 3, 3 rule for use of this adjunctive technique; Fixation with 3 screws across 3 cortices starting 3 cm above the tibial plafond.

The fibula pro-tibia construct utilizes the combined pull-out strength of locking screws to ensure a more biomechanical stronger construct. By using a tricortical fixation, it also ensures that the fixation is not as rigid as non-locking tetracortical fixation and provides some syndesmosis micro movement. There is therefore not a need for removal before weight bearing of the patient.

The increased biomechanical strength of the fibula pro-tibia construct demonstrates that there is merit to its use in patients with unstable osteoporotic ankle fractures.

Future research is required to evaluate if its use would aid improved clinical outcomes in this important group of patients.

CONCLUSION

This study compared a fibula pro-tibia construct to standard locking plate fixation in an ankle fracture saw bone model. The fibula pro-tibia construct demonstrated biomechanical superiority and there is merit to consideration of its use in patients with unstable osteoporotic ankle fractures.

ARTICLE HIGHLIGHTS

Research background

The lateral malleolus is key to the anatomical reduction of displaced bi-malleolar fractures, and restoring its structural integrity restores the integrity of the ankle. Various fixation techniques have been utilized in osteoporotic bone to ensure lateral malleolar integrity.

Research motivation

Biomechanical assessment of whether there is an increased strength to failure with a fibula pro-tibia construct when compared with standard locking plate fixation for ankle fractures in an ankle fracture saw bone model.

Research objectives

To compare a fibula pro-tibia construct to standard locking plate fixation in a saw bone model using biomechanical parameters.

Research methods

After simulation of supination/external rotation injuries in a series of n = 10 sawbones, n = 5 were fixed with the fibula pro-tibia construct and n = 5 were fixed with the standard locking plate. Biomechanical analysis was performed to assess torque (N/m) at 30 degrees external rotation, maximum failure torque (N/m) and external rotation angle (°) at failure. Students t test was used for comparison of both groups.

Research results

The fibula pro-tibia construct was biomechanically superior to the standard locking plate in torque at 30 degrees external rotation, and maximum failure torque. There was no statistically significant difference in the external rotation angle at failure.

Research conclusions

There is merit to considering the use of the fibula pro-tibia construct in fixation of bimalleolar ankle fractures in view of its biomechanical superiority over standard locking plates.

Research perspectives

Future research should evaluate the clinical significance of these findings.

ACKNOWLEDGEMENTS

We would like to thank King I and Lane H of Cardiff University School of Engineering for their assistance in providing access to the biomechanical testing equipment.

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World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2021 August 18; 12(8): 555-564

DOI: 10.5312/wjo.v12.i8.555

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Observational Study

Thromboelastography in elective total hip arthroplasty

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Author contributions: McNicol L and Liu GM were the main authors responsible for study design; Patients were primarily recruited, and data collection performed, by Liu GM and McNicol L; This existing data was inherited and analyzed primarily by Lee WS, McNicol L, Lloyd-Donald P and Weinberg L; The bulk of the manuscript was drafted by Lloyd-Donald P, Lee WS, Bellomo R and Weinberg L; all authors read and approved the final manuscript.

Institutional review board statement: The Austin Health Research and Ethics Committee approved this retrospective study (HREC ref number: LNR/19/Austin/21).

Informed consent statement: The informed consent was waived.

Conflict-of-interest statement: The authors declare that they have no competing interests.

Data sharing statement: The datasets used and/or analyzed during the current study are

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Abstract

BACKGROUND

Hypercoagulability plays an important role in predisposing patients to venous thromboembolism (VTE) after total hip arthroplasty (THA). We used thromboelastography (TEG) to examine the coagulation status of patients undergoing THA.

AIM

To examine coagulation as measured by TEG in patients undergoing THA who received standard VTE chemoprophylaxis with enoxaparin.

METHODS

After ethical approval, we performed a retrospective analysis of data collected in patients undergoing primary elective THA. We analyzed TEG data on samples performed before skin incision, intraoperatively and for 5 d postoperatively. Conventional coagulation tests were performed preoperatively and on postoperative day 5.

RESULTS

Twenty patients undergoing general anesthesia and 32 patients undergoing spinal anesthesia (SA) were included. TEG demonstrated a progressively hypercoagulable state postoperatively, characterized by elevated maximum amplitude. TEG also demonstrated transient intraoperative hypercoagulability in patients receiving SA. In contrast, conventional coagulation tests were normal in all patients, pre- and postoperatively, except for an increase in plasma fibrinogen day 5 postoperatively.

CONCLUSION

Despite VTE prophylaxis, patients following total hip replacement remain in a

available from the corresponding author on reasonable request. Original data is contained on old Minitab (.mtw) files that have compatibility issues with recent versions.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

Manuscript source: Unsolicited manuscript

Specialty type: Orthopedics

Country/Territory of origin: Australia

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

Received: February 15, 2021
Peer-review started: February 15, 2021
First decision: May 6, 2021
Revised: May 21, 2021
Accepted: July 9, 2021
Article in press: July 9, 2021
Published online: August 18, 2021

P-Reviewer: Costa G, Zhou S
S-Editor: Fan JR
L-Editor: A
P-Editor: Xing YX

hypercoagulable state as measured by both TEG and conventional tests. This group may benefit from more optimal anticoagulation and/or additional perioperative hemostatic monitoring, *via* TEG or otherwise.

Key Words: Surgery; Orthopedic; Anesthesia; Hip arthroplasty; Hypercoagulability; Thrombelastography

Core Tip: Patients undergoing total hip arthroplasty are a high-risk cohort for venous thromboembolism postoperatively. Thromboelastography (TEG) is a modality for investigating global coagulation status. There is limited evidence surrounding the use of TEG in this patient group. Our observational study revealed this patient cohort exhibits a progressively hypercoagulable state postoperatively, characterized primarily by elevated TEG maximum amplitude. The clinical significance of this hypercoagulability is yet to be fully elucidated, however suggests further outcome-based studies exploring anti-coagulation therapy in this cohort may be beneficial.

Citation: Lloyd-Donald P, Lee WS, Liu GM, Bellomo R, McNicol L, Weinberg L. Thromboelastography in elective total hip arthroplasty. *World J Orthop* 2021; 12(8): 555-564
URL: https://www.wjgnet.com/2218-5836/full/v12/i8/555.htm
DOI: https://dx.doi.org/10.5312/wjo.v12.i8.555

INTRODUCTION

Patients undergoing total hip replacement are at high risk of developing venous thromboembolism (VTE), with Australian incidence of postoperative deep vein thrombosis (DVT) approximately 9% in this group despite VTE prophylaxis[1]. An intrinsic hypercoagulable state is thought to be a major contributor to the development of DVT in this group, as well as postoperative stasis[2-6]. Despite routine postoperative prophylaxis, VTE remains a clinically important complication of joint arthroplasty, resulting in an incidence of pulmonary embolism of 0.14%-0.27% and associated mortality rate of 19.49%[7,8]. Recent major reviews on thromboembolism in this population have demonstrated that enoxaparin is effective in reducing DVT incidence [9]. The effect of enoxaparin on the overall global coagulation picture in this group remains limited, with our data augmenting evidence provided by other small observational studies in this cohort[10].

Thromboelastography (TEG) measures whole blood coagulation and fibrinolysis. Whilst neuraxial anesthesia techniques have been reported to diminish intra- and postoperative hypercoagulability by providing improved analgesia, the incidence of VTE after total hip arthroplasty (THA) appears to be similar in patients undergoing general anesthesia (GA)[11-14]. This study aims to describe the coagulation pattern observed by TEG in patients undergoing THA, and also to determine the impact of anesthetic technique on coagulation status.

MATERIALS AND METHODS

This study is a retrospective, observational study, using data from an electronic TEG database collected between 2000-2015 at a single tertiary center. The data was originally collected as part of routine clinical care, investigating the effect of routine enoxaparin administration on postoperative coagulation in THA patients, as measured by TEG. Our primary objective was to assess coagulation status in this group as measured by TEG, comparing baseline maximum amplitude (MA) to postoperative days 1, 2 and 5. Secondary outcomes were to: (1) Assess perioperative changes in other TEG parameters; (2) Compare perioperative TEG parameter changes based on the type of anesthetic used [either GA or spinal anesthesia (SA)]; and (3) Assess perioperative changes in conventional coagulation tests (international normalized ratio, activated partial thromboplastin time and fibrinogen). This study was not designed to investi-

gate clinical outcomes or incidence of VTE.

Participants

The Austin Health Research and Ethics Committee approved a retrospective analysis of historical data. The original data was collected using TEG as routine care (approval number: LNR/19/Austin/21). The study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12619000315112).

Original participants were recruited from perioperative anesthesia and orthopedic clinics at the Austin Hospital, Melbourne, Australia. Inclusion criteria included adult patients (> 18 years) undergoing primary, elective THA with American Society of Anesthesiologists (ASA) Grade 3 or lower. Exclusion criteria included patients with significant atherosclerotic disease, known coagulopathy or thrombophilia, abnormal liver function tests, impaired renal function (estimated glomerular filtration rate < 60 mL/min/1.73m^2, KDIGO stage 3A or greater) and use (< 10 d pre-operatively) of any of the following medications: Warfarin, heparin (high or low molecular weight), adenosine diphosphate receptor inhibitors, glycoprotein IIB/IIIA inhibitors, adenosine re-uptake inhibitors or thromboxane inhibitors. Patients were assessed for baseline comorbidities including ischemic heart disease, cerebrovascular disease, diabetes mellitus, smoking status and hypertension.

Standardization of setting

Anesthesia was managed by a group of anesthesiologists using a standardized care protocol. All patients scheduled for surgery underwent routine pre-operative investigations in a dedicated pre-operative anesthesiology clinic. This included a multidisciplinary review by an anesthesiologist, pharmacist, peri-operative nurse and orthopedic medical officer. Investigations included electrocardiogram (EKG), Chest X-ray and pathology testing including full blood count, urea and electrolytes and coagulation studies. Comorbidities were optimized which included smoking cessation counselling, optimization of cardiovascular risk factors and perioperative anemia and glycemic control. These were managed in accordance with National Australian Guidelines. Patients were provided with full informed consent in the pre-operative anesthesiology clinic and counselled regarding anesthetic technique. Anesthesia preference was for SA unless contraindicated (previous spinal surgery, aortic stenosis, patient refusal). Routine intraoperative anesthesia monitoring included continuous EKG and pulse oximetry as well as non-invasive blood pressure monitoring, with continuous blood pressure monitoring *via* an arterial line used in select patients (*i.e.* those with cardiorespiratory comorbidities). The threshold for blood transfusion was a hemoglobin less than 8 g/dL. No patient received intraoperative fibrinolytic therapy (*e.g.* tranexamic acid). All patients received non-pharmacologic methods of VTE prophylaxis. VTE chemoprophylaxis included enoxaparin (40 mg) administered immediately prior to skin closure, continued daily until hospital discharge. Patient charts were reviewed to ascertain the incidence of postoperative VTE.

Blood sampling and processing

Blood samples for TEG measurement were taken at 6 intervals: Immediately pre-operatively (baseline), midpoint intraoperatively (mid-point of surgery), immediately prior to skin closure (end of surgery), and on postoperative days 1, 2 and 5. Blood samples for conventional laboratory coagulation tests were pre-operatively (baseline) and postoperatively on day 5. All samples were collected using a single peripheral aseptic venepuncture. Viscoelasticity was measured on a TEG5000 system (Haemonetics®, United States) performed by a technician, expert in TEG, blinded to the choice of anesthesia technique. TEG was performed within 4 min of sampling, complying with our institution's standard technique at time of collection, which has been previously reported[15,16]. TEG variables measured were reaction time (R, min), coagulation time (K, min), clot formation angle (degree), MA (mm) and fibrinolytic index (LY60%).

Postoperatively, blood for TEG and conventional laboratory coagulation assays were sampled approximately 1 h before administration of daily VTE chemoprophylaxis using standard techniques (Supplementary Appendix 1).

No patients were eliminated from this study secondary to a lack of availability of TEG.

Statistical analysis

Non-parametric statistical analysis (Friedman's test) followed by the Wilcoxon signed rank test with Bonferroni correction was used to evaluate changes in TEG over time in

each group.

The Mann-Whitney *U* test was used to compare data between patients having GA and SA. Data are presented as medians with quartiles. A $P < 0.05$ was considered statistically significant.

RESULTS

A total of 52 patients were enrolled. Indications for THA were osteoarthritis ($n = 50$) and avascular necrosis of the femoral head ($n = 2$). Thirty patients were ASA 2 and 22 patients were ASA 3. Twenty patients received GA and 32 received SA. Patients receiving GA were younger than patients receiving SA [61 years (IQR: 56-70) *vs* 74 years (IQR: 66-79), $P < 0.01$]. There were no differences in patient weight (70 kg, IQR: 65-88 *vs* 70 kg; IQR: 62–74, $P = 0.67$), sex distribution (male/female: 7/13 *vs* 14/18, $P = 0.23$), ASA class ($P = 0.56$) or incidence of cardiovascular comorbidities ($P > 0.99$) based on type of anesthetic used (Table 1). Examining the primary end-point, baseline TEG MA was within normal limits with no differences based on anesthetic technique [GA: 62 mm (IQR: 56–68), SA: 61 mm (54–65)]. MA remained within normal limits without significant difference from baseline, and without difference between anesthetic groups throughout surgery. By days 2 and 5 post operatively, MA became significantly elevated *vs* baseline, and exceeding normal limits, in both anesthetic groups (Table 2). Regarding secondary aims, we observed decreased R time, decreased K time and increased alpha angle intraoperatively *vs* baseline (Table 2). This resolved postoperatively days 1 to 5. Fibrinogen levels were elevated *vs* baseline and exceeding normal limits in both anesthetic groups postoperatively [GA pre: 3.1 (IQR: 2.9–3.3), GA post: 4.6 (4.1–5.3), SA pre: 3.1 (2.9–3.6), SA post: 4.5 (4–4.9)] (Table 3). No changes were demonstrated in other conventional coagulation tests. There were zero cases of clinically significant VTE detected within five days postoperatively. Notably one patient in the spinal cohort complained of dyspnea and chest pain three days postoperative but returned a negative Computed Tomography Pulmonary Angiography (CTPA), while one patient in the GA cohort developed unilateral calf swelling five days postoperatively before returning a negative lower limb doppler ultrasound.

DISCUSSION

Key findings

We observed that TEG findings in the THA population demonstrated a hypercoagulable state postoperatively, characterized by a steady increase in MA regardless of anesthetic technique used. Other TEG parameters demonstrated a transient, intraoperative hypercoagulability using SA, with these parameters returning to baseline by day 5 postoperatively. Fibrinogen levels were significantly elevated postoperatively, in both anesthetic groups. No difference was demonstrated in any other conventional coagulation tests compared to baseline.

Relationship with previous studies

Our findings agree with and add to previously published research. A 2013 study examining 61 patients undergoing primary, elective THA found MA increased throughout postoperative day 1, peaked by day 7, and remained elevated until day 14 [17]. Like our study, this population all received routine enoxaparin prophylaxis. This study demonstrated a decline in platelet level postoperative day 1, increase after day 3, and peak between days 7-14, and again demonstrated elevated fibrinogen level postoperative day 3 to day 14. This study examined coagulation tests on differing days to our study, measuring TEG and conventional tests immediately postoperatively, day 1, 3, 7 and 14 postoperatively[17]. Similarly, a 2014 study examining 42 patients undergoing THA, also found an increasingly hypercoagulable picture postoperatively [10]. Unlike our data, which demonstrated no difference in any TEG parameter except MA *vs* baseline, this study demonstrated the hypercoagulable picture of this patient group was mostly attributed to a mixed enzymatic and platelet contribution. Importantly however, this study examined patients on days 1, 4 and 9 postoperatively, compared to days 1, 2 and 5 postoperatively for our study. This study also used a different form of low molecular weight heparin (fraxiparine) and did not report any conventional coagulation tests, as well as enrolling fewer patients. Our findings support other small, observational study data, wherein TEG demonstrates increase in

Table 1 Baseline patient comorbidities according to anesthetic technique

	Spinal (*n* = 32)	GA (*n* = 20)	*P* value
Median age	74	61	< 0.01
Median weight (kg)	70	70	0.67
Sex (male)	14	7	0.23
ASA class 2	17	13	0.56
ASA class 3	15	7	
Ischemic heart disease	1	0	> 0.99
Cerebrovascular disease	0	0	
Diabetes	3	1	
Hypertension	6	4	
Smoking history	4	4	

GA: General anesthesia; ASA: American society of anesthesiologists.

Table 2 Perioperative thromboelastography findings in patients undergoing total hip arthroplasty

TEG parameter	Type	Baseline	Mid-point of surgery	End of surgery	Post-op day 1	Post-op day 2	Post-op day 5
Reaction time (R time, min)	GA	3.0 (2.6-3.6)	2.4 (1.8-3.1)	2.2 (1.8-2.4)	2.9 (2.1-3.8)	3.1 (2.3-5.0)	4.0 (2.4-5.2)
	SA	3.0 (2.7-3.8)	2.5 (1.3-3.0)[a]	2.2 (1.4-2.4)[b]	2.9 (2.3-41)	2.8 (2.3-3.7)	3.8 (2.7-5.7)
Clot kinetics time (K time, min)	GA	4.2 (3.6-5.1)	3.3 (2.5-4.1)	3.0 (2.8-3.4)	3.9 (2.6-5.6)	3.7 (2.7-6.4)	5.3 (3.3-7.1)
	SA	4.4 (3.8-5.1)	3.2 (2.0-4.1)[a]	2.8 (2.3-3.3)[b]	4.2 (3.2-5.8)	3.7 (2.9-5.0)	5.4 (3.9-8.0)
Clot formation angle (degrees)	GA	36 (30-43)	50 (39-58)	43 (34-53)	44 (33-54)	46 (31-58)	41 (33-50)
	SA	35 (29-40)	47 (36-57)[b]	45 (40-57)[b]	43 (28-49)	49 (37-57)[b]	36 (25-47)
Maximum amplitude (mm)	GA	62 (56-68)	68 (63-71)	65 (54-71)	71 (66-76)[a]	77 (70-81)[b]	77 (74-81)[b]
	SA	61 (54-65)	64 (59-69)	63 (58-68)	69 (66-75)[b]	74 (70-81)[b]	78 (72-82)[b]
Clot lysis (LY60%)	GA	5 (3-6)	4 (3-7)	4 (2-7)	6 (2-7)	5 (3-6)	3 (1-4)
	SA	4 (4-6)	4 (2-5)	4 (2-4)	7 (5-10)[a]	5 (4-9)	3 (2-7)

All results are presented as median with interquartile range.

[a]$P < 0.05$.

[b]$P < 0.01$ compared to baseline in each group.

GA: General anesthesia; SA: Spinal anesthesia; TEG: Thromboelastography; LY60%: Fibrinolysis index. (Normal reference ranges: R time: 4-9 min, K time: 1-3 min. Angle: 59-74 degrees, Maximum amplitude: 55-70 millimeters, LY60: 0%-8%)

MA post THA[18]. Intraoperative hypercoagulable states detected by TEG have been reported in previous studies and attributed to either surgical trauma or acute blood loss and hemodilution[2,3,19]. The location of hip arthroplasty surgery makes it appropriate for neuraxial anesthesia techniques (epidural and SA). It has been demonstrated neuraxial techniques may attenuate the stress response and improve local blood flow, and have been associated with direct and indirect effects on the hemostatic system[11]. A previous study reported that epidural anesthesia and analgesia attenuated postoperative hypercoagulability as measured by TEG and reduced thromboembolic sequelae post major vascular surgery[20]. However, these findings have not been reproduced[21,22]. We failed to detect an association between coagulation state and anesthetic technique used for THA. Our findings are congruent with existing evidence, which demonstrate perioperative activation of the coagulation

Table 3 Perioperative conventional coagulation test findings in patients undergoing total hip arthroplasty

Conventional coagulation test	Anesthetic type	Baseline	Post-op day 5
Prothrombin time (min)	GA	12 (12-12)	12 (11-12)
	SA	12 (12-13)	12 (12-13)
INR	GA	0.9 (0.9-1.0)	0.9 (0.9-1.0)
	SA	1.0 (0.9-1.0)	1.0 (0.9-1.0)
aPTT (sec)	GA	32 (30-35)	32 (29-35)
	SA	32 (30-34)	32 (29-34)
Fibrinogen level (g/dL)	GA	3.1 (2.9-3.3)	4.6 (4.1-5.3)[b]
	SA	3.1 (2.9-3.6)	4.5 (4.0-4.9)[b]

All results are presented as median with interquartile range.

[b]$P < 0.01$ compared to baseline in each group.

GA: General anesthesia; SA: Spinal anesthesia; INR: International normalized ratio; aPTT: Activated partial thromboplastin time.

and fibrinolysis systems are similar regardless of anesthetic technique used, resulting in SA having no benefit in reducing hypercoagulability in this group[23-28]. The utility of TEG at predicting thromboembolic events in this patient population remains unknown. A comprehensive 2018 meta-analysis of 41 studies found the sensitivity and specificity of TEG at predicting thromboembolic events was 56% (95%CI: 44-67) and 76% (95%CI: 67-83), respectively[29]. This meta-analysis included data from over 10000 individuals from a heterogenous population. A prospective 2016 study focusing on the diagnostic predictive value of TEG in orthopedic patients revealed a sensitivity of 14% and specificity of 62%[30]. However, this study only performed pre-operative TEG, with several variables changing between pre-operative TEG sampling and the development of post-operative VTE limiting the interpretation of these results. To our knowledge, no evidence is currently available which examines the diagnostic predictive value of post-operative TEG at predicting VTE events in orthopedic patients. We believe our unique, novel findings add to the available evidence in this area and could help guide future outcome-based studies in this group.

Limitations

This study carried several significant limitations. It used data collected several years ago, however we feel that as anesthesia, chemoprophylaxis and surgical principles have not varied significantly *vs* when data was collected that our study results remain valid, and an important contribution to existing evidence. TEG was collected days 1, 2 and 5, compared to a single day 5 postoperative laboratory test. This was in keeping with the practice at our institution at the time of data collection. Importantly, no platelet counts were recorded for any patient during original data collection. We acknowledge that this is a major weakness in the original study design, given platelet contribution to thrombus formation, and subsequently the observed MA, and possibly the overall hypercoagulable state we observed. This is a single center, small observational study, which may limit the external validity of our findings. However, our hospital is representative of many tertiary institutions with patient outcomes equivalent to those of other tertiary hospitals in Australia[31]. The study was also observational and descriptive only and inadequately powered to assess clinical outcomes, including incidence of VTE or VTE associated complications, such as pulmonary embolism and overall morbidity/mortality. Patients were not actively investigated for venous thromboembolic complications including either the routine use of lower limb ultrasound or CTPA. However, this was never the intention of this research, and we seek to make valid data available to the broader scientific community. Ideally, further research conducted in this area would involve paired TEG and conventional coagulation tests sampling at dedicated, simultaneous time-points perioperatively, including platelet count (and ideally, platelet function).

Implications of study findings

Our findings imply that despite routine VTE chemoprophylaxis, patients undergoing THA remain in a hypercoagulable state as measured by both TEG and conventional tests. Going further, as TEG MA is a measure of thrombus size, it is influenced by both

fibrinogen and platelet number and function[32]. These are in turn both influenced by postoperative inflammatory mediators[33]. This leads us to question whether this patient group optimally anticoagulated. Existing evidence suggests solely targeting thrombin production (through administering low molecular weight heparin) may not provide sufficient protection against platelet activation, hence a hypercoagulable state may persist[34,35]. Increased TEG MA suggests that routine VTE chemoprophylaxis cannot prevent the development of platelet-dependent hypercoagulability after THA and that additional antiplatelet drugs may have a role[36,37]. A recent major review of thromboprophylaxis in major orthopedic surgery concluded that aspirin alone for VTE chemoprophylaxis is not recommended, however it's value as an adjunct remains unknown[9].

CONCLUSION

In conclusion, using TEG, we examined the coagulation status of over 50 patients undergoing elective, primary THA and found that in this patient group, TEG demonstrated a progressively hypercoagulable state postoperatively, characterized primarily by elevated MA. Hypercoagulability was also demonstrated by elevated conventional fibrinogen levels day 5 post-operatively. Our findings suggest that despite VTE prophylaxis, patients following total hip replacement remain in a hypercoagulable state as measured by both TEG and conventional tests. This group may benefit from further outcome-based studies to determine if additional perioperative hemostatic monitoring and/or anticoagulation is beneficial.

ARTICLE HIGHLIGHTS

Research background

Patients undergoing total hip arthroplasty (THA) are known to be at high risk of developing venous thromboembolism (VTE), causing significant morbidity and mortality. Thromboelastography (TEG) offers real-time information regarding the global coagulation state of a patient. This technology may be useful in investigating the coagulation of this high-risk population.

Research motivation

Available evidence surrounding the use of TEG in this patient cohort is limited, including both observational data, describing the coagulation status in these patients, and interventional data, guiding anticoagulant therapy. Our motivation for this study was to investigate the coagulation state observed in this patient group as assessed by TEG, and examine how these observations change according to time course post-operatively, and anesthetic technique, in order to ultimately improve perioperative care of these high-risk patients.

Research objectives

We aim primarily to demonstrate the coagulation profile of patients undergoing elective THA, using TEG. We secondarily aim to describe how this coagulation pattern varies according to anesthetic technique chosen [spinal neuraxial *vs* general anesthesia (GA)] and how TEG findings compare to traditional coagulation tests.

Research methods

We performed a retrospective, observational study, examining archived data of elective THA patients. Patients were selected from a dedicated orthopedic preadmission clinic, meeting strict inclusion criteria, and all received enoxaparin as routine post-operatively. We analyzed baseline TEG maximum amplitude (MA), compared to intraoperative and postoperative days 1, 2 and 5. We then compared observations based on anesthetic technique received (GA *vs* spinal) and those described by conventional coagulation tests.

Research results

We studied a total of 52 patients. We found that MA remained within normal limits, without significant difference from baseline, throughout surgery. We observed elevated MA postoperatively on days 1 and 2, before resolving day 5. This was

consistent regardless of anesthetic technique used. All patients had elevated fibrinogen levels day 5 post-operatively, with no other abnormalities detected by conventional coagulation tests.

Research conclusions

Patients undergoing elective THA demonstrate postoperative hypercoagulability when assessed by TEG (characterized by elevated TEG MA), despite routine VTE prophylaxis. Anesthetic technique (spinal *vs* GA) had no influence on the postoperative coagulation profile observed in these patients, as assessed by TEG.

Research perspectives

Our study findings imply that routine VTE prophylaxis in patients undergoing elective THA does not ablate the postoperative hypercoagulable state, according to TEG. These findings suggest that further research comparing TEG with both conventional coagulation tests, (including platelet count) and platelet function testing may be useful.

ACKNOWLEDGEMENTS

The authors would like to thank the Department of Anesthesia, Austin Hospital, Melbourne, Australia.

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World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2021 August 18; 12(8): 565-574

DOI: 10.5312/wjo.v12.i8.565

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Prospective Study

Performance of alpha-defensin lateral flow test after synovial fluid centrifugation for diagnosis of periprosthetic knee infection

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Supported by Fundação de

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Abstract

BACKGROUND

The quantitative alpha-defensin enzyme-linked immunosorbent assay (ELISA) demands a prior synovial fluid centrifugation, whereas this processing is not routinely required prior to the alpha-defensin lateral flow test.

AIM

To evaluate whether a prior synovial fluid centrifugation could lead the lateral flow performance to achieve comparable results to ELISA during periprosthetic joint infection (PJI) diagnosis.

METHODS

Fifty-three cases were included in this study: 22 classified as PJI and 31 classified as aseptic cases, according to Musculoskeletal Infection Society 2013 criteria. Synovial fluid samples were submitted to centrifugation, and the supernatant was evaluated by ELISA and lateral flow tests. The sensitivity (SE), specificity (SP) and accuracy of each method were calculated as well as the agreement between those two methods.

RESULTS

In all of the 31 samples from aseptic patients, alpha-defensin ELISA and lateral flow tests showed negative results for infection. Regarding the 22 infected patients, the lateral flow test was positive in 19 cases (86.4%) and the ELISA was positive in 21 (95.5%). Sensibility, SP and accuracy were, respectively, 86.4%

Amparo à Pesquisa do Estado de São Paulo.

Institutional review board statement: The study was approved by the local Institutional Review Board (2179456).

Informed consent statement: All study participants, or their legal guardian, provided written consent prior to study enrollment.

Conflict-of-interest statement: The authors declare that there are no any conflicts of interest.

Data sharing statement: There is no additional data available.

CONSORT 2010 statement: The authors have read the CONSORT 2010 Statement, and the manuscript was prepared and revised according to the CONSORT 2010 Statement.

Manuscript source: Unsolicited manuscript

Specialty type: Orthopedics

Country/Territory of origin: Brazil

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Received: April 24, 2021
Peer-review started: April 24, 2021
First decision: June 7, 2021

(95%CI: 65.1%-97.1%), 100% (95%CI: 88.8%-100%) and 93.2% (95%CI: 82.8%-98.3%) for the lateral flow test and 95.5% (95%CI: 77.2%-99.9%), 100% (95%CI: 88.8%-100%) and 98.1% (95%CI: 89.9%-100%) for ELISA. An agreement of 96.2% between those methods were observed. No statistical difference was found between them (P = 0.48).

CONCLUSION

Alpha-defensin lateral flow test showed high SE, SP and accuracy after a prior synovial fluid centrifugation, achieving comparable results to ELISA. Considering the lower complexity of the lateral flow and its equivalent performance obtained in this condition, a prior centrifugation might be added as a valuable step to enhance the PJI diagnosis.

Key Words: Alpha-defensin; Alpha-defensin lateral flow; Periprosthetic joint infection

Core Tip: This was a prospective study seeking to evaluate whether the synovial fluid centrifugation prior to the alpha-defensin lateral flow test leads to comparable results in relation to the alpha-defensin enzyme-linked immunosorbent assay (ELISA) during periprosthetic joint infection of the knee. Prior centrifugation of the synovial fluid showed to achieve high sensitivity, specificity and accuracy for the lateral flow test during periprosthetic joint infection diagnosis, leading to similar results in comparison to alpha-defensin ELISA.

Citation: Abdo RCT, Gobbi RG, Leite CBG, Pasoto SG, Leon EP, Lima ALLM, Bonfa E, Pécora JR, Demange MK. Performance of alpha-defensin lateral flow test after synovial fluid centrifugation for diagnosis of periprosthetic knee infection. *World J Orthop* 2021; 12(8): 565-574
URL: https://www.wjgnet.com/2218-5836/full/v12/i8/565.htm
DOI: https://dx.doi.org/10.5312/wjo.v12.i8.565

INTRODUCTION

Total knee arthroplasty (TKA) is one of the most successful orthopedic procedures, providing excellent improvement in knee pain, function and quality of life[1]. With the population ageing and the growth incidence of symptomatic osteoarthritis, an increased number of TKA has been observed over the years[2,3]. Despite the most satisfactory results, several complications can occur after TKA, such as long-term pain, periprosthetic fractures, and joint infection[4]. Periprosthetic joint infection (PJI) after TKA is a catastrophic postoperative complication, that ranges from 0.5% to 3% of cases [5-7]. PJI can lead to serious consequences, including death[8], and accounts for a quarter of TKA revision surgeries[6], leading to a substantial economic impact on the healthcare system[9].

Although timing and precision of PJI diagnosis is critical for the patient's evolution, there is no one-hundred percent exam to provide its confirmation. For that reason, the Musculoskeletal Infection Society (MSIS) has developed a score for unifying PJI definition[10,11]. Considering the most updated criteria, alpha-defensin has been included as a new biomarker during the investigation of PJI[10].

Alpha-defensin is a neutrophil-released antimicrobial peptide[12] that increases in response to pathogens[13]. Nowadays, both the synovial alpha-defensin tests available [the quantitative enzyme-linked immunosorbent assay (ELISA) and the qualitative lateral flow test] provide important information during the investigation of PJI[14]. However, given the higher performance of ELISA, this test has a slight advantage[15, 16]. The lateral flow test, despite the inferior performance, offers benefits regarding the ease of use, time-efficiency and cost[14]. One potential reason that could reduce the measurement of the lateral flow test is regarding the differences between fluid processing. While the synovial fluid sample has to be centrifuged preceding ELISA measurement, the same processing is not routinely performed before the lateral flow,

Revised: June 14, 2021
Accepted: July 9, 2021
Article in press: July 9, 2021
Published online: August 18, 2021

P-Reviewer: M'Koma A
S-Editor: Ma YJ
L-Editor: A
P-Editor: Xing YX

according to the manufacturer's instructions. Thus, the maintenance of cellular debris and other particles within the synovial fluid could interfere in the results.

Here, we aimed to evaluate the performance of the alpha-defensin lateral flow test post synovial fluid centrifugation, and compare these results with the synovial alpha-defensin ELISA. Our hypothesis was that a prior centrifugation of the synovial fluid would achieve high sensitivity and specificity to predict knee PJI, leading to equivalent performance as alpha-defensin ELISA.

MATERIALS AND METHODS

The study was approved by the local Institutional Review Board (2179456). Written informed consent was obtained from each patient prior to participation.

We conducted a prospective, cross-sectional diagnostic study to assess the performance of the alpha defensin lateral flow measured after synovial fluid centrifugation in patients under investigation of chronic knee PJI. Inclusion and exclusion criteria are displayed in Table 1.

The primary outcome was to evaluate the sensitivity, specificity and accuracy of the lateral flow test post fluid centrifugation. Secondarily, we assessed the performance of the alpha-defensin ELISA in the same population of study, and compared the results between both modalities.

Initially, 59 patients were selected. Of these, three patients had insufficient joint fluid aspirate for analysis, and three patients were using antibiotics, being excluded from the study. A total of 53 patients were included. Figure 1 represents the flowchart of enrolled patients. The recruitment was performed between August 2016 and July 2019.

Among those 53 patients, 22 were diagnosed as infected, and 31 as aseptic. The revised MSIS 2013 criteria were used for the diagnosis of knee PJI[11].

Intervention

Demographic data was recorded. Clinical examination and laboratory evaluations, including serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were collected on the same day as joint aspiration. Knee aspiration was conducted using the superolateral approach, with a 21-gauge needle and a 20-mL syringe. The possible maximum volume of synovial liquid was collected. In this study, at least 3 mL of joint fluid was required for proper analysis. All aspiration procedures were performed by the same author (RCTA).

After that, the synovial fluid samples were referred to the laboratory within 2 h. Part of the fluid from each sample was sent to analysis for cell count, percentage of polymorphonuclear leukocytes and cultures from aerobic, anaerobic and fungi. The remaining fluid was centrifuged for 10 minutes at 2700 rpm to separate all cell debris and particles. The supernatant was collected and divided into two aliquots, as following: approximately 1 mL of synovial fluid was referred to the qualitative alpha-defensin lateral flow test; the rest of the fluid was stored at -80° C until further immunoassay analyses. To quantify synovial alpha-defensin using ELISA, approximately 1.5 to 2 mL of synovial fluid was needed.

Qualitative alpha-defensin analysis

For the qualitative measurement, a lateral flow test (Synovasure® Zimmer-Biomet, Warsaw, IN, United States) was used according to the manufacturer's label. The centrifuged synovial fluid sample was diluted in the dilution buffer supplied by the kit, and deposited on the Synovasure® device. The qualitative result was read after 10 min. The result was considered positive for PJI if two lines appeared in the reading panel, regardless of its intensity.

Quantitative alpha-defensins analysis

For the quantitative alpha-defensin test, the commercial alpha-defensin (HNP1-3) ELISA kit (Hycult Biotech®, Uden, Netherlands) was employed. This ELISA kit is used to determine human HNP1-3. All assays were optimized and performed in duplicate by an experienced laboratory technician. The dilution optimization of the synovial fluid at 1:5000 was performed to decrease the effects of the fluid viscosity on the assay. Results were generated in optical density units (OD) using a spectrophotometer. The results in OD were plotted on the vertical axis with the corresponding concentration values on the horizontal axis (logarithmic scale). The concentration and the dilution factor were multiplied to reach alpha-defensin values in mg/L. The assay was

Table 1 Inclusion and exclusion criteria of the study

Inclusion criteria	Exclusion criteria
Any of the following suspicious signs or symptoms of chronic knee PJI (more than 90 d), as following:	Acute signs or symptoms of knee infection (less than 90 d)
Persistent knee pain (more than 3 mo), without other apparent cause	
Persistent joint effusion (more than 3 mo)	
Persistent local heat (more than 3 mo)	
Presence of draining sinus	
Early failure of the prosthesis (less than 5 yr)	
Radiographic findings suggesting infection[33]	
Have not used antibiotics for at least 4 wk before the evaluation	Insufficient synovial fluid volume during knee aspiration
	Insufficient data for fulfilling the periprosthesis infection criteria[11]

PJI: Periprosthetic joint infection.

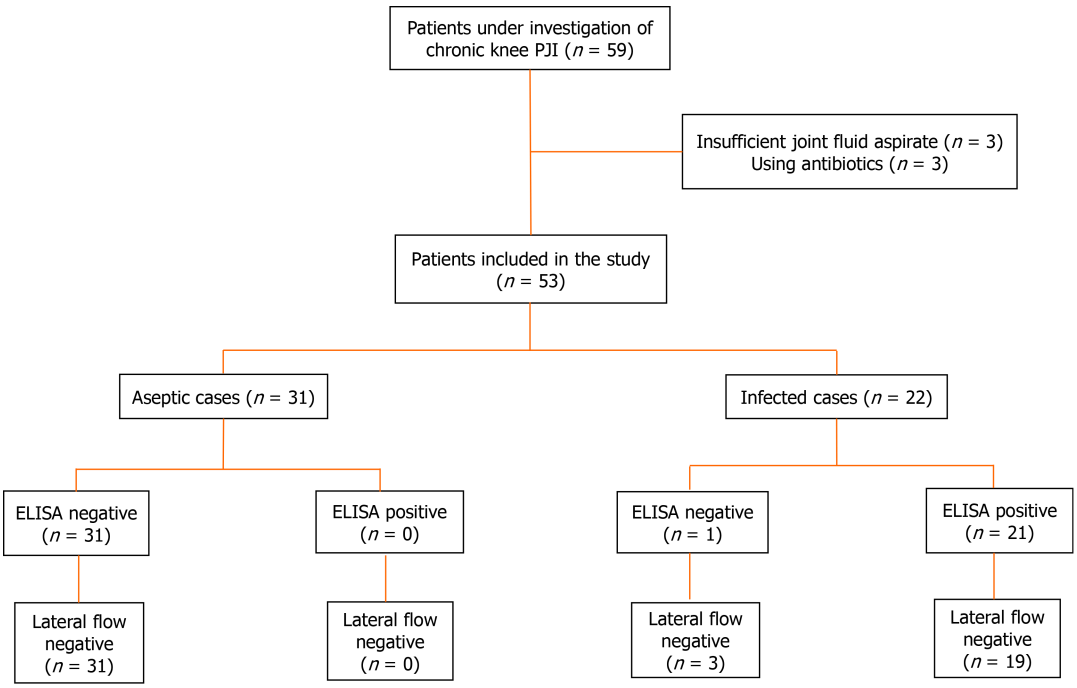

Figure 1 Flowchart of the patients included in the study.

optimized to operate at a cutoff value of 5.2 mg/L, based on previous studies[17,18].

Statistical analysis

Shapiro-Wilk test was applied to assess normality. Continuous variables were expressed as descriptive analysis, and categorical variables were expressed as proportions. To compare continuous variables, unpaired *t*-test or Mann-Whitney test were used, as appropriate. Fisher's exact test was applied to compare categorical variables. The cutoff value was obtained using the Receiver Operator Curve (ROC) through the SPSS software® (version 25.0 for Mac; SPSS, Chicago, IL), giving the results as a semiquantitative signal-to-cutoff ratio (S/CO) of 1.0. Sensitivity, specificity and accuracy (and 95%CI) of each method were calculated using the MSIS 2013 criteria as standard. The agreement between ELISA and lateral flow test was evaluated based on the percentage of concordant results, and McNemar's test was performed to calculate the statistical difference between those two alpha-defensin tests. Statistical significance was set at $P < 0.05$.

To further investigate whether draining sinus has influenced the tests results, we also calculated sensitivity, specificity and accuracy of each method excluding patients with fistulization.

RESULTS

Of the 53 patients included in the study, 31 were considered without infection (aseptic cases) and 22 were classified as infected. Table 2 shows the patient demographics.

In relation to the aseptic cases, all lateral flow tests showed negative results for infection. Likewise, alpha-defensin ELISA showed a mean S/CO of 0.28 ± 0.13, which was considered negative for all cases.

Regarding the infected patients, lateral flow showed positive results in 19 cases (86.4%). The 3 false negatives occurred in patients with sinus tract. The ELISA presented 21 positive (95.5%) (mean S/CO-4.93 ± 2.28) and one negative result (S/CO-0.24). Similarly, this false negative case referred to a patient with draining sinus.

Lateral flow test showed a sensitivity of 86.4% (95%CI: 65.1%-97.1%), a specificity of 100% (95%CI: 88.8%-100%) and an accuracy of 93.2% (95%CI: 82.8%-98.3%). Alpha-defensin ELISA presented a sensitivity of 95.5% (95%CI: 77.2%-99.9%), a specificity of 100% (95%CI: 88.8%-100%) and an accuracy of 98.1% (95%CI: 89.9%-100%). Table 3 summarizes those findings.

In terms of ROC analysis, area under curve was 93.2% (95%CI: 84.6%-100%) for the lateral flow test and 97.9% (95%CI: 93.6%-100%) for ELISA. The agreement between lateral flow and ELISA was observed in 51 cases (96.2%; 95%CI: 87.0%-99.5%). The two disagreement cases were false negatives for the lateral flow. No statistical difference between those two tests were found (P = 0.48).

Given that all false positive results occurred in patients with sinus tract, we performed an exploratory analysis to evaluate whether the lateral flow and the ELISA would change after excluding those selected patients (4 patients with sinus tract). In this situation, a sensitivity of 100% (95%CI: 81.5%-100%), specificity of 100% (95%CI: 88.8%-100%), accuracy of 100% (95%CI: 92.8%-100%) and agreement of 100% (95%CI: 92.9%-100%) were found for both tests (Table 4).

DISCUSSION

The findings of this study reinforce our hypothesis that a prior synovial fluid centrifugation before the lateral flow measurement provides high sensitivity, specificity and accuracy, leading to comparable performance of the alpha-defensin ELISA, so far the best method to measure synovial alpha-defensin[15]. This preliminary finding may bring a novel concept to the major topic of PJI.

Diagnosis of PJI is frequently defiant, particularly in chronic infections in which the clinical symptoms might be subtle and inflammatory markers might be normal[19]. In this regard, a great need for new diagnostic tests is observed[20]. Alpha-defensin is a small antimicrobial peptide that acts as part of the host's innate immune response against pathogens[12]. After the pathogen insult, the release of alpha-defensin increases, and a rapid interaction of this peptide with the pathogen's membrane occurs. As a consequence, the membrane depolarizes, and the pathogen is killed[21]. Under a knee infection, the concentration of alpha-defensin elevates into the joint. Indeed, this synovial fluid biomarker has been studied for PJI diagnosis, providing exciting findings in terms of sensitivity and specificity[14,22]. It has been demonstrated that, even in the presence of inflammatory disease or antibiotic use, the results are similar[17]. Here, we opted to exclude patients using antibiotics to avoid potential bias. However, we did include patients with inflammatory diseases, which in fact did not influence those tests' performance. Due to its relevance and applicability, alpha-defensin has been included as a diagnostic criterion in the updated consensus of PJI[10].

Currently, there are two commercially available methods for the determination of synovial alpha-defensin. The quantitative laboratory-based ELISA, that requires a centrifuged synovial fluid to assess the concentration of alpha-defensin[17], and the qualitative lateral flow test. As mentioned, both tests have shown to be successful for the investigation of PJI, with ELISA presenting the best performance[17,18,23,24]. However, alpha-defensin ELISA is much more complex, requiring a laboratory structure and an experienced professional to be performed. Conversely, the lateral flow test can be done by the physician at any location, and the result is rapidly

Table 2 Patient demographics

	Total	Aseptic cases	Infected cases	*P* value
n	53	31	22	
Sex				0.22[1]
Male	14 (26.4)	6 (19.4)	8 (36.4)	
Female	39 (73.6)	25 (80.6)	14 (63.6)	
Age (range)	68 (47-85)	67 (47-85)	70 (52-85)	0.30[2]
Laterality				> 0.99[1]
Right knee	28 (52.8)	16 (51.6)	12 (54.5)	
Left knee	25 (47.2)	15 (48.4)	10 (45.5)	
Inflammatory disease	12 (22.6)	7 (22.6)	5 (22.7)	> 0.99[1]
RA	10 (18.9)	7 (22.6)	3 (13.6)	
Gout	2 (3.8)	0	2 (9.1)	
Sinus tract	4 (7.5)	0	4 (18.2)	
Alpha-defensin S/CO	2.21 ± 2.73	0.28 ± 0.13	4.93 ± 2.28	< 0.01[3]

[1]Fisher's exact test.
[2]Unpaired *t* test.
[3]Mann-Whitney test. Values expressed in number (percentage). Age in years is presented as mean (range) and alpha-defensin S/CO in mean (standard deviation). RA: Rheumatoid arthritis.

Table 3 Statistical results of enzyme-linked immunosorbent assay and lateral flow test for all patients

	Aseptic	Infected	Sensitivity (95%CI)	Specificity (95%CI)	Accuracy (95%CI)
ELISA			95.5% (77.2%-99.9%)	100% (88.8%-100%)	98.1% (89.9%-100%)
Negative	31	1			
Positive	0	21			
Lateral flow			86.4% (65.1%-97.1%)	100% (88.8%-100%)	93.2% (82.8%-98.3%)
Negative	31	3			
Positive	0	19			

ELISA: Enzyme-linked immunosorbent assay.

expressed within 10 minutes.

As suggested by our team, one potential reason for the inferior results regarding the lateral flow test is that, during its execution, fluid centrifugation is not performed (in accordance with the manufacturer's instruction). Consequently, some particles and cellular debris could lead to false results. Although some evidence shows that blood contamination does not influence the lateral flow reading[19], the sample processing is not equivalent between ELISA and lateral flow test, which may interfere in the device reading[15,16]. In this study, we indirectly suggest this plausible issue, since a favorable performance of the lateral flow test was reached after centrifugation. Here, we obtained a sensitivity of 86.4%, a specificity of 100% and an accuracy of 93.2%, superior values than the ones observed in some previous non-centrifuged studies. Indeed, sensitivity of approximately 67%-69%, specificity of 93%-94%, and accuracy of 85% were previously reported for the lateral flow test[25,26]. It is noteworthy to mention that, although some recent systematic reviews and meta-analyses present higher pooled values for the lateral flow, the moderate-to-high heterogeneity among the included studies compels careful interpretation. Even so, the 83% sensitivity and 94% specificity found in these studies are still slightly lower than the achieved here[14,27]. In our series, the centrifuged lateral flow performed similarly to ELISA, which also demonstrated excellent results in concordance to the literature[16,27].

Table 4 Statistical results of enzyme-linked immunosorbent assay and lateral flow test for patients without sinus tract

	Aseptic	Infected	Sensitivity (95%CI)	Specificity (95%CI)	Accuracy (95%CI)
ELISA			100% (81.5%-100%)	100% (88.8%-100%)	100% (92.8%-100%)
Negative	31	0			
Positive	0	18			
Lateral flow			100% (81.5%-100%)	100% (88.8%-100%)	100% (92.8%-100%)
Negative	31	0			
Positive	0	18			

ELISA: Enzyme-linked immunosorbent assay.

Some authors have described false positive results using the lateral flow test in cases of metallosis[23,25] and crystal deposition disease[28,29]. This current study did not find any false positive case, despite the presence of four patients with gout. Once again, the centrifugation might improve the measurement by removing these particles. On the other hand, one false negative (by ELISA) and three false negatives (by the lateral flow test) were observed. All of those occurred in patients with sinus tract, as previously shown[30,31]. Although it was not directly investigated here, we speculate that the fistulization tends to drain the synovial fluid, avoiding the accumulation of pathogen and alpha-defensin within the knee. Considering the presence of draining sinus as a confirmation of PJI diagnosis, additional investigation would not be required. In this regard, excluding these specific patients, a sensitivity, specificity, accuracy and agreement of 100% were obtained for both tests.

The study has several limitations. First, we did not perform a direct comparison between centrifuged and non-centrifuged samples for the lateral flow test. Due to the high cost of lateral flow test in our region when this preliminary study was designed, we decided to compare these initial findings with the literature. As we know, there are several studies presenting remarkable data[14,25,26,32]. Further comparative trials are necessary and might add stronger conclusions. In addition, understanding the reason for false positive cases in patients with crystal arthropathy or metallosis, and the beneficial effects of synovial fluid centrifugation in these contexts may be valuable for its proper management. Moreover, despite the prospective design, the study was not randomized. Given the rarity of the cases that fit in our study, a randomization is impracticable. Therefore, we provide interesting data showing that a prior centrifugation may improve the lateral flow test performance. Considering the ease of execution and interpretation of the lateral flow, the addition of this prior step deserves further investigation and, potentially, a place in the PJI diagnosis.

CONCLUSION

In conclusion, we have identified that an extra step of synovial fluid centrifugation prior to the alpha-defensin lateral flow test achieved high sensitivity, specificity and accuracy. The results obtained using this methodology were comparable to those obtained with the alpha-defensin ELISA. Furthermore, centrifuged lateral flow demonstrated performance values slightly higher than the previously reported in the literature. Therefore, the use of the alpha-defensin lateral flow post synovial fluid centrifugation may represent a novel and interesting strategy during the PJI investigation given its lower complexity and equivalent performance in comparison to ELISA.

ARTICLE HIGHLIGHTS

Research background

Periprosthetic joint infection (PJI) is a serious postoperative complication that leads to severe morbidity as well as substantial financial burden to the healthcare system. Currently, two synovial alpha-defensin tests [the quantitative enzyme-linked

immunosorbent assay (ELISA) and the qualitative lateral flow test] are available and provide important information during PJI investigation, with the ELISA presenting slightly superior performance. However, the lateral flow test offers benefits in terms of the ease of use, time-efficiency and cost.

Research motivation

While the synovial fluid sample has to be centrifuged preceding ELISA, prior centrifugation is not routinely performed to the lateral flow test. The maintenance of synovial fluid debris could potentially interfere in the lateral flow results.

Research objectives

This study aimed to evaluate the performance of the alpha-defensin lateral flow test with prior synovial fluid centrifugation and compare the results with the synovial alpha-defensin ELISA.

Research methods

In this prospective study, 53 cases of total knee arthroplasty were evaluated: 22 classified as PJI and 31 classified as aseptic knees. Synovial fluid samples were collected and submitted to centrifugation, and the supernatant was evaluated by lateral flow test and ELISA. Sensitivity, specificity, and accuracy of each method as well as the agreement between those two methods were calculated.

Research results

Alpha-defensin ELISA and lateral flow tests showed negative results for infection in all 31 aseptic patient samples. In regard to the 22 infected cases, the lateral flow test showed positive results in 19 cases (86.4%) whereas the ELISA was positive in 21 cases (95.5%). Sensibility, specificity, and accuracy were 86.4% (95%CI: 65.1%-97.1%), 100% (95%CI: 88.8%-100%) and 93.2% (95%CI: 82.8%-98.3%), respectively, for the lateral flow test and 95.5% (95%CI: 77.2%-99.9%), 100% (95%CI: 88.8%-100%) and 98.1% (95%CI: 89.9%-100%) for ELISA. Agreement of 96.2% between these two methods were found, without statistical difference between them (P = 0.48).

Research conclusions

Alpha-defensin lateral flow test with prior synovial fluid centrifugation showed high sensitivity, specificity, and accuracy, achieving comparable results to ELISA. Given the lower complexity of the lateral flow test, a prior centrifugation might be a valuable strategy to enhance its performance.

Research perspectives

Prior synovial fluid centrifugation may be a novel and interesting strategy to improve the lateral flow performance during the PJI diagnosis. Further investigation is required to clarify its actual benefit.

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World Journal of Orthopedics

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World J Orthop 2021 August 18; 12(8): 575-583

DOI: 10.5312/wjo.v12.i8.575

ISSN 2218-5836 (online)

SYSTEMATIC REVIEWS

Limb lengthening with PRECICE magnetic nail in pediatric patients: A systematic review

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Author contributions: Palmacci O and Masci G designed the study; Cipolloni V and Vitiello R contributed to the data collection and data analyses; Masci G and Bonfiglio N contributed to the manuscript preparation; Bocchi MB and Pola E contributed to revising the manuscript content.

Conflict-of-interest statement: The authors declare that there are no conflict of interest.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

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Abstract

BACKGROUND

Limb lengthening techniques play an increasingly important role in the pediatric orthopedic field. The principles of the osteogenesis distraction bonded traditionally with external fixators; however, the recent deployment of fully implantable systems has been able to overcome severities related to external fixators. The PRECICE® is an implantable limb lengthening intramedullary nail system that is remotely controlled and magnetically driven.

AIM

To review the current literature available on this matter in order to assess the PRECICE clinical and radiological outcomes and its possible complications in a population of pediatric patients undergoing limb lengthening.

METHODS

Only five studies met the inclusion criteria and were consequently included in the review for a total of 131 patients and 135 femurs. The clinical and radiological outcomes of interest were: the main lengthening obtained, the distraction rate, the period of time to full weight bearing, the consolidation index, and the Association for the Study and Application of Methods of Ilizarov score.

RESULTS

In conclusion, data collected from the articles under investigation were comparable with the exception of the consolidation index. Unfortunately, the study population was too small and the patients' follow-up was too short to make definitive conclusions.

Manuscript source: Invited manuscript

Specialty type: Orthopedics

Country/Territory of origin: Italy

Peer-review report's scientific quality classification
Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: January 29, 2021
Peer-review started: January 29, 2021
First decision: May 3, 2021
Revised: May 12, 2021
Accepted: June 22, 2021
Article in press: June 22, 2021
Published online: August 18, 2021

P-Reviewer: Wang XQ
S-Editor: Ma YJ
L-Editor: Filipodia
P-Editor: Li X

CONCLUSION
This review shows that the PRECICE Nail System is still a therapeutic challenge in limb lengthening for pediatric orthopedic surgeons; however, careful preoperative planning and an accurate surgical technique could allow the correction of more complex deformities with a low rate of complications.

Key Words: Limbs lengthening; PRECICE; Nail; Pediatric; Dysmetria; Deformities

Core Tip: Limb lengthening techniques play an increasingly important role in the pediatric orthopedic field. The PRECICE® is an implantable limb lengthening intramedullary nail system that is remotely controlled and magnetically driven. The aim of our study was to review the current literature in order to assess the clinical and radiological outcomes and possible complications in a population of pediatric patients undergoing limb lengthening. This review shows that the PRECICE allows correction of the more complex deformities with a low rate of complications.

Citation: Masci G, Palmacci O, Vitiello R, Bonfiglio N, Bocchi MB, Cipolloni V, Maccauro G, Pola E. Limb lengthening with PRECICE magnetic nail in pediatric patients: A systematic review. *World J Orthop* 2021; 12(8): 575-583
URL: https://www.wjgnet.com/2218-5836/full/v12/i8/575.htm
DOI: https://dx.doi.org/10.5312/wjo.v12.i8.575

INTRODUCTION

Limb lengthening techniques play an increasingly important role in the field of pediatrics orthopedics with regard to length discrepancy, angular deformities (referable either to fractures sequelae or congenital malformations), and short stature correction[1-4]. The osteogenesis distraction is a reparative process involving not only the bone but also the soft tissues including the muscles, nerves, and skin. Therefore, accurate distraction control is required since too rapid correction could lead to nonunion, nerve damage, and joint contractures, while on the other hand a process that is too slow could result in premature consolidation[5].

The principles of the osteogenesis distraction bonded traditionally with the external fixators, considering both monolateral and circular fixators[6,7]. More recently, the deployment of fully implantable systems for limb lengthening has allowed overcoming external fixator-related severities such as pin-site infections, soft tissue tethering, and patient device intolerance during treatment, to name a few[8-10]. Intramedullary nails were initially used in conjunction with external fixation in hybrid techniques such as lengthening over nail or lengthening and then nailing[11,12], in order to reduce fixator time and prevent secondary deformities. However, these techniques are not free from external fixator-related complications. Over the past couple of decades, internal bone lengthening devices have been developed to obviate the need for external fixators. They seem to decrease patients' pain and discomfort and facilitate a more rapid and effective rehabilitation compared with external fixation[13].

At present, three types of telescopic nails are mainly used: mechanically activated nails, motorized nails, and magnetically driven nails[14-16]. The PRECICE® Intramedullary Limb Lengthening System (NuVasive Specialized Orthopedics, San Diego, CA, United States) is a remotely controlled, magnetically driven, implantable limb lengthening intramedullary nail system first used in Europe in 2012[17-19]. The PRECICE nail is a magnet-operated telescopic internal lengthening device with an ERC that contains two rotating magnets[20]. When placed by the patient on the skin, above the magnet which is within the nail, it causes this internal magnet to rotate, which translates to the thinner nail element telescoping out of the thicker surrounding nail; the nail can be both extended and retracted by altering the settings on the ERC as well as accurately setting the rate of distraction. A distance of 1 mm requires the ERC to be placed over the magnet within the nail for 7 min[21].

The PRECICE represents a safe and accurate technique able to correct both deformity and limb-length discrepancy, lengthening but also shortening (unlike other lengthening nails[22]) with reduced side effects . Among the advantages of opting for this implant, there is the ability to maintain the knee range of motion during the lengthening process and also the rapid bone healing allows a relatively early return to weight bearing[23,24].

The aim of our study was to review the current literature available on this matter in order to assess the PRECICE clinical and radiological outcomes and its possible complications in a population of pediatric patients undergoing limb lengthening.

MATERIALS AND METHODS

A systematic review of the literature indexed in PubMed MEDLINE and Cochrane Library databases using the search key word "PRECICE" was carried out. To minimize the number of missed studies, no filters were applied to the search strategy. The bibliography of the selected studies was accurately searched by hand, in order to identify further studies not found during our electronic search. No restrictions on the date of publication or language were applied. The title of the journal, name of authors, or supporting institutions were not masked at any stage. No attempt to contact authors in order to obtain individual patient data was made. The Preferred Reporting Items for Systematically Reviews and Meta-Analyses (PRISMA) was followed as reported in Figure 1. In order to be considered for this review, the articles needed to comply with the following inclusion criteria: use of the PRECICE® Intramedullary Limb Lengthening System (NuVasive Specialized Orthopedics) for femur lengthening and patient age under 18 years. No restrictions for surgical approach to nailing were applied. Abstracts and full texts were independently screened by two authors (Vitiello R and Maccauro G), and any discordance was solved by consensus with a third author (Palmacci O). The methodological quality of the studies was assessed using the modified Coleman Methodology Score (mCMS)[25]. Each article was evaluated by two independent investigators (Vitiello R and Bocchi MB); in cases with more than a five-point difference between their rating, the discrepancy was solved by consensus with a third author (Palmacci O). The mCMS ranges from 0 to 100 points, representing a well-designed study with no bias or confounding factors.

RESULTS

The electronic search resulted in 60 hits. Following the PRISMA flow chart[26], only five studies met the inclusion criteria and were taken into consideration in the review [27-31]. Eight papers partially followed the inclusion criteria; these studies included a non-specific pediatric population. An extra analysis was performed for these latter papers. All of the selected studies were retrospectively analyzed. The target population consisted of 131 patients for a total of 135 femurs. According to the mCMS evaluation, the mean score of the studies reached was 47 points (25-57 points) showing a poor-mediocre result. The papers we took into consideration had several methodological issues, particularly when considering the procedure in assessing the outcomes. Moreover, the study population was too small and the patient's follow-up was too short. However, all of the papers accurately reported the indications for surgical intervention and the surgical technique (respectively 5 points each). Studies by Szymczuk *et al*[30] and Hammouda *et al*[32] compared the PRECICE intramedullary nailing with external fixation, but in our analysis, we only took into account the PRECICE nailing results. In studies by Nasto *et al*[27] and Iliadis *et al*[29], both retrograde and antegrade approaches were used, and some tibia nailing was included. Other studies preferred the antegrade approach to the femur.

DISCUSSION

Demographic data and etiology

We reached a population of 131 male and female patients for a total of 135 femurs. Males and females numbered 69 and 62, respectively. The mean age was 14.8 years old, ranged between 7 and 18 years old[31]. All of the studies reported pre-operative discrepancy except one[31], with a mean value of 5.2 cm (range, 4.9 to 6.3). The mean

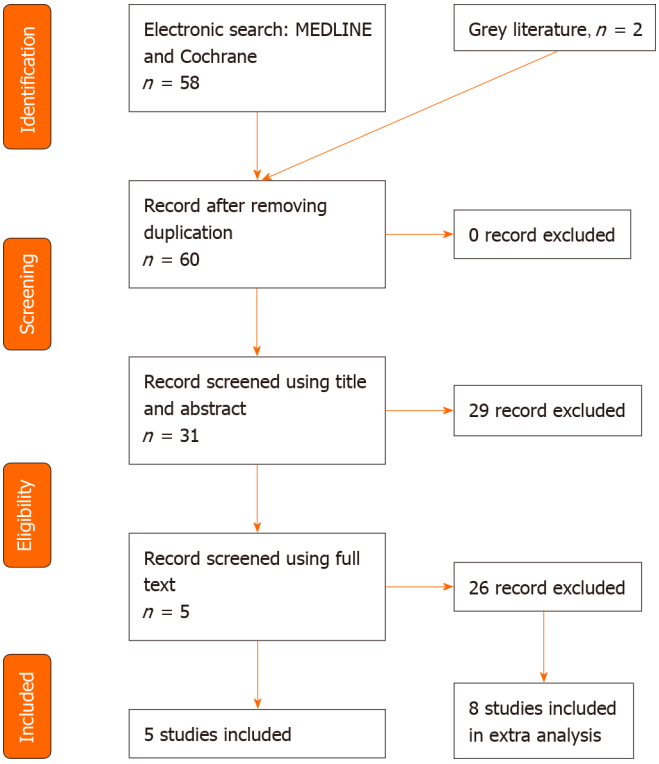

Figure 1 PRISMA flowchart.

follow-up was 1.7 years when reported (Table 1). Concerning surgical indications, one study only focused on a single pathology; in particular, Szymczuk *et al*[30] focused on congenital femoral deficiency treatment for a total of 30 femurs (Table 2). Among other papers, the principal surgical indication was congenital femoral deficiency (19 femurs), and yet post-traumatic malformations (18 femurs), achondroplasia (8 femurs), hemihypertrophy (8 femurs) and Ollier disease (6 femurs). Nevertheless, the main indication remained "miscellaneous" (46 femurs).

Clinical and radiological outcomes

Regarding the PRECICE system results, the studies examined focused on the following issues: The main lengthening obtained with particular reference to accuracy and reliability, the distraction rate, the period to reach full weight bearing, the consolidation index, and the Association for the Study and Application of Method of Ilizarov (ASAMI) score (Table 3 and Table 4). Nail accuracy is defined as the ratio between the lengthening obtained and the planned length, while nail reliability is the ratio between the number of implanted lengthening devices and the number of successfully ended lengthening treatments. Analyzing the main lengthening obtained, the results were similar across all studies. In particular, Hammouda *et al*[31] reported a mean lengthening of 5.6 (3-6.7), with no reference to accuracy and reliability. It is relevant to notice that the authors performed intramedullary nailing using the trochanteric entry. During the follow-up time no patients showed radiographic nor clinical signs of femoral head necrosis. The average lengthening achieved reported by Nasto *et al*[27] was 4.4 ± 1.2, with a nail accuracy and reliability of 91% and 88% respectively. Iliadis *et al*[29] reported a nail accuracy of 96% and a nail reliability of 98%, due to a single case where a nail was implanted without lengthening because of the patient's mental health issues.

The distraction index (DI), defined as the ratio between the number of days of distraction and the achieved length (days/cm), was reported in all of the studies analyzed, except for Hammouda *et al*[31]. Among the articles, the results were almost comparable. Szymczuk *et al*[30] described a DI of 0.7 ± 0.18, while Iliadis *et al*[29] reported a DI of 0.92 (0.67-1). Furthermore, this latter retrospective review was the only one considering the days to full weight bearing from lengthening accomplishment with a mean of 45 days. All patients in fact gradually obtained full weight bearing over a 4-wk period after the planned length achievement. The consolidation index (CI) is defined as the ratio between the total duration required to achieve bone healing and the achieved length (day/cm). The data collected in the articles under

Table 1 Demographic data

Ref.	Number of patients	Gender	Tibia nailing	Age (yr)	Discrepancy (cm)	Follow-up (yr)	mCMS
Hammouda *et al*[32]	28 patients; 31 femurs	17 males; 11 females	-	12.9	-	1.9	49
Szymczuk *et al*[30]	30	14 males; 16 females	-	15.4	4.9	1.9	51
Iliadis *et al*[29]	42 patients; 43 femurs	20 males; 22 females	7	15	4.9	-	54
Nasto *et al*[27]	26	15 males; 11 females	5	14.7	4.9	1.4	57
Tomaszewski *et al*[28]	5	3 males; 2 females	-	16.3	6.3	-	27

In brackets measurement unit; Data are reported as absolute value. mCMS: Modified Coleman Methodology Score.

Table 2 Etiology

Ref.	Congenital femoral deficiency	Achondroplasia	Post-traumatic	Hemihypertrophy	Ollier disease	Miscellaneous
Hammouda *et al*[32]	10	6	5	3	2	5
Szymczuk *et al*[30]	30	-	-	-	-	-
Iliadis *et al*[29]	5	2	7	5	1	23
Nasto *et al*[27]	4	-	4	-	3	15
Tomaszewski *et al*[28]	-	-	2	-	-	3

In brackets measurement unit; Data are reported as absolute values.

Table 3 Result

Ref.	Mean lengthening (cm)	Accuracy	Reliability	Distraction rate (mm/d)	Day to full weight bearing	Consolidation index (d/cm)	ASAMI functional score	ASAMI bone score
Hammouda *et al*[32]	5.6 (3-6.7)	-	-	-	-	-	-	-
Szymczuk *et al*[30]	4.75 ± 1.43	95%	-	0.7 ± 0.18	-	34.7 ± 11.2	-	-
Iliadis *et al*[29]	-	96%	98%	0.92 (0.67-1)	45 (21-132)	28 (18-43)	35 excellent; 11 good; 3 fairs; 1 poor	41 excellent; 8 good; 1 fair
Nasto *et al*[27]	4.4 ± 1.2	91%	88%	0.9 ± 0.1	-	11.9 ± 2.1	22 excellent; 3 good; 1 fair	24 excellent; 1 fair; 1 poor
Tomaszewski *et al*[28]	4.9 (4-5.8)	-	-	0.8 (0.8-1)	-	29.3 (21-33)	-	-

In brackets measurement unit; Data are reported as absolute values.

investigation were different. Nasto *et al*[27] in particular obtained a CI of 11.9 ± 2.1, while Szymczuk *et al*[30] obtained a CI of 34.7 ± 11.2. Nasto *et al*[27] and Iliadis *et al*[29] reported the modified ASAMI score, which is a scoring system that classifies clinical results into excellent, good, fair, and poor based on four different parameters. The data we collected were similar and encouraging, supporting the efficacy of this device. In the paper by Iliadis *et al*[29], patients reported a low pain score throughout the lengthening and consolidation period. No significant impact on daily living activities was reported by 66% of patients, to the extent that 92% of patients were satisfied with the surgical treatment results and felt that they had achieved their goals.

Complications

Adverse events were divided into problems, obstacles, and complications in accordance with the data previously described by Paley[17]. Problems were defined as

Table 4 Complication

Ref.	Number of patients	Problem	Obstacle	Complication
Hammouda *et al*[32]	28 patients; 31 femurs	-	-	2
Szymczuk *et al*[30]	30	8	19	4
Iliadis *et al*[29]	42 patients; 43 femurs	7	4	4
Nasto *et al*[27]	26	5	1	3
Tomaszewski *et al*[28]	5	1	-	-

In brackets measurement unit; Data are reported as absolute values. Problems are post-operative difficulties that resolved completely with non-operative intervention; obstacles were difficulties that needed an operative intervention, resolved completely after surgery; complications consisted of all intra- and post-operative complications that remained unresolved even after treatment was completed.

difficulties after the surgical procedure resolved with conservative treatment, obstacles were difficulties that required surgical treatment, and complications were true intra or post-operative complications that persisted after the treatment. Hammouda *et al*[31] reported no problems or obstacles in 28 patients and two complications. Among them, 1 patient developed hip subluxation and delayed union of the regenerate, which was treated surgically. In addition, the nail was exchanged 6 mo after surgery. Iliadis *et al*[29] reported instead seven problems, four obstacles, and four complications. In 7 cases, they reported joint stiffness during the lengthening period, which was resolved with physiotherapy and by slowing down the distraction. Two femoral nails required the locking bolts removal as they were causing discomfort after consolidation. One patient with fibrous dysplasia, who previously underwent proximal femoral osteotomy with locking plate fixation, had a periprosthetic fracture so the PRECICE was exchanged with a trauma nail, but with loss of about 30 mm of lengthening.

Tomaszewski *et al*[28] reported no inflammatory complications, but in 1 case, after a lengthening of more than 45 mm, they noted a knee flexion contracture of about 10° despite the physiotherapy. Moreover, they had to stop the lengthening treatment in 1 case due to the pain and femoral nerve paresthesia. In the retrospective multi-center study conducted by Nasto *et al*[27], a total of five problems (joint contractures), one obstacle (femur fracture), and three complications (hip subluxation, 1 deep infection and 1 nail running back) were encountered. No bone healing complications were reported. Considering the patient who developed deep infection, the treatment was suspended and the nail removed. Regarding the case of hip subluxation, we would like to note that the patient had a developmental hip dysplasia history treated with proximal femur varus derotation osteotomy (VDRO) and Dega osteotomy. This complication was surgically treated with periacetabular osteotomy and VDRO; at the latest follow-up, the patient was asymptomatic and pain free during walking.

Non-specific pediatric population

Analyzing the entire population, a great heterogeneity has emerged in terms of age (7-72), male/female ratio, surgical access and surgical site[18,19,21,32-36]. The rise in the average population age has led to an increase of post-traumatic etiology[32], although the congenital and syndromic causes are still well represented[18,32,36]. All of the reviewed articles analyzed both femoral and tibial lengthening nails outcomes, except one[32]. In a retrospective review by Wagner *et al*[18], both PRECICE nail accuracy and precision reached 97.3% and 92.4%, respectively, with a total of nine complications (28%), all of which were successfully resolved without any long-term sequelae. In his 24-nail series, Kirane *et al*[21] revealed an accuracy of 96% and a precision of 86% with only one (4%) implant-related failure caused by a non-functional distractor mechanism and 6 (24%) non-implant-related obstacles; the minimum follow-up was 3 wk (mean 14 wk). In a different 9 case series by Wiebking *et al*[34], there were significant differences regarding the lengthening goal achievement and thus also the full weight bearing among patients. Consequently, the accuracy and the precision rate were 78% *vs* 61%, respectively. Despite the complications, patient satisfaction was generally positive.

A slight improvement in the quality of life was shown in preoperative and 12-mo postoperative Enneking scores; no differences were revealed in the physical and mental SF-12 score[18].

Concerning complications, a low complication rate was demonstrated in a series of 17 post-traumatic femoral lengthening nails with 2.2-year follow-up[32]. Hammouda *et al*[32] reported 3 patients (18%) with non-implant related complications that all resolved without permanent sequelae. Similar outcomes were reported by Horn *et al* [35] who described 8 of 50 complications, which were treated by surgery without sequelae and therefore were graded as obstacles. However, in this study, 16 nails were not PRECICE[35].

CONCLUSION

This review shows that the PRECICE Nail System is still a therapeutic challenge in limb lengthening for pediatric orthopedic surgeons. In the literature, only few studies have been published; nevertheless, the outcome demonstrates excellent clinical results and patient satisfaction. Careful pre-operative planning and an accurate surgical technique could allow correction of the more complex deformities with a low rate of complications.

ARTICLE HIGHLIGHTS

Research background

Limb lengthening devices have evolved in the last century to correct limb length discrepancies, congenital short statures, and limb deformities. The unilateral external fixator has been the standard method of fixation for a long time; however, the method of fixation has rapidly evolved from unilateral external fixator to the ring fixator, to the computer-assisted fixator, and finally to the lengthening of intramedullary nails.

Research motivation

The large number of complications related to the use of external fixation has led to the development of alternatives. The PRECICE represents an innovative and less invasive option to external fixation with regard to limb lengthening, allowing a controlled lengthening phase with the ability to shorten and regulate the device if necessary.

Research objectives

To review the current literature available on the specific matter in order to assess the PRECICE clinical and radiological outcomes and its possible complications in a population of pediatric patients undergoing femur lengthening.

Research methods

The current study is the result of a systematic review of the available literature using a single search term "PRECICE". The articles were sorted according to both pre-determined inclusion and exclusion criteria. PRISMA was followed.

Research results

Five studies met the inclusion criteria for a total of 131 patients. The studies examined focused on the following issues: the main lengthening obtained, the distraction rate, the number of days necessary to reach full weight bearing, the consolidation index and the ASAMI score. Among the articles all the results were almost comparable with the only exception of the consolidation index. Adverse events that emerged in a low percentage were divided into problems, obstacles, and complications.

Research conclusions

Although the PRECICE nail system is still a therapeutic challenge, the results have shown excellent clinical results and patient satisfaction with a low rate of complications. Therefore this approach could represent a valid alternative to the traditional limb lengthening systems.

Research perspectives

Future studies on larger and more homogeneous samples are needed to validate the use of PRECICE.

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World J Orthop 2021 August 18; 12(8): 584-603

DOI: 10.5312/wjo.v12.i8.584

ISSN 2218-5836 (online)

SYSTEMATIC REVIEWS

Complications in growth-friendly spinal surgeries for early-onset scoliosis: Literature review

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Conflict-of-interest statement: The authors declare that there is no conflict of interest.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

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Abstract

BACKGROUND

The treatments for early-onset scoliosis (EOS), defined as curvature of the spine with onset before 10 years of age, continue to pose a great challenge for pediatric orthopedics. The treatment goals for EOS include minimizing spinal deformity while maximizing thoracic volume and pulmonary function. Different surgical techniques have different advantages and drawbacks; however, the two major concerns in the management of EOS are repeated surgeries and complications.

AIM

To review the current literature to assess the safety of EOS surgical treatment in terms of the rate of complications and unplanned surgeries.

METHODS

In January 2021 two independent reviewers systematically searched three electronic medical databases (PubMed, the Cochrane Library, and Embase) for relevant articles. Every step of the review was done according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Due to the heterogeneity of articles and topics after data analysis, a descriptive (synthetic) analysis was performed.

RESULTS

A total of 2136 articles were found. Forty articles were included in this systematic review, after applying our inclusion and exclusion criteria. EOS surgery has a varying but high rate of complications. The most frequent complications were categorized as implant (54%), general (17%), wound (15%) and alignment (12%).

Manuscript source: Invited manuscript

Specialty type: Orthopedics

Country/Territory of origin: Poland

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: February 25, 2021
Peer-review started: February 25, 2021
First decision: March 31, 2021
Revised: April 12, 2021
Accepted: August 2, 2021
Article in press: August 2, 2021
Published online: August 18, 2021

P-Reviewer: Liu HQ
S-Editor: Wang JL
L-Editor: A
P-Editor: Li JH

The rate of complications might have been even higher than reported, as some authors do not report all types of complications. About 54% of patients required unplanned surgeries due to complications, which comprised 15% of all surgeries.

CONCLUSION

The literature concerning the definitions, collection, and interpretation of data regarding EOS surgery complications is often difficult to interpret. This creates problems in the comparison, analysis, and improvement of spine surgery practice. Additionally, this observation indicates that data on the incidence of complications can be underestimated, and should be interpreted with caution. Awareness of the high rate of complications of EOS surgery is crucial, and an optimal strategy for prevention should become a priority.

Key Words: Scoliosis; Spine; Growth-friendly implant; Surgery; Complications; Treatment

Core Tip: Early-onset scoliosis (EOS) is defined as curvature of the spine ≥ 10° with onset before 10 years of age, regardless of etiology. The treatment for EOS is still a great challenge for pediatric orthopedics, and surgery is often necessary. Repeated surgeries and complications are two major concerns in EOS management. The literature on the definitions, collection, and interpretation of data regarding EOS surgery complications is often difficult to interpret. This creates problems in the comparison, analysis, and improvement of spine surgery practice. Data on the incidence of complications can be underestimated, and should be interpreted with caution.

Citation: Latalski M, Fatyga M, Sowa I, Wojciak M, Starobrat G, Danielewicz A. Complications in growth-friendly spinal surgeries for early-onset scoliosis: Literature review. *World J Orthop* 2021; 12(8): 584-603
URL: https://www.wjgnet.com/2218-5836/full/v12/i8/584.htm
DOI: https://dx.doi.org/10.5312/wjo.v12.i8.584

INTRODUCTION

Early-onset scoliosis (EOS) is defined as curvature of the spine ≥ 10° in the frontal plane with onset before 10 years of age[1]. EOS is not a diagnosis, but can rather be defined as the age of onset of a coronal plane spinal deformity. As such, EOS includes spinal deformities resulting from congenital malformations, neuromuscular conditions, inherited bone dysplasias and syndromes, and, in idiopathic cases, with no underlying disorder. As EOS has such a wide variety of etiologies, its natural history varies widely, and in many cases is established at the time of the child's diagnosis which reveals the spinal deformity[2]. The natural history of untreated progressive EOS was reported on by Scott and Morgan in 1955[3]. They documented the progression of curves from 30 to 100 degrees. Moreover, 4 patients out of 28 died before the age of 20 years, of cardiorespiratory disease. Relentless curve progression, in the absence of treatment, results in increasing chest wall deformity. Rib rotation and curve progression produce restrictive pulmonary disease, with worsening pulmonary function, as documented by diminishing forced vital capacity and total lung volume. If left untreated, the spinal deformity produces chest wall rotation, which obliterates the space available for the lungs[4]. The treatment for EOS remains a great challenge for pediatric orthopedics. The treatment goals for EOS, regardless of the diagnosis, are the same: minimizing spinal deformity while maximizing thoracic volume and pulmonary function[5]. When conservative treatment is ineffective, the option is surgery[6]. Different techniques have different advantages and drawbacks. Those most often used are traditional growing rods (TGR), vertical expandable prosthetic titanium ribs (VEPTR), magnetically controlled growing rods (MCGR), and the Shilla growth guidance system (SGGS). Repeated surgeries and complications are two major concerns in EOS management. The aim of the study was to review the current

literature to assess the safety of EOS surgical treatment in terms of the rate of complications and unplanned surgeries.

MATERIALS AND METHODS

Literature search strategy

The systematic review was conducted according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[7] (Figure 1). In January 2021, a search of three electronic medical databases (PubMed, the Cochrane Library, and Embase) was performed by three independent authors. We combined the terms: "early-onset scoliosis" OR "eos" OR "juvenile scoliosis" OR "infantile scoliosis" OR "tgr" OR "veptr" OR "MCGR" OR "Shilla" OR "growth-friendly" AND "complication". The reference lists of all retrieved articles were reviewed for the further identification of potentially relevant studies, and assessed using the inclusion and exclusion criteria.

Selection criteria

The eligible studies for the reference review included those dealing with complications in the operative treatment of EOS. The initial screening of titles and abstracts was made using the following inclusion criteria: studies of any level of evidence, reporting clinical results, published in peer review journals, and dealing with complications in operative EOS treatment. Exclusion criteria were: studies with complications in the non-operative treatment of EOS, in vitro, or animal model studies. We also excluded all the remaining duplicates, articles dealing with other topics, and those with poor scientific methodology, or without an accessible abstract. Reference lists were also manually searched for further relevant studies. Reviews, abstracts, case reports, conference presentations, and expert opinions, were excluded.

All papers were tagged: (1) according to the system used: TGR, VEPTR, MCGR, Shilla (guided growth); (2) the number of cases as a "big group" – more than 30 cases, "medium group" – 10-29 cases, and "small group" – less than 10 cases; and (3) the time of follow-up – "short" – less than 2 years, "minimum" – more than 2 years, and "optimum" – more than 5 years. The final inclusion criteria were primarily limited to "big group" and "optimum follow-up". During the paper extraction, no papers with VEPTR, and only one with Shilla and MCGR, were found, so that the groups' extracted papers had to be extended with "medium group" and "minimum" follow-up.

Data extraction and criteria appraisal

Three investigators independently reviewed each article. Discrepancies between the reviewers were resolved by discussion and consensus. All data were extracted from article texts, tables, and figures, and put into tables in an Excel sheet.

Complications were categorized as wound-related, implant-related, alignment-related, and general (surgical or medical). Surgical procedures were classified as planned [implantations, lengthenings, final fusions (FF)], and unplanned (revisions). Implantation procedures were included as equal to the number of patients. Not-given information was calculated using specific formulas based on the known data, *i.e.,* the mean number of operations per patient, the number of patients, and the number of operations. Some data – especially in TGR-group patients - like the number of lengthenings and derived information – were estimated based on the mean duration between lengthenings, using formulas, *i.e.,* the mean duration between lengthenings, and follow-up, *i.e.* the number of lengthenings. The mean durations between lengthenings, if not specified, were taken as the mean value of durations between lengthenings specified in other papers. These data were marked in the table with the symbol "1". In some papers the number of unplanned surgeries was not provided. In those cases, such complications as deep infections and implant fractures were estimated as an indication of at least one revision/unplanned surgery. Some fields were left empty when there were not enough data to estimate the value. When the data in the main text and the tables did not match, the higher value was taken.

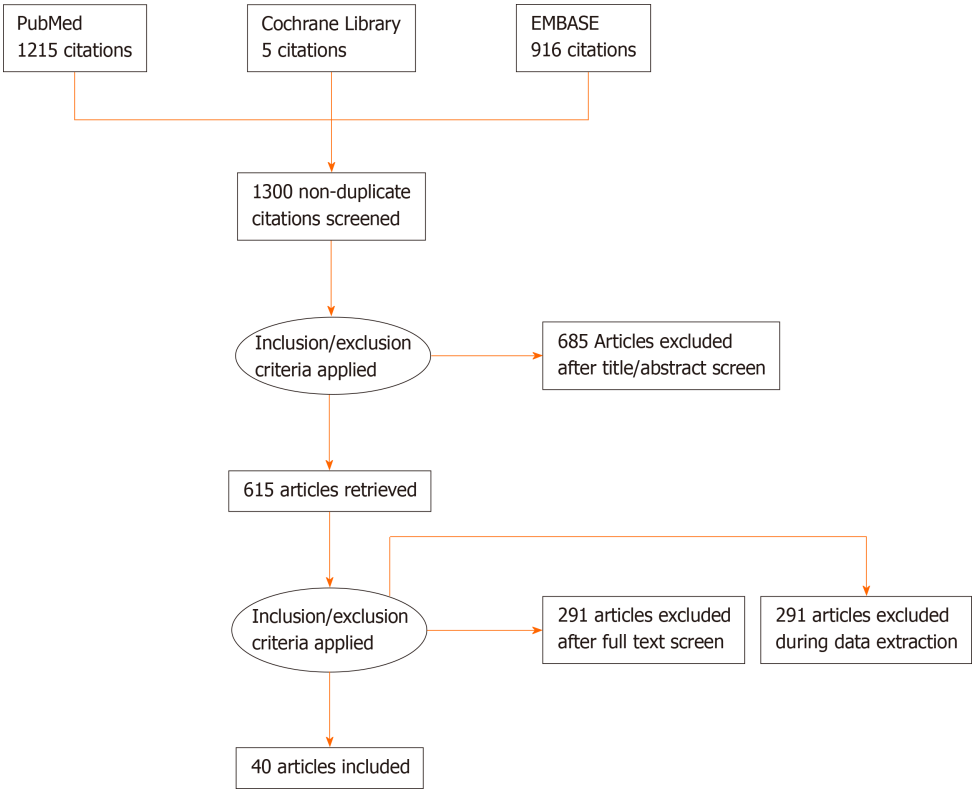

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the method of selection and screening.

RESULTS

Included studies

A total of 2136 articles were found. After the exclusion of duplicates, 1300 articles were selected. At the end of the first screening, following the previously described selection criteria, we selected 615 articles eligible for full-text reading. Ultimately, after full-text reading and reference-list checks, we selected n = 40 articles, following previously adopted criteria. A PRISMA flowchart of the method of selection and screening is presented in Figure 1. The included articles focus on complications in the most commonly used systems – TGR (17 papers), VEPTR (13 papers), MCGR (8 papers), and Shilla (guided growth) (7 papers). Data extracted from these papers were assigned to the appropriate system. Harris *et al*[8], 2020, in their paper analyzed the impact of patient and surgical factors on the proximal complications and revision rates of early-onset scoliosis patients using a multicenter database. Total 353 patients met the inclusion criteria: growing rods = 318 and VEPTR = 35. Helenius *et al*[9], 2018, analyzed the outcomes of surgeries using growing rods in patients with severe *vs* moderate early-onset scoliosis. From the group of 214 patients, 198 were treated with TGR and 14 with MCGR. As in the main texts, the data were not separated out, so we included them in the TGR group, as the vast majority were treated with this system. Papers by Akbarnia *et al*[10], Bachabi *et al*[11], Haapala *et al*[12], Andras *et al*[13], and Luhmann *et al*[14], dealt with comparisons between TGR and MCGR, TGR, and VEPTR, Shilla and MCGR, and TGR and Shilla, respectively, so they appear in the table for the applicable system. The demographic findings of the included articles are summarized in Table 1.

Tables 2-5 present the number of surgical procedures (planned and unplanned). The number of patients is re-listed for easier reference to the remaining data. As the quantitative data depends on the number of analyzed patients, the second part of the table presents the percentage data. It shows the percentage of unplanned surgeries, the percentage of unplanned surgeries to all surgeries, the percentage of unplanned surgeries to patients with at least one complication, and the ratio of planned to unplanned surgeries. Eight papers were excluded from these tables, as there were no data on unplanned surgeries. Some fields were left empty if there were insufficient data. From the 40 analyzed papers 12 described all 4 complications (wound and implant-related, alignment, and medical/surgical). These data are marked in the table with the symbol "2". In the others, some of these complications were not described. It

Table 1 Demographic data from the reviewed articles

	Ref.	Construct	Subject	Sex (male/female)	Age at IP	Follow up	Diagnosis	No of patient with final spinal fusion	Comments, kind of complication analyzed
1	Bess *et al*[15], 2010	TGR	140	71/59	6	5.0	Neuromuscular (*n* = 52), idiopathic (*n* = 40), congenital (*n* = 24), and other (*n* = 24)	50	W, I, A, M
2	Du *et al*[16], 2020		167	69/98	7,2	10.7	Idiopathic (*n* = 45), neuromuscular (*n* = 56), syndromic (*n* = 43), congenital (*n* = 21), other (*n* = 2)	167	Analyzed patients who had undergone a FF after growing-rod treatment, W, I, A, M
3	Andras *et al* [13], 2015		36	nd	6.1	4.3	Syndromal (*n* = 10), idiopathic (*n* = 11), congenital (*n* = 2), neuromuscular (*n* = 13)	nd	I, M
4	Myung *et al* [17], 2014		159	nd	5	4.7	Neuromuscular (*n* = 46), congenital (*n* = 42), idiopathic (*n* = 37), syndromal (*n* = 34)	nd	I
5	Arandi *et al* [18], 2014		175	78/97	5.9	5.2	Idiopathic (*n* = 69), syndromal (*n* = 62), neuromuscular (*n* = 44)	nd	I
6	Liang *et al* [19], 2015		55	16/39	6.8	38.4	Congenital (*n* = 28), idiopathic (*n* = 6), syndromal (*n* = 8), neuromuscular (*n* = 6) and miscellaneous disorders (*n* = 7)	10	W, I, A, M
7	Ramirez *et al* [20], 2020		67	32/35	6	4.1	Only non-ambulatory neuromuscular early-onset scoliosis	nd	W, I, M
8	Yamaguchi *et al*[21], 2014		176	nd	nd	4.7	Congenital (*n* = 48), neuromuscular (*n* = 42), syndromal (*n* = 37), idiopathic scoliosis (*n* = 32) and miscellaneous (*n* = 17)	nd	I
9	Poe-Kochert *et al*[22], 2016		100	42/58	7	4.3	Neuromuscular (*n* = 38), syndromic (*n* = 31), idiopathic (*n* = 22), congenital (*n* = 9)	100	Analyzed patients who had undergone a FF after growing-rod treatment; W, I
10	Kabirian *et al* [23], 2014		379	177/202	6.3	5.3	nd	nd	Only deep infection analyzed
11	Hosseini *et al* [24], 2018		274	114/160	6.7	6.3	Neuromuscular (*n* = 84), congenital (*n* = 43), syndromic (*n* = 89), idiopathic (*n* = 58)	nd	I
12	Johnston *et al* [25], 2013		27	nd	5.3	4.5	Neuromuscular (*n* = 6), idiopathic (*n* = 11), syndromic (*n* = 10)	6	Comparing with cast treatment, complications in total
13	Bachabi *et al* [11], 2020		50	nd	5.5	8.3	nd	nd	W, I, A, M
14	Luhmann *et al* [14], 2017		18	18	7.7	7.4	Idiopathic (*n* = 9), neuromuscular (*n* = 7), syndromic (*n* = 1), congenital (*n* = 1)	17	W, I, M
15	Akbarnia *et al* [10], 2014		12	5	6.5	4.1	Not given	nd	W, I, M
16	Harris *et al*[8], 2020		353	nd	6	6.0	Not given	nd	I, TGR -318 cases, 35 - VEPTR cases
17	Helenius *et al* [9], 2018		214	94/120	5.6	6.0	Neuromuscular (*n* = 68), congenital (*n* = 28), syndromic (*n* = 74), idiopathic (*n* = 44)	49	W, I, M TGR cases 198) MCGR cases 16
18	Gadepalli *et al* [26], 2011	VEPTR	26	16/10	7.58	7.0	Congenital or infantile scoliosis (*n* = 12), neuromuscular scoliosis (*n* = 5), unspecified structural thoracic disorder (*n* = 7), Jeune syndrome (*n* = 2)	nd	W, I, M
19	Bachabi *et al*		22	nd	4.3	7.7	nd	nd	W, I, M

	[11], 2020								
20	Crews *et al* [27], 2018		151	16/6	7.1	3+	nd	nd	Only SSIs following VEPTR implant or revision surgeries were identified
21	Murphy *et al* [28], 2016		25	12/13	5.7	4.5	Congenital (*n* = 25)	nd	W, I, M
22	Berger-Groch *et al*[29], 2020		13	7/6	2.2	7.6	Congenital (*n* = 13)	nd	W, I, M
23	Hasler *et al* [30], 2010		23	8/15	6.5	3.6	Early onset idiopathic scoliosis (*n* = 1), neuromuscular (*n* = 11), post-thoracotomy scoliosis (*n* = 2), Sprengel deformity (*n* = 1), hyperkyphosis (*n* = 2), myopathy (*n* = 1), syndromic (*n* = 5)	nd	W, I, A, M
24	Latalski *et al* [31], 2011		12	nd	5.25	2.5	Congenital (*n* = 3), neuromuscular (*n* = 9)	0	W, I, A, M
25	Hell *et al*[32], 2005		15	8/7	6	nd	Congenital (*n* = 9), neuromuscular (*n* = 6)	0	W, I, M
26	Garg *et al*[33], 2014		103	57/46	5.3		Neuromuscular (*n* = 30), congenital (*n* = 44), syndromic (*n* = 18), idiopathic (*n* = 11)		Only wound complications following VEPTR implant or revision surgeries were identified
27	Waldhausen *et al*[34], 2016		65	nd	6.9	6.9	Congenital (*n* = 23), neuromuscular (*n* = 12), syndromic (*n* = 14), idiopathic (*n* = 2), other (*n* = 14)	28	W, I, M
28	Striano *et al* [35], 2019		166		6.81		Neuromuscular (*n* = 61), syndromic (*n* = 38), congenital (*n* = 64), idiopathic (*n* = 3)	nd	Only wound complications following VEPTR implant or revision surgeries were identified
29	Lucas *et al* [36], 2013		54	21/33	7	2.0	Neuromuscular (*n* = 19), congenital (*n* = 30), syndromic (*n* = 7), idiopathic (*n* = 3)	nd	W, I, A, M
30	Garg *et al*[37], 2016		38	22/16	5.51	4.1	Neuromuscular (*n* = 18), congenital (*n* = 13), syndromic (*n* = 5), idiopathic (*n* = 2)	nd	Only wound complications following VEPTR implant or revision surgeries were identified
31	Subramanian *et al*[38], 2018	MCGR	31	15/16	7.7	3.9	Neuromuscular (*n* = 4), syndromic (*n* = 19), idiopathic (*n* = 6), congenital (*n* = 2)	nd	W, I, A, M
32	Urbański *et al* [39], 2020		47	14/18	8.8	1-2.5	Neuromuscular (*n* = 10), syndromic (*n* = 11), idiopathic (*n* = 20), congenital (*n* = 6)	0	W, I, A, M
33	Akbarnia *et al* [10], 2014		12	5/7	6.8	2.5	Neuromuscular (*n* = 4), syndromic (*n* = 4), idiopathic (*n* = 3), congenital (*n* = 1)	nd	I, M
34	Studer *et al* [40], 2019		30	10/20	9.4	2.1	Congenital (*n* = 11), neuromuscular (*n* = 10), syndromic (*n* = 4), idiopathic (*n* = 5)	nd	W, I, A
35	Kwan *et al* [41], 2017		30	11/19	7.3	3.0	Syndromal (*n* = 8), idiopathic (*n* = 8), congenital (*n* = 6), neuromuscular (*n* = 8)	5	W, I, A,
36	Obid *et al*[42], 2020		22	4/18	9.5	4.0	Idiopathic (*n* = 14), neurofbromatosis (*n* = 2), neuromuscular and syndromic (*n* = 6)	9	W, I, A, M
37	Lampe *et al* [43], 2019		24	7/17	10.5	3.5	Syndromal (*n* = 4), idiopathic (*n* = 9), congenital (*n* = 1), neuromuscular (*n* = 10)	nd	W, I, A, M

38	Haapala *et al* [12], 2020		18	11/7	6.8	3.2	Neuromuscular (*n* = 12) II, syndromic (*n* = 8) EOS two NFI (*n* = 2)	5	I, A, M
39	Haapala *et al* [12], 2020	Shilla	13	8/5	6	4.0	Neuromuscular (*n* = 11), syndromic (*n* = 2)	4	W, I, M
40	Andras *et al* [13], 2015	Shilla	36	nd	6.1	4.6	Syndromal (*n* = 10), idiopathic (*n* = 11), congenital (*n* = 2), neuromuscular (*n* = 13)	nd	I, M
41	Nazareth *et al* [44], 2020	Shilla	20	10/10	5.7	5.2	Syndromic (*n* = 9), neuromuscular (*n* = 5), idiopathic (*n* = 3), congenital (*n* = 3).	7	W, I, M
42	Miękisiak *et al* [45], 2019	GGS	57	13/44	9.8	2+	Not given	nd	GGS – the same principle as Shilla. System made of Ti. W, I, A, M
43	McCarthy *et al* [46], 2014	Shilla	10	2/8	7.5	2.0	Idiopathic (*n* = 3), congenital scoliosis (*n* = 1), syndromic (*n* = 2), neuromuscular scoliosis (*n* = 4)	nd	W, I
44	Luhmann *et al* [14], 2017	Shilla	18	nd	7.9	6.1	Idiopathic (*n* = 8), neuromuscular (*n* = 7), syndromic (*n* = 3)	15 and 3 implant removals	W, I, M
45	McCarthy *et al* [47], 2015	Shilla	40	17/23	6.11	5.0	Idiopathic (*n* = 9), congenital (*n* = 1), neuromuscular (*n* = 16), syndromic (*n* = 14)	15 and 3 Implant removals	W, I, A

Type of complications: Wound (W), implant-related (I), alignment (A), and medical/surgical complications (M). FF: Final fusions; GGS: Growth guidance system; VEPTR: Vertical expandable prosthetic titanium ribs; TGR: Traditional growing rods; MCGR: Magnetically controlled growing rods.

probably means that the number of unplanned surgeries was understated.

Excluded from these tables were papers in which the number of unplanned surgeries was not specified, and were not calculated; some cases referred to final fusion, but it was not specified when, so the total number based on the duration between lengthenings was not possible to estimate.

Unplanned surgeries are due to complications which cannot be resolved conservatively. The total number of complications is much higher. Table 6 presents the total number of complications, the number of patients with a minimum of one complication, the percentage of complications in all patients, the percentage of patients with a minimum of one complication, the number of complications in complicated patients, the complication rate per surgical procedure in percentage terms, and the percentage complications requiring surgical procedures. Some cells in the table are empty because of insufficient data in the corresponding papers.

In Table 7 the total number of complications are divided into wound-related, implant-related, alignment, and surgical/medical-related. Only 12 out of 40 papers include analyses of all these types. The paper by Johnston *et al*[25], 2013, did not differentiate the types of complications, so this reference was excluded from Table 7.

Smith *et al*[48] published in 2015 a New Classification System to Report Complications in Growing Spine Surgery, and only 4 out of 23 papers published in 2016 used this system (Table 8).

DISCUSSION

Currently there is great interest in the concept of the continued growth of the spine and chest while treating spinal deformity in EOS patients. The risk of complications is inherent in correction surgeries, regardless of etiology. Many studies agree that in the case of neuromuscular scoliosis the probability of a complication is 35%, while for EOS the probability increases to 48%[49]. Watanabe *et al*[50] identified risk factors for complications in the treatment of early-onset scoliosis using the dual growing rod technique. Postoperative complications occurred after 119 out of 538 procedures (22%) and affected 50 patients (57%). Complications mostly included implant-related failures (72%), and infections (16%). The authors suggested that independent risk factors for postoperative complications included an increase of every 20° in the proximal thoracic Cobb angle, an increase of every 20° in the thoracic kyphosis angle, and 6 or more rod-

Table 2 The number of planned and unplanned surgical procedures in the traditional growing rods group

Ref.	Subject	Surgical procedures (*n*)	Planned surgical procedures (*n*)	Unplanned surgical procedure		% unplanned surgeries to all surgeries	% unplanned surgery to patients with at least one complication	Ratio of planned to unplanned surgery
				n	%			
Bess *et al* [15], 2010	140	897	823	74	52.9[2]	8.2[2]	91.4[2]	11.12
Du *et al*[16], 2020	167	199	167	32	19.2[3]	16.1[3]	100.0[3]	5.22
Andras *et al* [13], 2015	36	288	259	29	80.6	10.1	100.0	8.9
Myung *et al* [17], 2014	159	1081[1]	1050[1]	31[1]	19.5	2.9	83.8	33.87
Arandi *et al* [18], 2014	175	1247[1]	1190	57[1]	32.6	4.6	71.3	20.88
Liang *et al* [19], 2015	55	272	263	23[1]	41.8[2]	8.5[2]	100.0[2]	11.43
Ramirez *et al* [20], 2020	67	463[1]	396[1]	67	100	14.5	163.4	5.91
Poe-Kochert *et al*[22], 2016	100	157[1]	100[1]	57	57[3]	36.3[3]	285.0[3]	1.75
Kabirian e *et al*[23], 2014	379	2344	2274[1]	70	18.5	3.0	166.7	32.49
Luhmann *et al*[14], 2017	18	167	141	26	144.4	15.6		5.42
Akbarnia *et al*[10], 2014	12	73	68	5	41.7	6.8	45.5	13.6
Harris *et al* [8], 2020	353	3141[1]	2895[1]	246	69.7	7.8	174.5	11.77
Helenius *et al* [9], 2018	214	1971	1836	133	62.1	6.7	137.1	13.8

[1]Data estimated based on the mean values of duration between lengthenings.
[2]The values of the % of unplanned surgeries in which all four complications were analyzed in the paper.
[3]Corresponds to the papers in which all the patients were after the final fusion.

lengthening procedures. According to Bess *et al*[15], the patients' early age when carrying out the index surgery influenced the incidence of complications, but Watanabe did not confirm this. He believed that a patient's being young at the time of the index surgery significantly reduced the risk of the child's developing a significant deformity, the degree of which at the start of the treatment significantly affects the risk of its course. However, one should be aware of the inverse relationship between the age of the index surgery and the number of lengthenings in distraction-based methods [4].

Bess, and the Growing Spine Study Group, stated in publications that there was a 24% complication rate each time a growing-rod construct was surgically lengthened, and a 13% decrease in complications for each additional year of age at the time of the initial growing rod implantation[15]. Rod implantation below age 7 years, increasing kyphosis, and more severe major curve magnitude, have been shown to correlate with a higher rate of complications overall[51].

Surgical difficulties, as well as the potentially harmful effect of repeated anesthesia, have led to the adoption of magnetically controlled growing rods, and guided growth systems like Shilla. However, problems with the loss of fixation and failure of the implants in some cases persist[10,47]. Some authors have pointed out an additional problem connected with metal debris which appears in the serum and surrounding tissues[52]. Although it does not directly affect the outcome of the treatment, it is worth considering this occurrence as undesirable/a complication.

The most important issue is that authors define complications in different ways. In Andras *et al*[13], major complications are defined as any neurological injury and any

Table 3 The number of planned and unplanned surgical procedures in the vertical expandable prosthetic titanium ribs group

Ref.	Subject	Surgical procedures (*n*)	Planned surgical procedures (*n*)	Unplanned surgical procedure		% unplanned surgeries to all surgeries	% unplanned surgery to patients with at least one complication	Ratio of planned to unplanned surgery
				n	%			
Murphy *et al* [28], 2016	25	232	188	40	160	17.2	266.7	4.69
Gadepalli *et al*[26], 2011	26	100	86	14	53.8	14.0		6.14
Berger-Groch *et al*[29], 2020	13	182	178	5	38.5	2.7		35.6
Hasler *et al* [30], 2010	23	187	172	15	65.2[2]	8.0[2]	166.7[2]	11.47
Latalski *et al* [31], 2011	12	44	38	6	50[2]	13.6[2]	75.0[2]	6.33
Striano *et al* [35], 2019	166	670	560	110	66.3	16.4	275.0	5.09
Lucas *et al* [36], 2013	54	184	152	30	55.6[2]	16.3[2]	83.3[2]	5.07
Garg *et al* [37], 2016	38	410	350[1]	60[1]	157.9	14.6		5.83

[1]Data estimated based on the mean values of duration between lengthenings.
[2]The values of the % of unplanned surgeries in which all four complications were analyzed in the paper.

Table 4 The number of planned and unplanned surgical procedures in the magnetically controlled growing rods group

Ref.	Subject	Surgical procedures (*n*)	Planned surgical procedures (*n*)	Unplanned surgical procedure		% unplanned surgeries to all surgeries	% unplanned surgery to patients with at least one complication	Ratio of planned to unplanned surgery
				n	%			
Subramanian *et al*[38], 2018	31	53	31	22	71[2]	41.5[2]	104.8	1.41
Urbański *et al* [39], 2020	47	60	47	13	27.7[2]	21.7[2]	81.3	3.62
Akbarnia *et al* [10], 2014	12	16	12	4	33.3	25.0	100.0	3
Studer *et al*[40], 2019	30	43	30	13	43.3	30.2	118.2	2.31
Kwan *et al*[41], 2017	30	44	30	14	46.7	31.8	100.0	2.14
Obid *et al*[42], 2020	22	46	19	5	22.7[2]	10.9[2]	41.7[2]	3.8
Lampe *et al*[43], 2019	24	43	24	19	79.2[2]	44.2[2]	172.7[2]	1.26

[2]The values of the % of unplanned surgeries in which all four complications were analyzed in the paper.

issue requiring surgery for implant revision or infection. In Ramirez *et al*[20], complications are defined as any change from the normal postoperative course which occurred from the time of the surgery until the most recent follow-up visit. In McCarthy *et al*[47], 2015, complications are defined as any problem requiring a return to the operating room, so all returns to the operating room were considered unanticipated. Some authors report major complications and some report the whole range of general complications.

Table 5 The number of planned and unplanned surgical procedures in guided growth group – the Shilla and growth guidance system groups

Ref.	Subject	Surgical procedures (*n*)	Planned surgical procedures (*n*)	Unplanned surgical procedure		% unplanned surgeries to all surgeries	% unplanned surgeries to patients with at least one complication	Ratio of planned to unplanned surgery
				n	%			
Haapala *et al* [12], 2020	13	19	17	2	15.4	10.5	40.0	8.5
Andras *et al* [13], 2015	36	101	36	65	180.6	64.4	224.1	0.55
Nazareth *et al*[44], 2020	20	41	20	21	105	51.2	140.0	0.95
Miękisiak *et al*[45], 2019	57	82	57	25	43.9[2]	30.5[2]		2.28
McCarthy *et al*[46], 2014	10	15	10	5	50	33.3	100.0	2
Luhmann *et al*[14], 2017	18	56	36	20	111.1			1.8
McCarthy *et al*[47], 2015	40	109	58	51	127.5			1.14

[2]The values of the % of unplanned surgeries in which all four complications were analyzed in the paper.

For this study, complications were categorized as wound, implant, alignment, or general [surgical or medical]. Wound problems were classified as either superficial or deep infections, and other wound-related problems, such as painful scars. Implant complications included rod breakage, failure of foundation fixation such as hook or screw pullout, and implant prominence. Alignment complications included junctional kyphosis (proximal or distal), curve progression above or below the instrumented levels, and curve progression after definitive fusion. General complications included, but were not limited to, dural tears, hematomas, and postoperative cardiopulmonary and gastrointestinal complications. Unfortunately, not all authors evaluated all these kinds of complications together – 4 out of 17 in TGR, 3 out of 13 in VEPTR, 4 out of 8 in MCGR, and 1 out of 7 in Shilla. Only 16 out of 44 papers (36%) referred to alignment complication in the evaluation – mostly in MCGR (88%), and conversely to VEPTR (23%). Five papers (11%) (TGR) described only implant-related complications, and 5 only wound-related (4 VEPTR and 1 TGR). The most frequently evaluated set of complications were wound, implant, and medical-related – 13 papers (30% of the papers). The original idea of the paper was to evaluate the number of procedures used to treat complications categorized as either planned or unplanned. Planned procedures were defined as procedures which were scheduled as part of the routine growing-rod-treatment protocol. Unplanned procedures were defined as unscheduled surgical procedures performed to manage a complication. Unfortunately, there was no division into such treatments, so the data were simplified and surgical procedures were classified as planned (implantations, lengthenings, final fusions) and unplanned (revisions). In that case, the number of complications requiring surgical treatment could have been greater, as some of them could have been repaired during the planned lengthening procedure. Only 10 papers (23%) (2 TGR, 3 VEPTR, 4 MAGEC, 1 Shilla) included data with unplanned surgeries, and all described complications concurrently. FF significantly influenced the number of surgeries. Despite the number of patients with FFs being known, there were no data about the time of the FFs – so estimated data based on the mean follow-up times and durations between lengthening procedures were understated. Deleting these references from the statements in question leaves 6 papers with no TGR patients. Adding Smith's classification for evaluation as a criterion further reduces the number of papers to only one. That is why the analysis had to be simplified.

TGRs constitute the most commonly applied technique, and are considered the gold standard for EOS with long curves[53]. In the reviewed papers, the complication rate per patient of the growing rod technique was very high and ranged from 19% to 208% (median 84%). Interestingly, Akbarnia *et al*[10], presented a complication rate of 208%

Table 6 Number of complications analyzed in extracted papers

Ref.	Subject	Total No. of complications	No. of patients with a minimum of one complication	% of complications in all patients	% of patients with a minimum one complication	No. of complications in complicated patients	Complication rate per surgical procedure (%)	% complications requiring surgical procedures
TGR								
Bess *et al*[15], 2010	140	171	81	122.1[2]	57.9[2]	2.1[2]	19.1[2]	43.3[2]
Du *et al*[16], 2020	167	49	32	29.3[2,3]	19.2[3]	1.5[3]	nd	nd
Andras *et al* [13], 2015	36	47	29	130.6	80.6	1.6	16.3	61.7
Myung *et al* [17], 2014	159	64	37	40.3	23.3	1.7	5.9	48.4
Arandi *et al* [18], 2014	175	146	80	83.4	45.7	1.8	11.7	39.0
Liang *et al* [19], 2015	55	42	23	76.4[2]	41.8[2]	1.8[2]	15.4[2]	54.8[2]
Ramirez *et al* [20], 2020	67	92	41	137.3	61.2	2.2	19.9	72.8
Yamaguchi *et al*[21], 2014	176	44	26	25.0	14.8	1.7		
Poe-Kochert *et al*[22], 2016	100	30	20	30.0[3]	20.0[3]	1.5[3]	19.1[3]	190.0
Kabirian *et al* [23], 2014	379	70	42	18.5	11.1	1.7	3.0	
Johnston *et al* [25], 2013	27	23	12	85.2	44.4	1.9	12.8	
Bachabi *et al* [11], 2020	50	45	33	90.0[2]	66.0[2]	1.4[2]	9.4[2]	
Luhmann *et al*[14], 2017	18	26		144.4	nd		15.6	
Akbarnia *et al* [10], 2014	12	25	11	208.3	91.7	2.3	34.2	
Harris *et al* [8], 2020	353	264	141	74.8	39.9	1.9	nd	93.2
Helenius *et al* [9], 2018	214	216	97	100.9	45.3	2.2	11.0	61.6
VEPTR								
Bachabi *et al* [11], 2020	22	26	18	118.2	81.8	1.4	7.9	
Crews *et al* [27], 2018	151	26	22	17.2	14.6	1.2	8.0	
Murphy *et al* [28], 2016	25	41	15	164.0	60.0	2.7	17.7	97.6
Gadepalli *et al*[26], 2011	26	36	nd	138.5	nd	nd		38.9
Berger-Groch *et al*[29], 2020	13	21	nd	161.5	nd	nd	11.5	23.8
Hasler *et al* [30], 2010	23	31	9	134.8[2]	39.1[2]	3.4	16.6[2]	48.4
Latalski *et al* [31], 2011	12	15	8	125.0[2]	66.7[2]	1.9	34.1[2]	40.0
Hell, *et al*	15	3	3	20.0	20.0	1.0	10.7	

[32]. 2005								
Garg *et al* [33], 2014	103	33	25	32.0	24.3	1.3	nd	
Waldhausen *et al*[34], 2016	65	37	22	56.9	33.8	1.7		
Striano *et al* [35], 2019	166	47	40	28.3	24.1	1.2	7.0	234.0
Lucas *et al* [36], 2013	54	74	36	137.0[2]	66.7[2]	2.1[2]	40.2[2]	40.5
Garg *et al* [37], 2016	38	86		226.3	nd			69.8
MCGR								
Subramanian *et al*[38], 2018	31	25	21	80.6[2]	67.7[2]	1.2[2]	47.2[2]	88.0
Urbański *et al* [39], 2020	47	17	16	36.2[2]	34.0[2]	1.1[2]	28.3[2]	76.5
Akbarnia *et al* [10], 2014	12	12	4	100.0	33.3	3.0	75.0	33.3
Studer *et al* [40], 2019	30	12	11	40.0	36.7	1.1	27.9	108.3
Kwan *et al* [41], 2017	30	15	14	50.0	46.7	1.1	34.1	93.3
Obid *et al* [42], 2020	22	12	12	54.5[2]	54.5[2]	1.0[2]	26.1[2]	41.7
Lampe *et al* [43], 2019	24	20	11	83.3[2]	45.8	1.8	46.5	95.0
Haapala *et al* [12], 2020	18	10	6	55.6	33.3	1.7	20.0	
Shilla								
Haapala *et al* [12], 2020	13	5	5	38.5	38.5	1.0	26.3	
Andras *et al* [13], 2015	36	69	29	191.7	80.6	2.4	68.3	
Nazareth *et al* [44], 2020	20	31	15	155.0	75.0	2.1	75.6	
Miękisiak *et al*[45], 2019	57	57		100.0[2]	0.0		69.5	
McCarthy *et al*[46], 2014	10	5	5	50.0	50.0	1.0	33.3	
Luhmann *et al*[14], 2017	18	20		111.1	0.0		35.7	
McCarthy *et al*[47], 2015	40	59	38	147.5	95.0	1.6	54.1	

[2]The values of the % of unplanned surgeries in which all four complications were analyzed in the paper.

[3]Corresponds to the papers in which all patients were after final fusion.

TGR: Traditional growing rods; VEPTR: Vertical expandable prosthetic titanium ribs; MCGR: Magnetically controlled growing rods.

(wound, implant-related and medical) in only 12 patients, whereas the rate for deep infections was 19% in 379 cases[23]. Comparing only implant-related complications, this parameter varied from 25%[21] to 40%[17], to 83%[18] – the authors analyzed a similar group of approximately 160 patients. The complication rate per surgical procedure varied from 3% to 34% (median 15%). There were two complications in complication-affected patients. In the analyzed papers, an average of 946 surgical procedures were performed. The incidence of unplanned surgeries in all patients varied from 19% to 144% (median 53%). The percentage of unplanned surgeries for all surgeries was 8% (3%-36%). The ratio of planned to unplanned surgeries was 11.6% (1.8%-33.9%). The most frequent complications were implant-related (61%) and

Table 7 Total number of complications divided into wound-related, implant-related, alignment and surgical/medical related

Ref.	Total No. of complications	Wound complications total/infection		Implant complications mechanical complication		Alignment complications		Surgical or medical complications	
		n	%	*n*	%	*n*	%	*n*	%
TGR									
Bess *et al*[15], 2010	171	34	20	105	61	10	6	22	13
Du *et al*[16], 2020	49	19	39	13	27	9	18	8	16
Andras *et al*[13], 2015	32			24	75			8	25
Myung *et al*[17], 2014	64			64	100				
Arandi *et al*[18], 2014	146			146	100				
Liang *et al*[19], 2015	42	5	12	25	60	4	10	8	19
Ramirez *et al*[20], 2020	92	49	53	30	33			13	14
Yamaguchi *et al* [21], 2014	44			44	100				
Poe-Kochert *et al* [22], 2016	29	16	55	13	45				
Kabirian *et al*[23], 2014	70	70	100						
Hosseini *et al*[24], 2018	134			134	100				
Bachabi *et al*[11], 2020	45	7	16	28	62	2	4	8	18
Luhmann *et al*[14], 2017	26	9	35	11	42			6	23
Akbarnia *et al*[10], 2014	25	4	16	13	52			8	32
Harris *et al*[8], 2020	264			264	100				
Helenius *et al*[9], 2018	216	40	19	127	59			49	23
VEPTR									
Bachabi *et al*[11], 2020	26	9	35	15	58			2	8
Crews *et al*[27], 2018	26	26	100						
Murphy *et al*[28], 2016	57	16	28	28	49			13	23
Gadepalli *et al*[26], 2011	25	6	24	3	12			16	64
Berger-Groch *et al* [29], 2020	24	1	4			2	8	21	88
Hasler *et al*[30], 2010	31	16	52	7	23	7	23	1	3
Latalski *et al*[31], 2011	15	1	7	7	47	1	7	6	40
Hell, *et al*[32], 2005	3	1	33	1	33			1	33
Garg *et al*[33], 2014	34	34	100						
Waldhausen *et al* [34], 2016	37	12	32	21	57			4	11
Striano *et al*[35],	47	47	100						

2019									
Lucas *et al*[36], 2013	49	11	22	28	57	7	14	3	6
Garg *et al*[37], 2016	86	86	100						
MCGR									
Subramanian *et al*[38], 2018	24	6	25	16	67	1	4	1	4
Urbański *et al*[39], 2020	16	2	13	8	50	1	6	5	31
Akbarnia *et al*[10], 2014	12			8	67			4	33
Studer *et al*[40], 2019	12	3	25	6	50	3	25		
Kwan *et al*[41], 2017	15	2	13	12	80	1	7		
Obid *et al*[42], 2020	12	1	8	3	25	7	58	1	8
Lampe *et al*[43], 2019	20	3	15	7	35	6	30	4	20
Haapala *et al*[12], 2020	10			6	60	1	10	3	30
Shilla									
Haapala *et al*[12], 2020	5	1	20	3	60			1	20
Andras *et al*[13], 2015	56			55	98			1	2
Nazareth *et al*[44], 2020	31	4	13	26	84			1	3
Miękisiak *et al*[45], 2019	57	3	5	34	60	10	18	10	18
McCarthy *et al*[46], 2014	5	2	40	3	60				
Luhmann *et al*[14], 2017	20	6	30	13	65			1	5
McCarthy *et al*[47], 2015	59	6	10	42	71	11	19		

TGR: Traditional growing rods; VEPTR: Vertical expandable prosthetic titanium ribs; MCGR: Magnetically controlled growing rods.

wound-related (27%), while medical complications and alignments accounted for 19% and 8%, respectively. The most concerning problem related to TGRs is the high complication rate. The risks for implant failure, infections, and wound healing problems are significantly increased as a consequence of the repeated lengthening procedures and an unfused spine. If rod breakage or screw displacement occurs, revision surgeries are indicated to change the rod or extend the instrumented segments. Additionally, repeated general anesthesia can pose a threat to mental health. Adequate informed consent and close follow-ups are necessary.

VEPTR was developed for patients with thoracic insufficiency syndrome (TIS), but it is sometimes indicated for individuals with EOS who are at risk of secondary TIS[54, 55]. The complication rate per patient was as high as 125% (17%-226%) with a 9% rate per surgical procedure (7%-18%). Such a discrepancy is very confusing. Garg *et al*[37] identified only wound complications following VEPTR implant or revision surgeries. If so, adding implant, alignment, and medical-related complications, the final percentage of complications should be expected at a much higher level. On the other hand, Crews *et al*[27] analyzed wound, implant, and general complications at the level of 17%. The most frequent complications were implant-related 48%, and wound-related 33%, while medical complications and alignments accounted for 23% and 11%. respectively. which limits their applications. In the analyzed papers, an average of 251 surgical procedures were performed. The percentage of unplanned surgeries in all patients varied from 39% to 160% (median 60%). The percentage of unplanned

Table 8 Complication grades according to Smith

Ref.	Total No. of complications	Related to disease				Related to device				
		Complication grade I	Complication grade II	Complication grade III	Complication grade IV	Complication grade I	Complication grade IIA	Complication grade IIB	Complication grade III	Complication grade IV
Ramirez *et al* [20], 2020	92					8	8	17	4	4
Murphy *et al* [28], 2016	57	5	6	2	1	13	8	3	4	
Studer *et al*[40], 2019	12					2	7			
Miękisiak *et al* [45], 2019	57	32	17	8	0					

surgeries to all surgeries was 14% (3%-17%). The proportion of planned to unplanned surgeries was 6% (4.7%-35.6%).

MCGRs were introduced by Takaso *et al*[56] in 1998 as remote-controlled growing-rod spinal instrumentation. The system did not require open lengthening as TGRs did, and the effect could instead be achieved by external remote control without repeated anesthesia. The complication rate of the magnetically controlled growing rod technique per patient varied from 36% to 100% (median 55%). In this group of patients, the distribution of complications is fairly homogeneous. Only Akbarnia *et al* [10] described such a high level of complications while omitting wound-related and alignment problems. The complication rate per surgical procedure varied from 20% to 75% (median 31%). In the analyzed papers, an average of 44 surgical procedures were performed. The percentage of unplanned surgeries in all patients varied from 23% to 79% (median 43%). The percentage of unplanned surgeries in all surgeries was 30% (11%-34%). The ratio of planned to unplanned surgeries was 2.3 (1.3-3.8). The most frequently occurring complication was implant-related – 55%, then general (25%), wound (14%), and alignment (10%). La Rosa *et al*[57] stated that MCGRs can prevent surgical scarring, surgical site infections, and psychological distress, which occur in patients with TGRs and VEPTR due to the multiple surgeries. The decreased rate of infections and wound healing problems in patients who received MCGRs is of great benefit to patients. However, Aslan *et al*[58] used psychosocial tools to compare the mental state of patients receiving MCGRs and TGRs. He affirmed that if the patient noticed benefit from the growing rods, and did not experience major complications, the non-invasiveness of the lengthening procedures did not show an advantage on the patients' psychosocial state. Besides, although MCGRs were associated with a lower rate of infections [both deep and superficial], they were associated with a significantly increased risk of metalwork problems and unplanned revisions[59].

The Shilla technique guides spinal growth towards a normal alignment[60]. The technique first corrects the apical deformity towards a neutral alignment. Then the upper and lower growth guidance portions extend into the distal and proximal areas of the curve, using special screws and caps, allowing the rod to slide with growth in a longitudinal direction. Multiple open lengthening surgeries are avoided, as in MCGRs. The complication rate was as high as 111% of the patients (39%-192%), and the complication rate per surgical procedure was 54%. Haapala *et al*[12] showed the fewest complications – 39%. The remaining authors assessed the number of complications at a similar level. The most frequently appearing complications were implant-related (65%). Wound-related and alignment problems were 16% and 18%, respectively. General complications were only 5%. The percentage of unplanned surgeries in all patients varied from 15% to 181% (median 105%). The percentage of unplanned surgeries to all surgeries was 33% (11%-64%). The ratio of planned to unplanned surgeries was 1.8 (0.6-8.5). Luhmann *et al*[14] found that the Shilla growth guidance system compared favorably with TGRs in terms of the degree of correction of the major curve, spinal length, and growth, and the maintenance of the sagittal alignment. Looking at these data the benefits are not so obvious. Similar to MCGR and TGR, the SGGS is associated with a very high rate of implant-related complications, which usually results in revision surgery. Additionally, for patients with great growth potential, the distal and proximal screws can slide off the rod, requiring the rods to be changed.

EOS surgery has a varying but high rate of complications. Based on this review of 40 papers, 3249 cases, and 15037 surgical procedures, the most-frequent implant complications (total 54%), the general, wound, and alignment were 17%, 15%, and 12%, respectively. These data are simplified and certainly underestimated, because of the reasons described earlier. The rate of complications might have been higher than reported, as some authors did not report every type of complication. Due to complications, 54% of the patients required unplanned surgeries, which equated to 15% of all surgeries.

The long-term risks of EOS surgery have not yet been reported on in research. There is a lack of papers with homogenous cases, long-term follow-up, all revision surgeries, and complication data.

One would expect that successful treatment which encourages the growth of the spine and chest would lead to favorable outcomes in patients with early-onset idiopathic scoliosis. But it is not unambiguous with patients with, *e.g.*, progressive neuromuscular conditions such as congenital muscular dystrophies and spinal muscular atrophy. Surgery can effect spinal growth with expandable instrumentation, but worsening muscle weakness can negate the positive effects of growth-friendly procedures[2]. Tsirikos *et al*[61] showed that the life expectancy of patients with cerebral palsy and other neurogenic deformities subjected to deformation correction does not change, but only an additional source of data such as the number of days in the intensive care unit after surgery, and the presence of severe preoperative thoracic hyperkyphosis, were the only factors affecting survival rates.

As highlighted by Hawes[62], the complexity of spinal surgery is reflected in the diversity of complications which might occur months or even years later. Given the time delay and difficulty in diagnosis, it is likely that some of the events are not recognized as surgical complications. Therefore, clear uniformity of definitions and the carefulness of the surgeon are important in assessing patient follow-up and treatment outcomes.

CONCLUSION

The literature concerning the definitions, collection, and interpretation of data regarding EOS surgery complications is often difficult to interpret. This causes problems in the comparison, analysis, and improvement of spine surgery practice. Additionally, this observation indicates that data on the incidence of complications can be underestimated and should be interpreted with caution. Awareness of the high rate of complications of EOS surgery is crucial, and an optimal strategy for prevention should become a priority.

ARTICLE HIGHLIGHTS

Research background

The treatment for early-onset scoliosis (EOS) remains a great challenge for pediatric orthopedics. The treatment goals for EOS, regardless of the diagnosis, are the same: minimizing spinal deformity while maximizing thoracic volume and pulmonary function. When conservative treatment is ineffective, the option is surgery.

Research motivation

Different surgical techniques have different advantages and drawbacks. Those most often used are traditional growing rods (TGR), vertical expandable prosthetic titanium ribs (VEPTR), magnetically controlled growing rods (MCGR), and the Shilla growth guidance system (SGGS). Repeated surgeries and complications are two major concerns in EOS management.

Research objectives

The aim of the study was to review the current literature to assess the safety of EOS surgical treatment in terms of the rate of complications and unplanned surgeries.

Research methods

The systematic review was conducted according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. In January 2021, a search of three electronic medical databases (PubMed, the Cochrane Library, and Embase) was performed by three independent authors. We combined the terms: "early-onset scoliosis" OR "eos" OR "juvenile scoliosis" OR "infantile scoliosis" OR "tgr" OR "veptr" OR "MCGR" OR "Shilla" OR "growth-friendly" AND "complication".

Research results

EOS surgery has a varying but high rate of complications. The most frequent complications were categorized as implant, general, wound and alignment. The rate of complications might have been even higher than reported, as some authors do not report all types of complications.

Research conclusions

The literature concerning the definitions, collection, and interpretation of data regarding EOS surgery complications is often difficult to interpret. This creates problems in the comparison, analysis, and improvement of spine surgery practice. Awareness of the high rate of complications of EOS surgery is crucial, and an optimal strategy for prevention should become a priority.

Research perspectives

This observation indicates that data on the incidence of complications can be underestimated, and should be interpreted with caution. Further studies are needed to confirm the study results, especially concerning longitudinal data.

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World Journal of Orthopedics

Submit a Manuscript: https://www.f6publishing.com

World J Orthop 2021 August 18; 12(8): 604-619

DOI: 10.5312/wjo.v12.i8.604

ISSN 2218-5836 (online)

SYSTEMATIC REVIEWS

Safety and efficacy of surgical hip dislocation in managing femoral head fractures: A systematic review and meta-analysis

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Author contributions: Khalifa AA carried out the study conception and design; Haridy MA and Fergany A carried out data acquisition; Khalifa AA, Haridy MA, and Fergany A carried out interpretation of data; all authors drafted the manuscript and designed the figures and tables; Khalifa AA did the critical revision; all authors discussed the results and commented on the manuscript; All authors read and approved the final manuscript and are responsible for the content and similarity index of the manuscript.

Conflict-of-interest statement: The authors deny any conflict of interest.

PRISMA 2009 Checklist statement: We admit that the guidelines of the PRISMA 2009 Statement have been adopted for preparation of the manuscript.

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Abstract

BACKGROUND

Femoral head fractures (FHFs) are considered relatively uncommon injuries; however, open reduction and internal fixation is preferred for most displaced fractures. Several surgical approaches had been utilized with controversial results; surgical hip dislocation (SHD) is among these approaches, with the reputation of being demanding and leading to higher complication rates.

AIM

To determine the efficacy and safety of SHD in managing FHFs by reviewing the results reported in the literature.

METHODS

Major databases including PubMed, Embase, Web of Science, and Cochrane Central Register of Controlled Trials were searched to identify studies reporting on outcomes of SHD utilized as an approach in treating FHFs. We extracted basic studies data, surgery-related data, functional outcomes, radiological outcomes, and postoperative complications. We calculated the mean differences for continuous data with 95% confidence intervals for each outcome and the odds ratio with 95% confidence intervals for binary outcomes. $P < 0.05$ was considered significant.

RESULTS

Our search retrieved nine studies meeting our inclusion criteria, with a total of 129 FHFs. The results of our analysis revealed that the average operation time was 123.74 min, while the average blood loss was 491.89 mL. After an average follow-up of 38.4 mo, a satisfactory clinical outcome was achieved in 85% of patients,

Manuscript source: Invited manuscript

Specialty type: Orthopedics

Country/Territory of origin: Egypt

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Received: April 26, 2021
Peer-review started: April 26, 2021
First decision: June 16, 2021
Revised: June 20, 2021
Accepted: July 20, 2021
Article in press: July 20, 2021
Published online: August 18, 2021

P-Reviewer: Maslennikov R
S-Editor: Wang JL
L-Editor: Filipodia
P-Editor: Li JH

with 74% obtained anatomical fracture reduction. Overall complication rate ranged from 30% to 86%, with avascular necrosis, heterotopic ossification, and osteoarthritis being the most common complications occurring at an incidence of 12%, 25%, and 16%, respectively. Trochanteric flip osteotomy nonunion and trochanteric bursitis as a unique complication of SHD occurred at an incidence of 3.4% and 3.8%, respectively.

CONCLUSION

The integration of SHD approach for dealing with FHFs offered acceptable functional and radiological outcomes with a wide range of safety in regards to the hip joint vascularity and the development of avascular necrosis, the formation of heterotopic ossification, and the development of posttraumatic osteoarthritis; however, it still carries its unique risk of trochanteric flip osteotomy nonunion and persistent lateral thigh pain.

Key Words: Femoral head; Pipkin fracture; Surgical hip dislocation; Ganz; Systematic review; Meta-analysis

Core Tip: In the past few years, surgical hip dislocation had been adopted by many trauma surgeons as an approach for femoral head fractures management. The current systematic review and metanalysis collected data from the most recent literature showed the efficacy of this approach in regards to obtaining acceptable functional and radiological outcomes as well as resulting in relatively low complication rates when compared with other approaches reported in the literature. However, it carries some unique complications such as trochanteric bursitis and trochanteric flip osteotomy nonunion.

Citation: Khalifa AA, Haridy MA, Fergany A. Safety and efficacy of surgical hip dislocation in managing femoral head fractures: A systematic review and meta-analysis. *World J Orthop* 2021; 12(8): 604-619
URL: https://www.wjgnet.com/2218-5836/full/v12/i8/604.htm
DOI: https://dx.doi.org/10.5312/wjo.v12.i8.604

INTRODUCTION

Femoral head fractures (FHFs) are considered rare injuries resulting from high energy trauma, which is usually associated with posterior hip dislocation and rarely anterior subluxation [1,2]. The rarity of this injury makes it difficult to report on large numbers of patients, and the performance of high quality prospective randomized studies is even more challenging [1,3].

The commonly used classification system for this injury is the Pipkin classification, where four types were identified according to the fracture location and the presence of associated injuries (Type I where the fracture fragment is distal to the fovea, Type II where the fracture fragment including or above the fovea, Type III if the fracture is associated with a femoral neck fracture, and Type IV if it was associated with acetabular wall fractures)[4].

The management of FHFs follows a broad spectrum of options (primarily based on its Pipkin type), where conservative management is kept for the minimally displaced Pipkin I fracture, and at the end of the spectrum, total hip arthroplasty could be offered for older patients with highly comminuted fractures[5].

The basic principles of intraarticular fracture management still apply to FHFs, where obtaining anatomical reduction and stable fixation [achieved by open reduction and internal fixation (ORIF)] is mandatory for good long-term results. The controversy exists regarding the optimum approach that should be used safely for ORIF[2,3,6], either anterior, lateral, or posterior based approaches including the use of safe surgical hip dislocation (SHD), which was initially described by Ganz *et al*[7] as a safe approach for management of different intraarticular hip pathologies with no or few complic-

ations especially those related to femoral head vascularity[3,7].

One of the significant complications occurring either due to the trauma itself or as a consequence of surgical management is avascular necrosis (AVN) of the femoral head [2,3]. After Ganz popularized the safety of SHD in regard to hip vascularity preservation[7], this encouraged more trauma surgeons to introduce this approach in the armamentarium of approaches in the management of FHFs[2,3,6,8].

As a trial to collect large data on these injuries, a systematic review was performed by Giannoudis *et al*[2] in 2009, pooling the data from 29 studies that constituted a total of 453 FHFs treated through different approaches, where they evaluated various aspects related to management; however, one drawback of this review was the heterogenicity of the reported studies, and the inclusion of relatively few numbers of patients (36 FHFs) treated through SHD[2].

Recently, more studies with a larger number of patients reported the utilization of SHD in the management of FHFs; this encouraged us to carry out this systematic review and metanalysis to update the knowledge regarding the clinical and radiological outcomes as well as the safety (by reporting the incidence of complications) of using SHD in the management of FHFs.

MATERIALS AND METHODS

Search protocol and information sources

We conducted a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist[9]. PubMed, Embase, Web of Science, and Cochrane Central Register of Controlled Trials databases were searched for the last 20 years (until January 2021) using a combination of the following search terms: Femoral head fracture, Pipkin fracture, surgical hip dislocation, Ganz.

Eligibility criteria, study selection, and data items

Retrieved results were imported into Endnote X9 software (Thomson Reuters, New York, NY, United States), where a check for duplicates was conducted. The titles and abstracts of the remaining articles were then screened, and the selection was based on the following exclusion criteria: (1) Articles published in languages other than English; (2) Reviews, guidelines, or classifications; (3) Letters to the editor, case reports, or conference papers; (4) *In vitro* and animal experiment studies; and (5) Irrelevant studies.

Subsequently, full-text articles of potentially relevant studies were obtained and assessed for eligibility. We included studies that met the following inclusion criteria: (1) Prospective or retrospective cohorts or case series investigating SHD *via* a trochanteric flip osteotomy (TFO) (as described initially by Ganz *et al*[7]) as an approach to treat FHFs in adult populations or studies from which data could be extracted independently; (2) A minimum sample size of 5 patients; and (3) The ability to extract data related to the outcomes of interest (data should be genuine and not reported in another study).

Data collection process

Two independent reviewers reviewed the list of potentially eligible articles (they also performed data extraction), and a third reviewer was consulted, when necessary, to decide any uncertainties regarding eligibility. The following information was extracted from studies that met the inclusion criteria: The name of the first author, year of publication, study design, number of cases, patients age and gender, classification of the fracture according to Pipkin classification system, the strategy of management (ORIF or fragment excision), type of the implant used for fixation, operation time, blood loss, length of follow-up time, and outcomes of interest including functional outcome, radiological outcome, complication rate, and reoperation or revision surgery details.

Summary measures, synthesis of results, and risk of bias across studies

When mean or standard deviation values were not available in the publications, we used statistical methods described in previous literature to derive the needed numerical values[10]. We performed all data analyses using Review Manager version 5.4.1. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). We calculated the odds ratio with a 95% confidence interval (CI) for binary outcomes, while the mean difference with 95%CI for continuous outcomes was calculated. To

calculate the overall effect estimate with 95%CI, we used a fixed-effect model with the method of Mantel-Haenszel when there was no evidence of heterogeneity between studies. Otherwise, a random-effects model with the method of DerSiomonian and Laird was chosen. Heterogeneity between studies was evaluated using the Q statistic and I^2 test, which describes the percentage of variability in the effect estimates. A P value of < 0.05 was considered significant.

RESULTS

Study selection

The electronic search yielded 1002 references from the four databases. After excluding 192 duplicates, 810 records remained for a title and abstract screening. We had 18 relevant articles for full-text screening: Eight fulfilled the inclusion criteria, and ten were excluded (one article not in English, six articles were case reports or included less than five cases, two articles the data of interest could not be extracted, and in one article the same data was reported in one of the included articles). The manual search of the included articles references imported one additional article. Nine studies[11-19] were ultimately included in the qualitative and quantitative analyses. The flow diagram of the study selection process is shown in Figure 1.

Study characteristics

Nine studies included a total of 129 FHFs from which basic demographic data were extracted (the data on outcomes were extracted from 127 FHFs, as in one study[15], the authors reported missing the assessment of two patients in their results section). Two studies[15,16] were prospective, while seven[11-14,17-19] were retrospective. Across studies, the mean age was 38.2 years (range from 17 to 64). The average follow-up period was 38.4 mo (ranged from 10.8 to 77.0). The majority of participants were males (76.4%). In one study[18], the fracture classification was not reported, while in the remaining eight studies, the fracture classification according to Pipkin was as follows, 77 (62.6%) type I and II, while 46 (37.4%) were type IV, and none (0%) were Pipkin type III. All patients underwent fixation (96.9%) except four (3.1%) patients who underwent fragment excision; no patient underwent total hip arthroplasty as the primary management. Details for included studies are summarized in (Table 1).

Surgical data

Associated intraarticular injuries: Regarding the intraarticular associated injuries (other than the primary fractures either in the femoral head or the acetabulum), in four studies[12,14,15,19], the authors reported intraoperative diagnosis of Labral injuries at an incidence of 41.3% (33 out of 80 hips). Head impaction injury was reported in three studies[14,15,19], which occurred at an incidence of 23.5% (16 out of 68 hips).

Operation time: It was reported in five studies[12-14,16,18]. However, we were able to pool the results of four studies[12-14,16] due to incomplete data from the fifth study. No significant heterogeneity was detected (I^2 = 41.33%, P = 0.164) using the fixed-effect model for analysis. The mean operation time ranged from 120.0 to 155.2 min, with the pooled estimate being 123.7 (95%CI: 116.58–130.89). The result was statistically significant (Z = 33.91, P = 0.000). Details of operation time in included studies are shown in (Table 2).

Blood loss: It was reported in six studies[12-14,16-18]. However, we were able to pool the results of five studies[12-14,16,17] due to incomplete data from the sixth study. We used the random effect model for analysis as significant heterogeneity was detected (I^2 = 91.52%, P = 0.000). The mean amount of blood loss ranged from 283.0 to 1436.9 mL, with the pooled estimate being 491.9 (95%CI: 347.01–636.77). The result was statistically significant (Z = 6.66, P = 0.000). Details of blood loss in included studies are shown in (Table 2).

Functional outcomes

Functional outcomes (Figure 2) of the hip were reported in eight studies[11-16,18,19], but the assessment methods used were different. The Harris Hip Score (HHS) was used in three studies[14,18,19], in six studies[11-13,15,16,19] Merle d'Aubigne-Postel score was used, Thompson–Epstein scale was used in three studies[11-13], and the Oxford Hip Score was used in one study[15]. In the current meta-analysis, a satisfactory functional outcome was defined as HHS or Merle d'Aubigne-Postel score

Table 1 Baseline characteristics of included studies

Ref.	Study design	Sample size	Age[1], yr	Sex		Pipkin classification (I/II/III/IV)	Management		Implant	Follow up[1], mo
				M	F		Fixation	Excision		
Henle *et al* [11], 2007	Retrospective	12	39.8 (26-71)	10	2	1/3/0/8	12	0	Mini or small fragment cortical screws (2.0-2.7 mm) or Herbert screws or absorbable pins	31.1 (3-96)
Solberg *et al* [12], 2009	Retrospective	12	-	10	2	0/0/0/12	11	1	Headless variable-pitch screws or Herbert screws	47 (24-71)
Mostafa *et al* [13], 2014	Retrospective	12	-	-	-	12/0/0	12	0	Partially threaded cancellous screws or Herbert headless screws	31 (24-84)
Massè*et al* [14], 2015	Retrospective	13	34 (22-54)	11	2	5/2/0/6	13	0	2.7 mm nonabsorbable screws	77 (26-122)
Gavaskar *et al*[15], 2015	Prospective	28	-	-	-	6/22/0/0	26	2	2.4 mm headless screws (Synthes-India).	36 (25-46)
Wang *et al* [16], 2019	Prospective	12	39.9 ± 12.2	8	4	4/3/0/5	12	0	3.2 mm Herbert screws or partially threaded screws	35 (25-48)
Engel *et al* [17], 2020	Retrospective	7	39.57 (17-64)	4	3	0/0/0/7	6	1	Buried headless screw	29.8 (11.6-67.2)
Rana *et al* [18], 2020	Retrospective	6	42 (32-54)	4	2	-	6	0	Herbert (headless) screw	10.8 (8-18)
Khalifa *et al* [19], 2020	Retrospective	27	33.8 (18-45)	21	6	6/13/0/8	27	0	4 mm partially threaded cancellous screws or Herbert headless screws	48 (24-72)

[1]Data are presented as mean ± SD or mean (range). M: Male; F: Female.

Table 2 Operation time and blood loss (six studies)

Ref.	Operation time	Blood loss
Solberg *et al*[12], 2009	121.0 ± 28.3 (102-215)	350.00 ± 125.00 (250-750)
Mostafa *et al*[13], 2014	120.0 ± 19.7	283.00 ± 124.90
Massè*et al*[14], 2015	155.2 ± 53.1	1436.90 ± 663.80
Wang *et al*[16], 2019	124.2 ± 22.1	437.50 ± 113.10
Engel *et al*[17], 2020	NR	503.00 ± 181.25
Rana *et al*[18], 2020	90.0	450.00

NR: Not reported.

graded as excellent or good. No significant heterogeneity was detected (I^2 = 0%, P = 0.893) using the fixed-effect model for analysis. The event rates of satisfactory outcome ranged from 0.62 to 0.98, with the pooled estimate being 0.85 (95%CI: 0.77-0.91). The result was statistically significant (Z = 6.55, P = 0.000). According to individual assessment score or scale, excellent or good results were obtained in 87.9% (29 of 33 hips), 87.1% (88 of 101 hips), and 83.3% (30 of 36 hips) according to HHS, Merle d'Aubigne-Postel score, and Thompson–Epstein scale, respectively.

Radiological outcome

Four studies[14-16,19] reported radiological outcomes in terms of obtaining fracture anatomical reduction. No significant heterogeneity was detected (I^2 = 49.66%, P = 0.114) using the fixed-effect model for analysis. The overall incidence of anatomic reduction ranged from 0.30 to 0.86, with the pooled estimate being 0.74 (95%CI: 0.61–0.83). The result was statistically significant (Z = 3.37, P = 0.001, Figure 3).

Complication rate

All nine studies[11-19] reported on the postoperative complications, namely AVN of

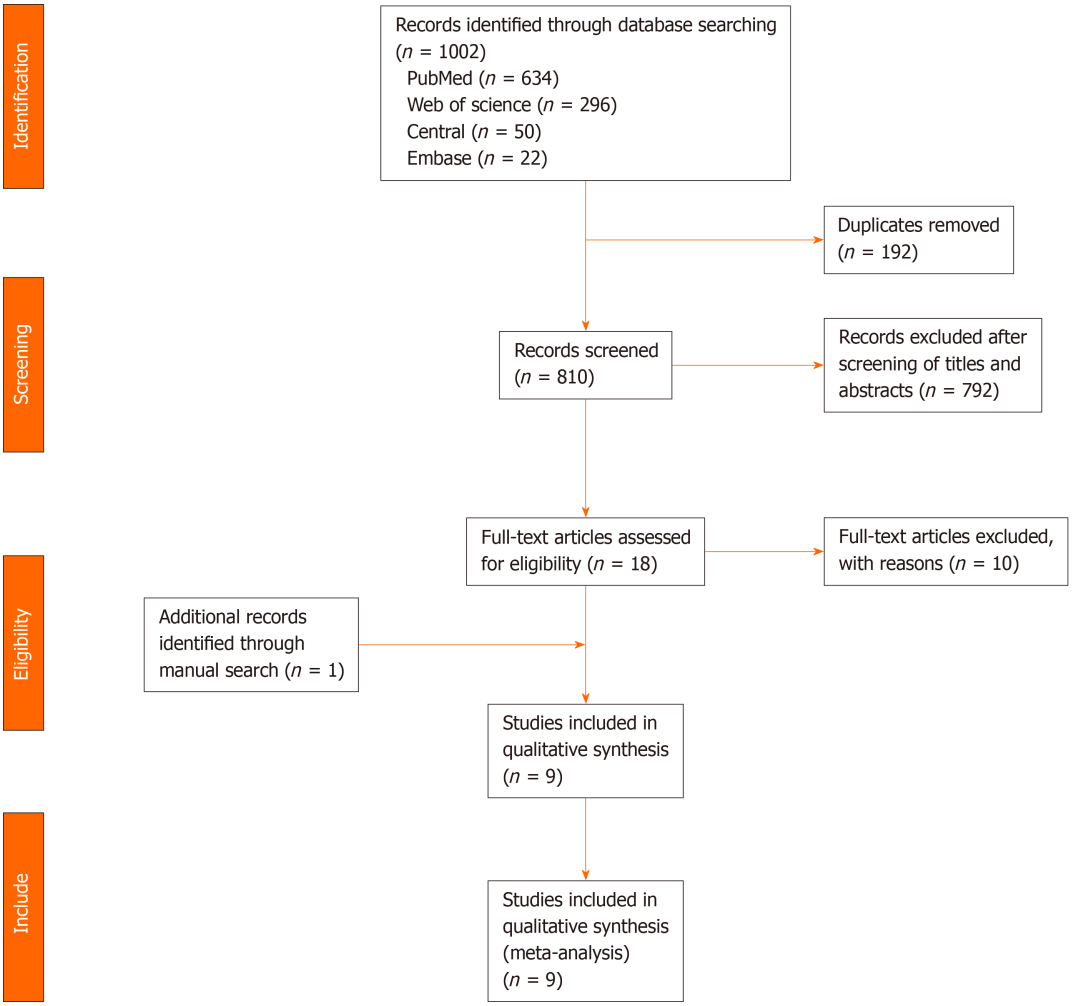

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of search results, studies' screening, and selection.

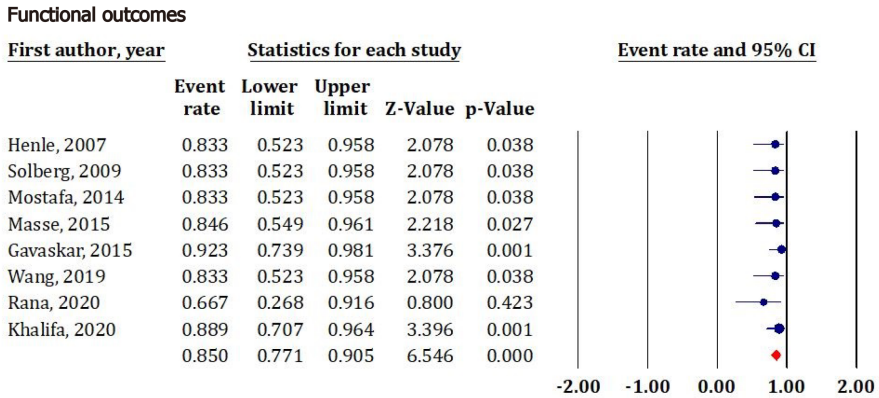

Figure 2 Forest plot diagram shows postoperative functional outcomes. CI: Confidence interval.

the femoral head, heterotopic ossification (HO) formation, posttraumatic osteoarthritis (OA), deep infection, trochanteric bursitis, and nonunion of the TFO. No significant heterogeneity was detected (I^2 = 11.18%, P = 0.342) using the fixed-effect model for analysis. The overall incidence of postoperative complications ranged from 0.30 to 0.86, with the pooled estimate being 0.44 (95%CI: 0.35–0.53). The result was statistically insignificant (Z = -1.27, P = 0.205) (Figure 4A).

AVN of the femoral head: AVN was reported in all nine studies[11-19]. No significant heterogeneity was detected (I^2 = 0%, P = 0.509) using the fixed-effect model for

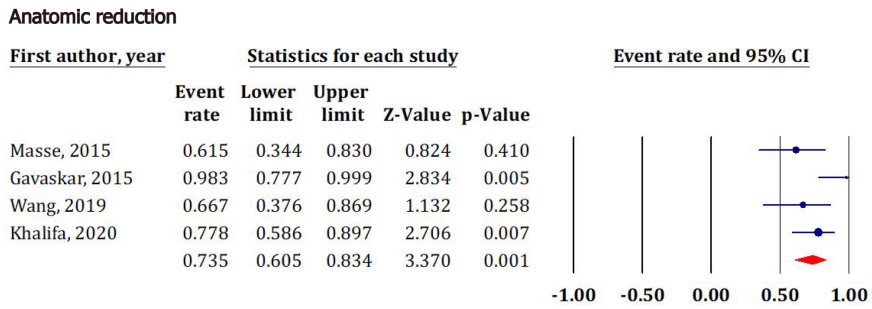

Figure 3 Forest plot diagram shows postoperative anatomical reduction as a representative of radiological outcomes. CI: Confidence interval.

analysis. The incidence of AVN ranged from 0.02 to 0.33, with the pooled estimate being 0.12 (95%CI: 0.07–0.21). The result was statistically significant (Z = -6.32, *P* = 0.000) (Figure 4B).

HO formation: HO was reported in eight studies[11-17,19]. No significant heterogeneity was detected (I^2 = 0%, *P* = 0.798) using the fixed-effect model for analysis. The incidence of HO ranged from 0.14 to 0.33, with the pooled estimate being 0.25 (95%CI: 0.18–0.34). The result was statistically significant (Z = -5.12, *P* = 0.000) (Figure 4C). According to the Brooker classification system[20], there was grade I in ten (33.3%) patients, grade II in 13 (43.3%), grade III in six (20%), and grade IV in one (3.4%). Excision was required in three (10%) patients.

Posttraumatic OA: OA was reported in five studies[11,15,17,19]. We used the random effect model for analysis as significant heterogeneity was detected (I^2 = 71.82%, *P* = 6.696). The incidence of OA ranged from 0.04 to 0.86, with the pooled estimate being 0.16 (95%CI: 0.04–0.47). The result was statistically significant (Z = -2.12, *P* = 0.034) (Figure 4D).

Other complications: Further complications that were not included in the meta-analysis were presented as follows. Nonunion of the TFO was reported in five studies [11,13-16,19] and occurred at an incidence of 3.4% (3 out of 89 hips). Presence of infection was reported in six studies[13-17,19] and occurred at an incidence of 2.1% (2 out of 97 hips). Trochanteric bursitis was reported in one study[15], which occurred at an incidence of 3.8% (1 out of 26 hips).

Reoperation rate

Reoperation rate was reported in eight studies[11-17,19]. No significant heterogeneity was detected (I^2 = 36.16%, *P* = 0.140) using the fixed effect model for analysis. The event rate for reoperation ranged from 0.08 to 0.57, with the pooled estimate being 0.20 (95%CI: 0.13–0.29) (Figure 5). The result was statistically significant (Z = -5.53, *P* = 0.000). Details of the reoperations required are in Table 3.

DISCUSSION

FHFs possess a challenge to the trauma surgeon, owing to the lack of a standard protocol for management and the various controversial issues around the best management option. The surgeon has to choose between conservative and surgical management. If the latter was chosen, then the surgeon must decide whether will it be excision or ORIF and through which approach it would be carried out[16,21,22]. Various surgical approaches have been utilized, including medial (Ludloff), anterior Smith-Petersen (S-P), posterior Kocher-Langenbeck (K-L), and anterolateral (Watson-Jones) approaches. Even hip arthroscopy was reported to be a way of management; SHD has emerged in the past few years and gained popularity as an option to approach and treat FHFs[2,3,6,23].

The most important findings in the current systematic review and metanalysis are that a large percentage of patients with FHFs obtained proper postoperative hip joint function after being managed through SHD; this approach enabled the surgeon to achieve anatomical fracture reduction and an acceptable rate of postoperative complic-

Table 3 Details of reoperation (eight studies)

Ref.	Indication of reoperation	Intervention
Henle *et al*[11], 2007	2 AVN	THA
	2 HO	Excision
Solberg *et al*[12], 2009	1 AVN	THA
Mostafa *et al*[13], 2014	1 AVN	THA
	1 TFO Nonunion	Revision of fixation
Massè*et al*[14], 2015	1 AVN	THA
	1 OA	THA
Gavaskar *et al*[15], 2015	1 Infection	Debridement
	1 Bursitis	Screw removal
Wang *et al*[16], 2019	1 AVN	THA
	1 HO	Excision
	1 TFO Nonunion	Revision of fixation
Engel *et al*[17], 2020	2 OA/ AVN	THA
	1 OA/HO	THA
	1 OA/Metal failure/Infection	Revision/Girdlestone/THA
Khalifa *et al*[19], 2020	2 AVN	THA
	1 OA	THA

AVN: Avascular necrosis; HO: Heterotopic ossification; THA: Total hip arthroplasty; OA: Osteoarthritis; TFO: Trochanteric flip osteotomy.

ations, mainly femoral head AVN, HO formation, and posttraumatic OA development.

In the systematic review by Giannoudis *et al*[2], the data regarding the surgical approaches were collected from 14 articles forming 177 surgical cases and was distributed as follows: The K-L was the most commonly used in 72 (40.7%) cases, followed by the S-P in 44 (24.9%), in third place was the SHD through TFO, which was used in 36 (20.3%). The remaining were other approaches reported in fewer numbers (lateral, anterolateral, medial, and dual approach). Thirty-six FHFs were treated through SHD, which was driven from four studies[2], while in the current systematic review, we included data of 129 FHFs from nine studies, meaning that in the past 10 years, the cases treated through SHD nearly tripled, indicating that this approach is gaining popularity among trauma surgeons.

Surgical data

In the current systematic review, the reported average operative time was 123.7 minutes, which is considered to be shorter than the operative time reported with the K-L approach but longer than the S-P. In a study by Wang *et al*[24], the authors compared managing Pipkin type I and II FHFs (21 through S-P and 18 through K-L). The average operative time for the S-P approach group was 96.9 ± 14.8 min, which was significantly shorter than the K-L approach group where the average operative time was 131.8 ± 21.2 min ($P < 0.001$)[24]. Many factors could affect the operative time, such as the presence of a concomitant injury that needed further management, such as an acetabular fracture (which was present in the current systematic review in 37.4% of the patients) or the presence of intra-articular injuries, mainly labral and head impaction injuries that were reported in the current systematic review in 41.3% and 23.5% of patients, respectively. Another factor that might play a role is the surgical skill and familiarity of the surgeon with the SHD approach and the learning curve needed to master managing such injuries through SHD, which we were unable to assess.

The relatively prolonged operative time and the presence of associated injuries led to an increase in the blood loss, as the reported average blood loss in the current systematic review was 491.9 mL, with a maximum blood loss of 1436.9 mL as reported in one study[14]. In Wang *et al*[24] study, the average blood loss was lower in both

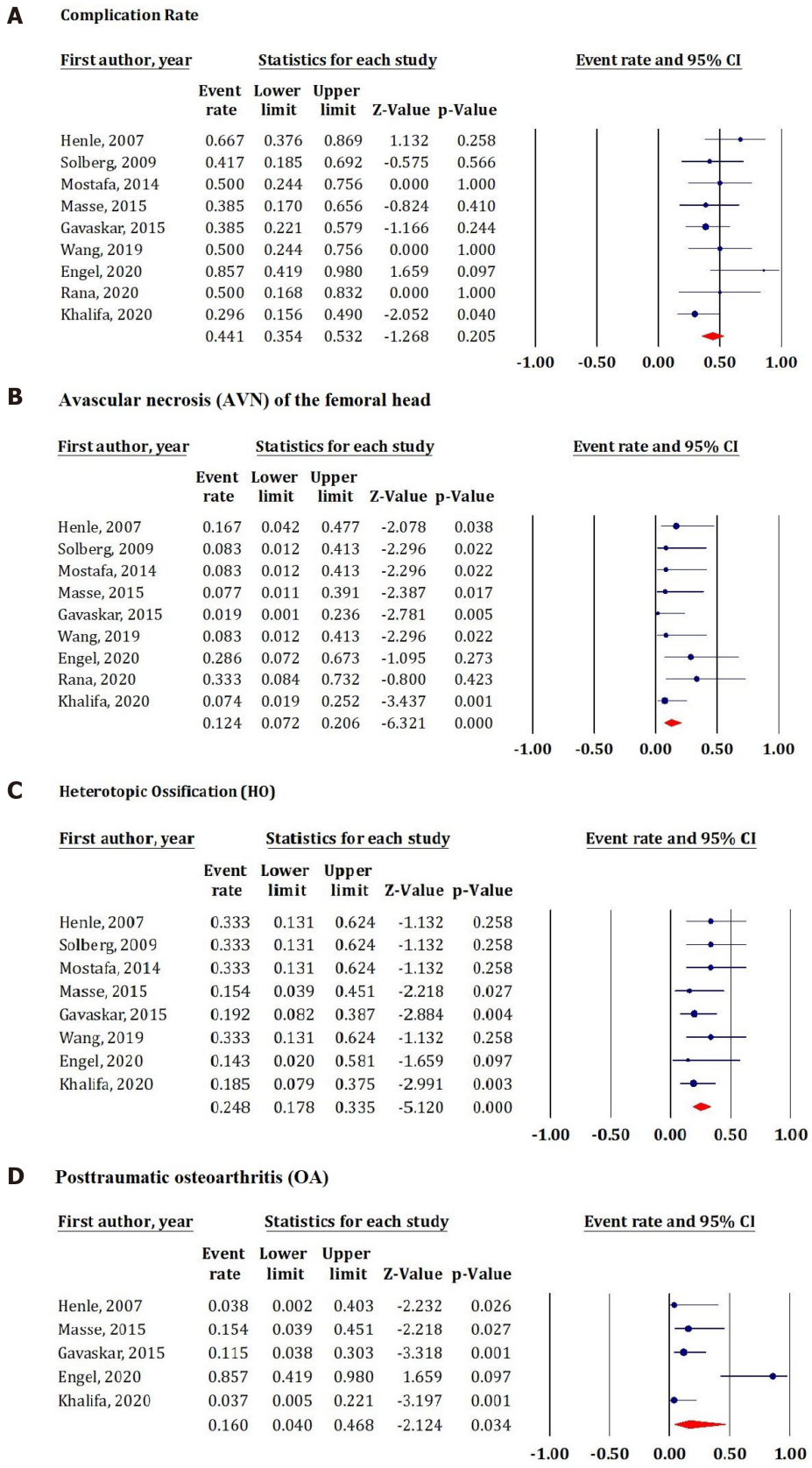

Figure 4 Forest plot diagram shows postoperative complications. A: Overall complications incidence; B: Avascular necrosis of the femoral head; C: Heterotopic ossification formation; D: Posttraumatic osteoarthritis. AVN: Avascular necrosis; CI: Confidence interval; HO: Heterotopic ossification; OA: Osteoarthritis.

approaches than what was reported with SHD in the current review, and the S-P approach group was even significantly lower than the K-L group, 103.3 ± 28.5 *vs* 334.5 ± 58.9, respectively ($P < 0.001$).

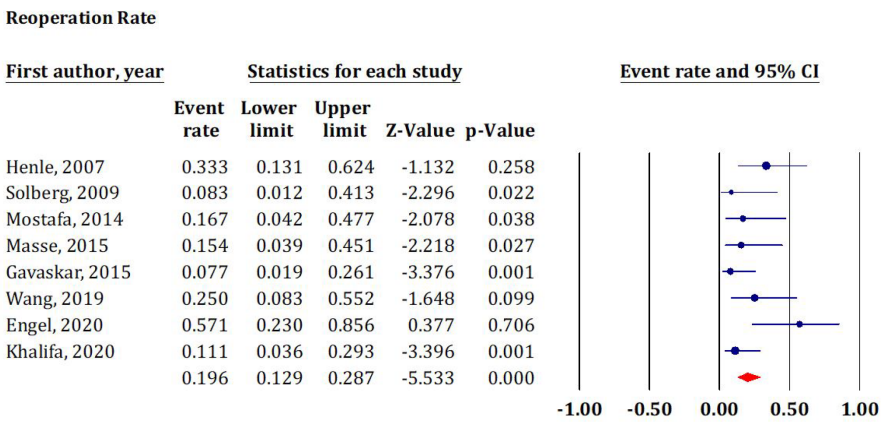

Figure 5 Forest plot diagram shows postoperative reoperation rate. CI: Confidence interval.

Many fixation devices could be used when ORIF is decided, such as headless subchondral screws, countersinking lag screws, bioabsorbable pins or screws, and suture fixation[15,25-27]. The same diversity was reported in the current systematic review, as various implants were used for fracture fixation, as reported in (Table 1). Some of the fixation devices had been criticized for causing foreign body reactions such as biodegradable screws or pins[26]; metal implants may lead to stress shielding besides causing an allergic reaction in susceptible patients[28].

Functional outcomes

Although there was diversity in reporting the functional outcomes among the studies included in this meta-analysis owing to implementing different assessment scales and scores, an overall satisfactory functional outcome (defined as excellent or good according to HHS or Merle d'Aubigne-Postel) was reported in 85% of the patients. Giannoudis *et al*[2] studied the relation between the functional outcomes and the utilized approach in 119 cases from nine studies. Excellent and good results according to the Thompson–Epstein scale was reported in 83.4% of patients treated through SHD compared to 65.4% and 49% in patients who received S-P or K-L approaches, respectively. In the current systematic review, we found nearly the same result as 83.3% of the patients where the Thompson–Epstein scale was used for functional assessment reported being excellent or good. However, the functional results obtained in patients treated through SHD were better than what was reported in other studies using the K-L or S-P approaches. In a study by Del Core *et al*[29], they retrospectively reviewed the results of 22 patient managed for FHFs (five Pipkin I, three Pipkin II, 0 Pipkin III, and 14 Pipkin IV). Surgical intervention was needed in 18 (82%) patients: S-P approach was used in 5 (28%) patients, and K-L approach in 13 (72%). Overall functional results (regardless of the approach used) according to the Thompson and Epstein scale were excellent and good in 12 (54%) patients, fair and poor in 10 (46%) [29]. In a systematic review and meta-analysis carried out by Wang *et al*[21] comparing the S-P *vs* K-L approaches for managing Pipkin type I and II fractures, five case-control trials were evaluated, including data of 68 patients (34 in each approach). An acceptable hip function (excellent or good) according to Thompson and Epstein scale was achieved in 67.6% (23/34) treated through the S-P approach, and this was not different from the K-L approach (P = 0.82)[21].

Radiological outcomes

There is no agreement on a scale or specific criteria to assess the quality of FHF reduction (as what is to be considered as non-anatomical or mal-reduction) in the postoperative period and follow-up radiographs, which makes comparison across studies difficult. However, Massè *et al*[14] was the first to describe using the Matta criteria[30] (originally described for acetabular fracture quality of reduction assessment) and applied it to the FHFs. In the current systematic review, a postoperative anatomic reduction was reported in about 74% of the patients reported from four studies. Three of them[14,16,19] reported using the Matta criteria, while in the fourth study[15], the authors did not report a specific method of assessment. As the SHD allows for 360 degrees of head exposure, it is postulated that it will allow a better anatomical reduction of the fracture compared with the limited visualization offered by other approaches[7].

Complications

The three major reported complications after FHF management had been alternating between AVN of the femoral head, HO formation, and posttraumatic OA as reported in many studies regardless of the approach used for surgery[1-3,25]. Controversy exists as to whether the trauma incident itself or the surgical intervention (including the surgical approach) is the cause leading to these complications; for example, the timing of reduction (if the patient presented with a dislocated hip) could affect the complication incidence[8,11,31], and disruption of the femoral head vascularity (leading to AVN) can occur at the time of trauma rather than being a consequence of surgical intervention[32].

The overall incidence of postoperative complications in the current systematic review was 44%; however, only half of those patients needed further intervention. This incidence was higher than what was reported in the initial series by Ganz *et al*[7] (treating non-traumatic conditions), where they reported a major complication rate of 3.3% in 213 patients. However, the incidence was lower than the overall complications reported in the Giannoudis *et al*[2] systematic review, where the major three complications were reported to occur at an incidence of 68%, which reached 84.4% when cases treated through SHD were excluded.

AVN of the femoral head

Ganz *et al*[7] reported 0% of AVN in their study; however, the cases they reported were non-traumatic conditions. The authors proved the safety of SHD in regard to hip vascularity preservation. In the systematic review by Giannoudis *et al*[2], after a mean follow-up of 59.7 mo, AVN was reported in 2 (5.3%) out of 38 patients treated through the S-P approach, 3 (8.3%) out of 36 patients treated through SHD, and 11 (16.9%) patients out of 65 treated through the K-L approach. The authors reported that the chance of a patient to develop AVN when treated through a K-L approach was 3.67 and 2.24 times higher compared to S-P or SHD approach, respectively ($P > 0.05$)[2]. In the current systematic review, we reported an incidence of AVN of 12%, which was better than the K-L approach and higher than the S-P approach, as reported in the previous study.

The same previous finding was confirmed in further studies as follows. In a study by Scolaro *et al*[1] on 147 FHFs classified according to Pipkin classification into type I (27%), II (42%), III (4.7%), IV (15%), and as others which included impaction injuries (10%). ORIF was performed in 78 (53.1%) fractures; 97% of these were approached through the S–P approach. After a mean follow-up of 12.4 months, 6 (8.7%) patients developed AVN, mostly all Pipkin III fractures ($n = 5$) had AVN[1]. In a study by Stannard *et al*[33] where they surgically treated 17 patients diagnosed with FHFs, in 6 patients (35%) the S-P approach was used, 10 (59%) underwent the K-L approach, and 1 (6%) underwent dual anterior and posterior approaches. The authors reported that 4 of the 5 patients who had AVN were managed through the K-L approach. They reported that the odds ratio was 3.2 times higher for AVN when the K-L approach was used compared to the S-P approach[33].

In a retrospective analysis by Swiontkowski *et al*[34] of 24 patients presented with Pipkin types I and II (12 patients were treated through the K-L approach and 12 through the S-P approach), the authors reported an incidence of AVN of 16.7% with the K-L approach compared to 0% when the surgery was performed through the S-P approach[34]. In the systematic review by Guo *et al*[35], they included studies from 1980 to April 2009 to evaluate the relation of the surgical approach to the development of AVN; ten studies were eligible to be included with a total of 176 cases. The incidence of AVN was more with the K-L approach (16.9%) than the S-P (7.9%); however, the difference was not significant[35].

HO formation

It is not clearly defined if HO formation relates to the surgical approach or the traumatic muscle injury[25]. The exact pathogenesis is still unclear, but other factors rather than the type of the approach have been accused such as being a polytrauma patient, concomitant craniocerebral or thoracoabdominal trauma, male sex, the time to hip reduction (if dislocated), delay to surgery, and associated fractures as in type III and IV injuries[36-38]. In the current systematic review, SHD was associated with HO formation at an incidence of 25%; surprisingly, this incidence was lower than the incidence reported with treating non-traumatic conditions as Ganz *et al*[7] reported 37% of their patients having HO formation.

In another study by Kargin *et al*[39] where they evaluated 44 patients who underwent SHD for non-traumatic causes with a mean follow up of 66 mo, they

reported an incidence of HO formation of 36.5%. The incidence reported in the current systematic review was lower than what was reported by Giannoudis *et al*[2], as they noted that HO of any grade occurred in 44.7% of patients treated with the S-P approach and in 32.3% of patients treated through the K-L approach. However, the difference between approaches was not significant ($P > 0.05$). The authors reported an incidence of 47.2% in the patients treated through SHD included in their review (which was nearly double the incidence in the current review). They estimated a 1.87 times higher rate of HO following SHD; however, they noted that this higher incidence did not affect the functional outcomes[2].

In the systematic review by Guo *et al*[35], HO formation was lower in the SHD group (33.3%) compared to the S-P or K-L approaches (42.1% and 36.9%), although the difference was not statistically significant. In a study by Peng *et al*[40] reporting their results of treating FHFs at an average follow up of 3.3 years, 18 patients treated through the S-P approach, and 6 through the K-L approach, the overall incidence of HO was 43%. No surgical intervention was needed.

In the current systematic review, lower grades of HO (Brooker I and II) occurred in 76.5 % of the patients, while higher grades (III and IV) occurred in 23.4 %. This was nearly similar to the results obtained from the study by Scolaro *et al*[1] where low-grade HO developed in 74% of the patients, while higher grades developed in 24%. However, they had a lower incidence of surgical intervention for HO in only 2.9% of patients who required surgical excision compared to 10% of the patients in the current systematic review. The lower incidence of HO formation in the current systematic review compared to the previous reports may be attributed to the advancement in HO prophylaxis techniques, more orientation about the problem, which was gained from previous studies, and to increasing experience of surgeons with the SHD technique paying more respect to soft tissues.

Posttraumatic OA

This complication could develop due to improper fracture reduction or as a consequence of AVN, as in some studies the authors reported AVN and OA as a single entity[1]. In the current systematic review, we reported an incidence of posttraumatic OA of 16% after SHD, which is considered higher than the incidence reported with cases managed through SHD in the Giannoudis *et al*[2] systematic review, where the authors reported 0% incidence. However, the incidence reported with SHD was still lower than other approaches, as Giannoudis *et al*[2] reported an incidence of 21.0% and 29.2% in patients treated through the S-P and K-L approaches, respectively. They estimated a 20.3 ($P = 0.04$) and 30.6 ($P = 0.018$) times higher incidence of posttraumatic OA development when the S-P or K-L approach was used, respectively, compared to SHD[2]. An increased incidence with other approaches was reported in other studies, as in the study by Wang *et al*[24] the authors reported a posttraumatic OA incidence of 14.3% and 16.7% with the S-P and K-L approaches, respectively. The difference was insignificant ($P = 1.000$). Del Core *et al*[29] reported an overall incidence of 23% in their patients. In the current systematic review, the increased incidence of OA development could be attributed to the fact that 6 of the 12 patients who developed posttraumatic OA were reported from Engel *et al*[17] study, where all the included cases were Pipkin type IV with an incidence of OA of 85.7% (6 out of 7 patients), owing to the severity and complexity of this type of injury.

Infection

This was the lowest reported complication in the current systematic review, which occurred at an incidence of 2.1%. Only 2 patients required further surgical intervention; this was in accordance with previous studies, as in the systematic review by Giannoudis *et al*[2] the incidence of infection was 3.2%. In the study by Del Core *et al*[29], 1 patient (5%) developed a postoperative infection. In a study by Peng *et al*[40], no deep infection was reported.

SHD unique complications

The possibility of TFO nonunion and the development of trochanteric bursitis with lateral thigh pain secondary to irritation by the screws used to fix the TFO are unique complications to the SHD approach[7,13,41,42]. An incidence of TFO nonunion was reported in five studies in the current review giving an incidence of 3.4%, and two patients required refixation. The incidence was even lower in the studies reported on non-traumatic conditions, as in a multicentre study by Sink *et al*[43]. They evaluated 334 hips from eight different North American centres with a minimum of 12 months follow-up. TFO nonunion was reported in six hips (1.8%), all united after revision of

the internal fixation. Ganz *et al*[7] reported three (1.4%) cases with TFO nonunion. In the current systematic review, we reported an incidence of trochanteric bursitis with lateral thigh pain in 1 (3.8%) patient out of 26 hips, which required screw removal. In the study by Kargin *et al*[39], lateral thigh pain was reported to occur in 28.8% of their patients.

Advantages of the SHD approach

Trauma surgeons were encouraged to incorporate SHD in the management of FHFs as it offered many advantages. Firstly, the wide exposure (360 degrees) of both the femoral head and the acetabulum makes it possible to treat both pathologies if present (as in Pipkin Type 4) at the same time. Secondly, it enables the detection and dealing with other intraarticular injuries such as labrum injury or head impaction injuries, which may be difficult to diagnose in preoperative imaging studies[44-46]. Thirdly, the ability of the approach allows the surgeon to perform better reduction and fixation of the fractured fragments. Lastly, it enables the ability to check the vascularity of the femoral head intraoperatively by using the drill test [7,8].

Limitations of the current systematic review

First, we did not compare the results obtained from SHD with other approaches, which might be due to the lack of comparative studies in this field. Second, one crucial point that was not assessed is the experience of the surgeon with this approach. Some authors reported having no familiarity with this approach[40]. On the other hand, in two studies[14,19] included in the meta-analysis, the authors reported having previous experience with the SHD approach; however, we found it unmeasurable and challenging to state the learning curve needed to master this technique. Lastly, limiting the article search to the past 20 years might lead to missing some earlier articles; however, we aimed at presenting as updated data as possible.

CONCLUSION

Incorporating SHD as an optional approach in the armamentarium of approaches in dealing with FHFs enables trauma surgeons to properly manage these intraarticular fractures and detect and deal with additional intraarticular injuries. It offered acceptable functional and radiological outcomes with a wide range of safety in regards to the hip joint vascularity and the development of AVN, the formation of HO, and the development of posttraumatic OA; however, it still carries its unique risk of complications such as TFO nonunion and persistent lateral thigh pain.

ARTICLE HIGHLIGHTS

Research background

Surgical hip dislocation (SHD) was introduced as a safe approach for managing various hip pathologies. It gained popularity among trauma surgeons as a new approach for the management of femoral head fractures (FHFs). Several studies were published on this subject. However, no systematic reviews were carried pooling these data together to generate stronger evidence of this approach utility.

Research motivation

FHFs are considered as intraarticular fractures. Anatomical reduction and preservation of its vascularity are two mandatory perquisites for obtaining optimum outcomes; SHD was introduced for the management of these fractures with the advantage of preserving femoral head vascularity and providing 360 degree visualization of the femoral head.

Research objectives

We carried out this systematic review and meta-analysis to evaluate the efficacy (functional and radiological outcomes) as well as the safety (complications incidence) of using the SHD approach for management of FHFs, which could help encourage more surgeons to widely adopting this approach in their practice.

Research methods

Four major databases were searched (PubMed, Embase, Web of Science, and Cochrane Central Register of Controlled Trials) to collect eligible studies reporting on various outcomes (functional, radiological, and complications) after utilizing SHD as described by Ganz in the management of FHFs. Articles basic, surgical, functional, radiographic, and complications data were collected from the included articles.

Research results

Nine studies were eligible and included in the analysis, forming a total of 129 FHFs with an average follow up of 38.4 mo. The average operative time and blood loss were 123.74 min and 491.89 mL, respectively. Excellent and good functional outcomes were obtained in 85% of the patients, while anatomical fracture reduction could be obtained in 74%. The overall complication rate was 44%; the main reported complications were femoral head avascular necrosis, heterotopic ossification, and osteoarthritis, which occurred at an incidence of 12%, 25%, and 16%, respectively. A unique complication to SHD was trochanteric flip osteotomy nonunion and trochanteric bursitis, which occurred at an incidence of 3.4% and 3.8%, respectively. The issue of surgeon experience and its relation to the results and utilization of this approach is still to be studied.

Research conclusions

We believe that this was the most recent systematic review collecting and reporting the data regarding the efficacy and safety of SHD as an approach for management of FHFs; the results of this systematic review suggest the high safety profile of this approach with acceptable functional outcomes.

Research perspectives

We believe that there is a need for further studies and systematic reviews comparing the SHD approach to conventional approaches (anterior and posterior) in the management of FHFs to prove its safety and efficacy.

ACKNOWLEDGEMENTS

We would like to thank Dr. Ahmed M Ahmed for his great effort in performing the statistical analysis for the current systematic review and metanalysis.

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