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EDITORIAL

Three-dimensional printing in paediatric orthopaedic surgery

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Abstract

Three-dimensional (3D) printing is a rapidly evolving and promising field to improve outcomes of orthopaedic surgery. The use of patient-specific 3D-printed models is specifically interesting in paediatric orthopaedic surgery, as limb deformity corrections often require an individual 3D treatment. In this editorial, various operative applications of 3D printing in paediatric orthopaedic surgery are discussed. The technical aspects and the imaging acquisition with computed tomography and magnetic resonance imaging are outlined. Next, there is a focus on the intraoperative applications of 3D printing during paediatric orthopaedic surgical procedures. An overview of various upper and lower limb deformities in paediatrics is given, in which 3D printing is already implemented, including post-traumatic forearm corrections and proximal femoral osteotomies. The use of patient-specific instrumentation (PSI) or guiding templates during the surgical procedure shows to be promising in reducing operation time, intraoperative haemorrhage and radiation exposure. Moreover, 3D-printed models for the use of PSI or patient-specific navigation templates are promising in improving the accuracy of complex limb deformity surgery in children. Lastly, the future of 3D printing in paediatric orthopaedics extends beyond the intraoperative applications; various other medical applications include 3D casting and prosthetic limb replacement. In conclusion, 3D printing opportunities are numerous, and the fast developments are exciting, but more evidence is required to prove its superiority over conventional paediatric orthopaedic surgery.

Key Words: Three-dimensional printing; Paediatric; Orthopaedic surgery; Intraoperative; Patient-specific instrumentation; Guiding

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Core Tip: Three-dimensional (3D) printing for intraoperative use in paediatric orthopaedic surgery is a relatively novel field. Research has shown that 3D anatomic models can be used for patient-specific instrumentation and patient-specific templates, that possibly allow the orthopedic surgeon to perform complex surgery more accurately. Based on the latest scientific evidence, this editorial provides an overview of the overall role of 3D printing in intraoperative applications of upper and lower limb surgery in paediatric orthopaedics.

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INTRODUCTION

Over the last decade, three-dimensional (3D) printing–or additive/layer manufacturing-has become a more and more interesting application in medicine. It has been used in various surgical specialties, including neurosurgery, oral and maxillofacial surgery, plastic surgery and cardiothoracic surgery[1-3]. Also in the field of orthopaedic surgery the interest and use of 3D printing has grown over the years, since it started in 1999 in a case of complex spinal surgery[4].

In the orthopaedic field, 3D technology can be used in three different sections: Including preoperative planning, 3D-printed models and 3D printing for patient-specific instrumentation (PSI). A recent meta-analysis reported that the use of 3D-printed models in preoperative planning significantly reduced the operative time, intraoperative blood loss and fluoroscopy use during orthopedic trauma surgery[5]. These outcomes may be the result of a better understanding of the pathological anatomy in complex cases. Moreover, 3D printing helps the surgeon in preoperative planning of the surgical procedure by means of fracture reduction and the sizes and positioning of plates and screws for internal fixation. This could possibly reduce operation time and the amount of dissection of surrounding tissues and therefore blood loss[5]. In addition to trauma surgical applications, PSI allows the surgeon to perform precise osteotomies for deformity correction[5-8], which is specifically interesting for paediatric patients[9].

Correcting limb deformities in children is a challenging and complex type of surgery. Therefore, novel technologies such as 3D printing are increasingly applied, aiming to achieve more accurate corrections and improved outcomes[9]. The use of patient-specific 3D-printed models is specifically interesting and promising in paediatric orthopaedic surgery, as limb deformity corrections require [sh6] an individual 3D treatment. For example, the use of 3D printing in preoperative planning of hip preservation surgery created an improvement in trainee and patient education for understanding the abnormality of the patient's disorder[6]. However, due to its novelty, evidence on the use of 3D printing in pediatric orthopedics is still limited.

This editorial provides an overview of the various intraoperative applications of 3D printing in pediatric orthopedic surgery and assesses the overall role, challenges and future of this relatively novel technique.

TECHNICAL ASPECTS OF 3D PRINTING

3D printing, or additive layer manufacturing, is a technique to create a 3D object from a digital model. It is an advanced, computer-controlled technology that deposits successive layers of materials (*e.g.*, metals or plastic) to create an object. In contrast to traditional subtractive manufacturing processes that take away or shape material, 3D printing has the advantage to create complex structures by adding hundreds of miniscule layers that are fused together. Another advantage of 3D printing is the

possibility to create shapes of different materials including plastic, rubber, metals or ceramics[7,10].

The process of creating 3D-printed models for medical applications starts with high-resolution imaging (Figure 1)[7,8,10-12]. Multi-row detecting computed tomography (MDCT) and magnetic resonance imaging (MRI) are frequently used in orthopedics for diagnostics of complex anatomy or severe deformities[7,11-13]. MDCT is a high-contrast computed tomography (CT) that produces thin-section slices of less than 1 mm and therefore highly suitable for analysing bony structures. After acquiring the clinical dataset, MDCT images are stored according to a universal data format; standardized digital imaging and communications in medicine (DICOM). Post-processing software extracts these DICOM files[7,8,14]. This extraction process is called segmentation. It separates the outlines of different anatomical structures in each individual 2D image (slice) by using colour contrast to create separate objects. In the next phase, computer-aided design (CAD) software (*e.g.*, MIMICS or InPrint) combines all the individual 2D images (slices) and creates a virtual 3D initial object (Mesh creation)[7,8,10,14]. This makes it possible to see depth, angulation and diameters of the anatomical structure or pathology. Next, the 3D object is transformed into a file that is ready for printing. In some cases, the resolution of the radiology is suboptimal, or the 3D object has no clear boundaries. In these cases, a manual reconstruction of a 3D object can be performed (*i.e.*, ReplicatorG software) and anatomical corrections of the model can be made in this CAD software[7,8,14]. It also provides control of the filling of the model, with possibilities between 0% filling (shell alone) to 100% filling and makes the model more suitable for 3D printing or material of preference[7,8,10,14]. Once the CAD model is finalised, it is converted into a common 3D file format, stereolithography (SLA) file and sent to the appropriate 3D printer[2,7,8,14]. Post process, the materials first need to cool down before they can be used and consequently sterilization is required for intraoperative use[12].

Different types of 3D printing techniques have been used over the last years, including printers that use powder, melted polymers, gel, liquids, or a combination of these substances[7,8]. In the past, Fused Deposition Modeling (FDM) was used as a 3D printing technique, in which a movable nozzle places long, thin wire of thermoplastic material on top of each other. A 3D object is created layer by layer. It is a relatively cheap and fast production method to create anatomical models. However, the shape of a FDM print differs greatly in quality from a professional 3D printer[7,8,15,16]. Therefore, different 3D printing procedures are used for the production of patient-specific models and patient-specific surgical guides at this moment. Selective laser sintering (SLS) is a powder-based fusion technology that uses a laser beam to locally sinter polymer powder to build 3D objects layer by layer[7,8,15,16]. SLS uses bio-based polyamide materials and metals for 3D printing. Other 3D printing techniques are SLA and digital light processing (DLP) that use UV laser and a liquid bath containing a UV-sensitive liquid polymer[8,10,12,17]. This liquid is illuminated layer by layer by the laser where the liquid has to cure. The surface cures into a solid state and subsequently the surface raises one layer. The next layer is then exposed and cured. 3D-printed objects that are generated SLS, DLP and SLA can be sterilized and therefore can be used in the operating room.

INTRAOPERATIVE APPLICATIONS OF 3D PRINTING IN PEDIATRIC ORTHOPEDIC SURGERY

Intraoperative applications of 3D printing in pediatric orthopedics involve the creation of PSI to perform more accurate complex surgery or correct deformities. There are increasingly interesting and promising applications in both upper limb and lower limb deformities.

Upper limb

Currently, the most commonly described application of 3D printing in the upper extremity is the forearm, usually rotational impairment after malunited forearm fractures. Byrne *et al*[18] used 3D-printed patient-specific osteotomy guides and custom-made plates for multiplanar corrective osteotomies in 5 patients with posttraumatic malunion of the forearm. An angular correction of the ulna and radius of 9.9° and 10.0° was planned, respectively. They reported mean postoperative corrections of 10.1° and 10.8°, respectively. Forearm pronation improved from 68° to 87° and supination improved from 47° to 89°. Furthermore, a significant improvement in pain relief and grip strength was seen. Another prospective study enrolled 16

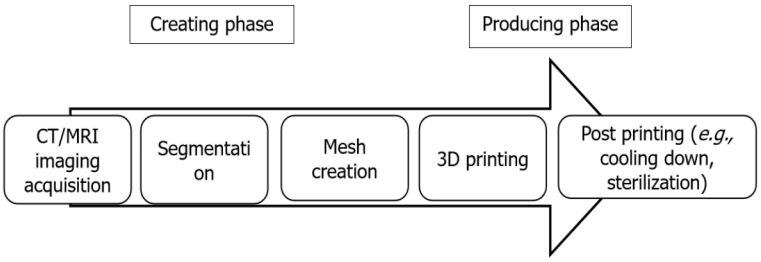

Figure 1 The process of three-dimensional printing. A high-resolution computed tomography (CT) or magnetic resonance imaging (MRI) scan is required for the data acquisition of the limb deformity. The data are used for the segmentation process where each anatomical structure is processed as an individual entity. Mesh creation uses this data to generate the process from the segmented anatomy models into a model that only retains the specific structures that must be used for three-dimensional (3D) printing. Then, the 3D-printed model is manufactured. The post-printing process includes cooling down the created model or sterilization for the use in the operating room. CT: Computed tomography; MRI: Magnetic resonance imaging; 3D: Three-dimensional.

patients with a total of 17 bone deformities, including distal radial malunion, distal humeral malunion and forearm diaphyseal malunion[19]. They reported that the use of 3D patient-matched instruments for corrective osteotomies showed a significant deformity improvement of 22.2°. Also, in patients treated for distal radial malunion and diaphyseal malunion, the flexion, extension and pronation of the forearm were significantly improved. Clinical implications as pain, range of motion, and grip strength were also significantly improved compared to the preoperative situation. Another study used 3D-printed templates to guide the osteotomy orientation in a posttraumatic forearm malunion of a 15-year-old female[3]. The authors reported that 3D-printed templates made it possible to achieve near-anatomical reduction close to 1° residual deformity in all three planes and a recovery to full function within 3 mo. One of our own cases presented with decreased rotational range of motion after sustaining a forearm fracture as a child, without improvement after extensive rehabilitation. 3D analysis determined the deformity and optimal planes of correction (Figure 2). Patient-specific osteotomy guides with predrilling of the screw holes were designed, and hardware for fixation was selected (Figure 2). The surgical procedure was then completed according to plan, which resulted in a vast improvement in range of motion and high patient satisfaction. In the period 2014-2020, 42 cases were operated using this technique, of which 16 were malunited forearms with rotational impairment. Most patients had a severe supination deficit (mean -10 degrees), which improved to a mean supination of +60 degrees. Pronation limitation was much less severe (mean +45 degrees) with a mean improvement to +55 degrees. We experienced one complication due to a transient posterior interosseous nerve paralysis, which recovered spontaneously within the first 6 wk after surgery. Thus, in deformities of the forearm due to malunion, the use of 3D PSI shows improvement in correction angles as well as in clinical outcomes as grip strength and pain relief[1,18,19]**.** Nevertheless, it is important to realize that the studies mentioned above are low-grade evidence and therefore the results need to be analysed with a critical view.

Cubitus varus deformities are sometimes seen after elbow fractures in children. Correction of this deformity is a complex surgical procedure and requires a 3D approach. Hu *et al*[20] included 35 patients and assigned them into two different groups comparing traditional surgery to surgery using an intraoperative patient-specific 3D-printed navigation template. All patients underwent similar surgery with wedge osteotomy of the lateral distal humerus. The 3D-printed patient-specific template significantly reduced the operation time with a mean of 11 min and significantly improves the accuracy of the correction by a mean of 3°. However, the question remains whether and accuracy of 3° is clinically relevant. Another study analysed 25 patients with cubitus varus deformity and compared a group of patient-specific 3D-printed osteotomy guides with a traditional group[21]. The 3D guiding template procedure resulted in a significant decrease of the operation time (almost 30 min), less intraoperative blood loss (17.5 mL) and higher satisfaction. However, the most important achievement of correcting deformities in pediatric orthopedics is recovery of function.

Lower limb

For lower limb paediatrics, 3D printing has been used for various complex techniques, including femoral and pelvic osteotomies and tarsal coalition resection[15,22]. Femoral and pelvic osteotomies with use of 3D guides have been applied for late sequelae of

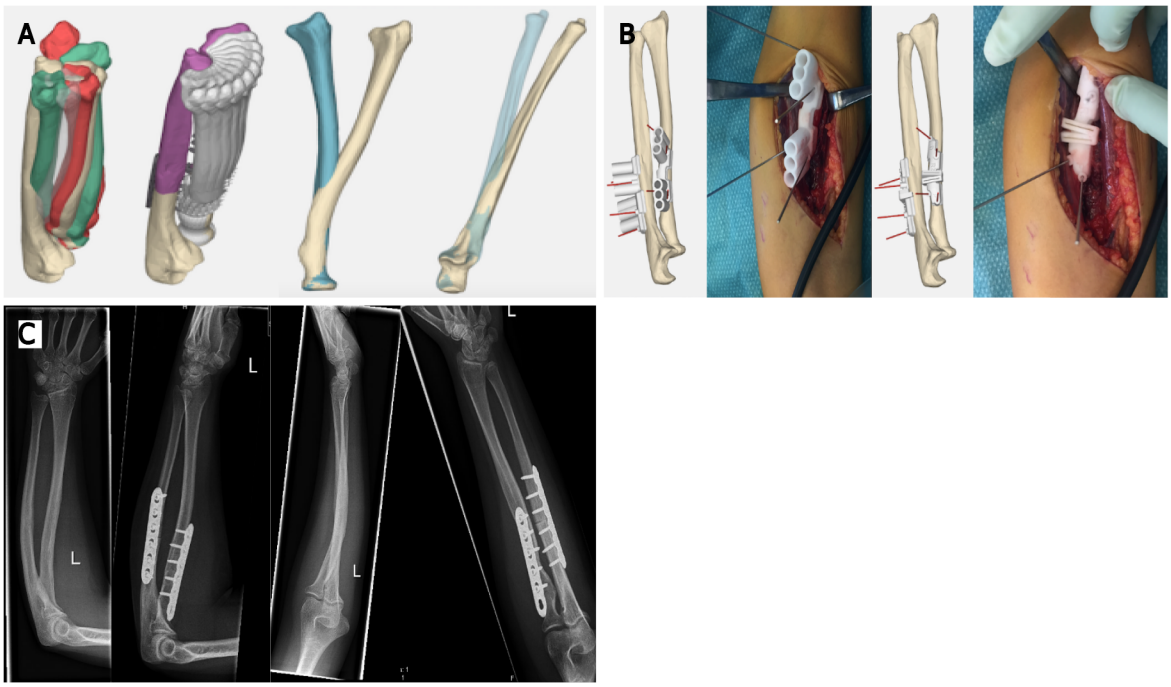

Figure 2 Three-dimensional-printed guides in posttraumatic rotational impairment of the forearm. This patient suffered from a decreased rotational range of motion due to malunion after a forearm fracture. The three-dimensional (3D) deformity in both bones of the forearm was assessed with 3D analysis. During this analysis the optimal planes of correction were determined, and potential gains were calculated with simulation of rotation of the forearm comparing the preoperative and postoperative situation. Patient-specific guides to perform the desired osteotomies with predrilling of the screw holes for the radius and ulna are shown here. The surgical procedure was completed as planned and resulted in a vast improvement in range of motion. A: Preoperative planning; B: Intraoperative use of 3D-printed patient specific guides; C: Preoperative and postoperative radiographs, showing correction of the flexion deformity of the ulna to an ulna with a normalized proximal ulna dorsal angulation, as well as correction of an S-shaped radial shaft to a normalized bowing configuration of the radial shaft.

developmental dysplasia of the hip (DDH), slipped capital femoral epiphysis (SCFE) and Legg-Calvé-Parthes (LCP) disease[15].

Severe DDH can lead to hip deformity that may require surgical correction. Zheng *et al*[23] compared 12 cases of femoral corrective osteotomy after DDH using patient-specific 3D navigation templates with 13 cases using conventional approaches[23]. No differences in varus and angles were reported. However, significantly decreased operation time (26 min) and fluoroscopy were reported in favour of the 3D-printed model group.

SCFE leads to a posterior and inferior displacement of the femoral head, giving an altered mobility of the hip joint and a syphon-shaped femoral neck after consolidation. A 3D sub- or intertrochanteric osteotomy can be performed for correction of the varus, internal rotation and flexion of the hip and thereby restoring its function. Cherkasskiy *et al*[24] used 3D models for proximal femoral osteotomy following SCFE and also found decreased operation and fluoroscopy times. We have used a CT-based 3D-printed model to plan and perform a complex osteotomy in a previously pinned SCFE case, with favourable results with regard to osteotomy precision, positioning of the implant, surgical time and use of the image intensifier (Figure 3). In this case the patient had a pre-operative externally rotated right hip of 40 degrees. Post-operatively, she was able to internally rotate the hip 10 degrees, compared to 20 degrees of internal rotation on the contralateral left side (Figure 3).

LCP disease can lead to deformity of the femoral head and an adaptive deformity of the acetabulum. Six patients with LCP disease were treated with a 3D-printed patient-specific osteotomy model[25]. The model allowed the surgeon to correct the femoral head almost identical to the contralateral healthy side[25].

A recent review confirmed that use of PSI for the above indications has led to improved accuracy and precision, decreased procedure times, and decreased intra-operative imaging requirements, compared to conventional methods of performing femoral or pelvic osteotomy[15].

3D techniques have also been used in pediatric foot orthopaedics. De Wouters *et al* [22] used 3D-printed PSI to guide the surgeon in removal of talocalcaneal and calcaneonavicular coalitions. It helped to orientate the saw blade for the resection of the bone bridge at the correct depth, which resulted in complete resections with no

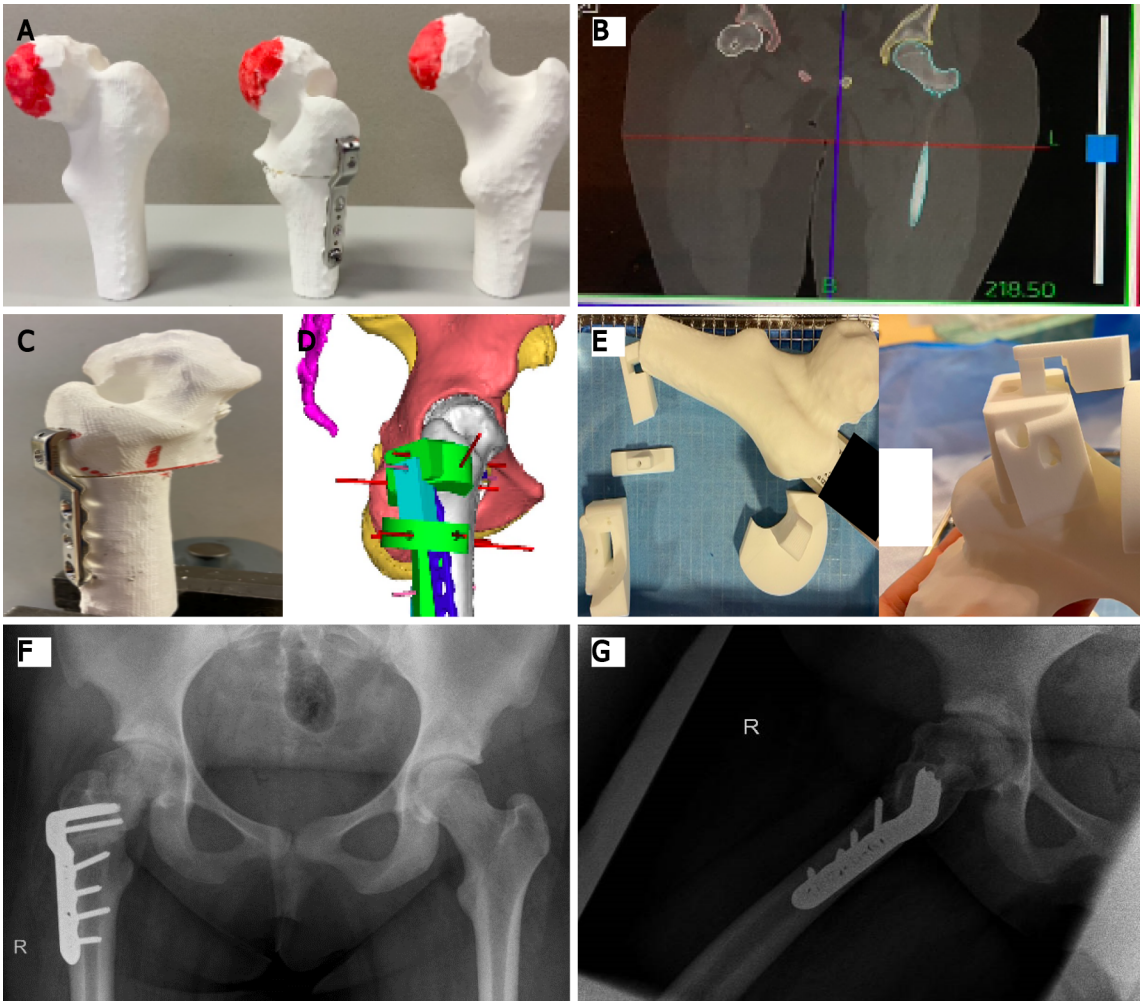

Figure 3 Three-dimensional printing for grade 3 slipped capital femoral epiphysis. This figure shows different steps required in a case of grade 3 slipped capital femoral epiphysis where three-dimensional (3D)-based templates for positioning of the implant were used, and guidance of the osteotomy during the surgical procedure was performed. A: Preoperative 3D-printed model of the deformed femoral head; B: High-resolution computed tomography scan for exact preoperative planning of deformity correction; C: Preoperative 3D-printed model of the deformed femoral head after correction; D: Analysis of the unique blade plate through 3D-computed view; E: The 3D-printed unique locking system; F: Postoperative anteroposterior radiograph; G: Postoperative lateral radiograph.

recurrence after a mean follow-up period of 18 mo. We have promising experience with 3D-guided resection of a calcaneonavicular coalition based on preoperative MRI (Figure 4).

ADDITIONAL APPLICATIONS OF 3D PRINTING IN PAEDIATRIC ORTHOPAEDICS

Over the last years, 3D printing has been successfully introduced in pediatric orthopaedics. Because of its seemingly endless possibilities, this relatively novel technique expands further than surgical applications alone.

In the technology of prosthetic limbs, 3D printing is increasingly used. Traditional prostheses for children with upper extremity amputees have been considered to be too heavy or too expensive to be a true benefit for a child[22]. In addition, children outgrow prostheses and may damage them[26]. In 3D printed prostheses, there is the possibility to replace a part of the prosthesis instead of the complete device[13]. Children are also allowed to choose the design and colour schemes, which make 3D-printed model prostheses more tailored to a child's choices. Therefore, children may be more self-confident, as described in various studies of 3D-printed upper limb replacement[13,27-29].

In the conservative treatment of paediatric fractures, two studies described the treatment of nondisplaced forearm fractures with a 3D-printed device compared to a traditional plaster cast[30,31]. The results showed an improvement of wrist function

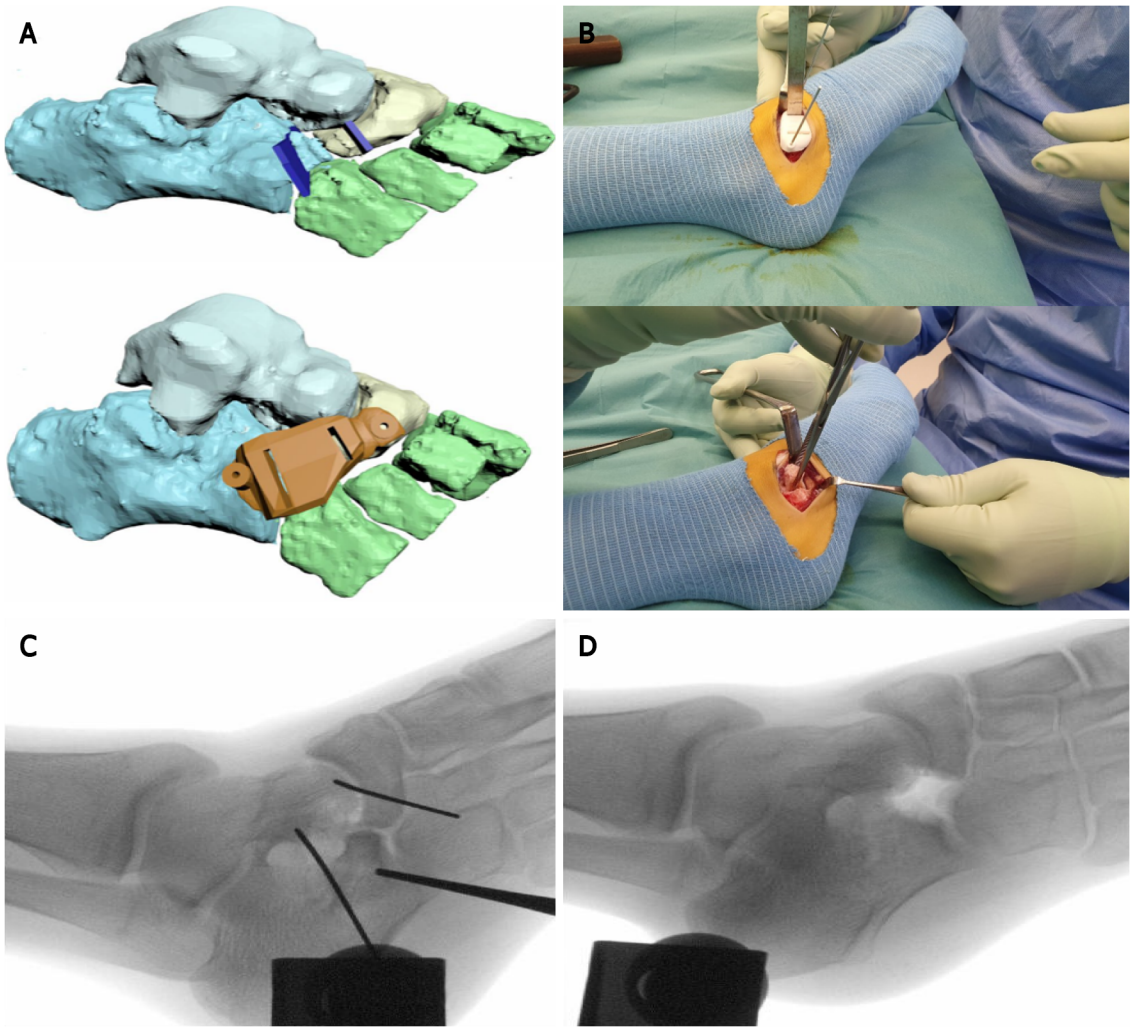

Figure 4 Preoperative planning and intraoperative use of three-dimensional-printing for a calcaneonaviculair coalition in a 14-year-old girl. A preoperative magnetic resonane imaging scan was used to manufacture a three-dimensional (3D)-printed osteotomy guide for removal of a calcaneonavicular coalition. A: Preoperative 3D-planning; B: Intraoperative use of the manufactured 3D-printed guide and coalition resection; C: Intraoperative fluoroscopy shows the position of K-wires to hold the 3D-printed guide; D: Intraoperative fluoroscopy shows the resected bone.

after immobilization with a 3D-printed device. Moreover, activities of everyday life, patient satisfaction and patient comfort during the immobilization were improved compared to the traditional cast group. In addition, the 3D-printed devices were reported to be lighter than traditional casts and removable, which make them more patient-friendly (*e.g.* when taking a shower). This suggests that a 3D device can also be an effective alternative approach in the conservative treatment of fractures in paediatric orthopaedics.

CHALLENGES AND FUTURE OF 3D PRINTING IN PAEDIATRIC ORTHOPAEDIC SURGERY

As outlined, 3D printing seems to have great potential in numerous paediatric orthopaedic applications. However, there are several challenges in this field that need further investigation and improvement.

Although the production time of a 3D product has decreased since it was invented, preparation and production of PSI still take at least several days[32]. Therefore, the application in the acute setting is challenging (*e.g.*, for fractures). However, research and development in 3D printing is a growing field of interest, resulting in new upcoming materials with better biomechanical and biocompatible characteristics. Furthermore, the development of 3D printers that can create models within hours is very promising.

Another challenge is reduction of radiation exposure. Although the use of fluoroscopy during the surgical procedure is reduced by using 3D PSI or 3D-printed model guiding templates[23,33], the total dose of radiation might not be decreased *per* case. A preoperative high-resolution CT scan is usually obtained to produce a 3D image, which is additional radiation exposure to the child[16,32]. Instead, the use of MRI would help reduce the radiation exposure, with the possible additional advantage of a more detailed image of the paediatric anatomic structures (*e.g.*, physeal bar, periosteum and soft tissue)[10]. However, the process of undergoing an MRI scan is more difficult for very young children (under the age of 5), because of the necessity of sedation, motion reduction and/or accelerated imaging[7,8,17,34,35]. Moreover, studies using MRI for preoperative imaging acquisition in 3D processes are scarce. Our case shows the potential of MRI to produce surgical 3D guides (Figure 4).

In addition, 3D printing requires advanced technology and financial resources, which may not be available in developing countries[32]. However, printing costs seem to decrease over time[36] and costs of 3D printing may be outweighed by saving operation time. A cost analysis showed that using 3D-printed models saved a mean operating time of 62 min, translated to $3720 *per* case compared to conventional techniques[37]. Due to the ambiguity in evidence on the cost-savings of using 3D-printed models in paediatric orthopaedic surgery, an in-depth cost analysis is required of production costs *vs* potential savings obtained by improved intraoperative results [5].

Finally, more scientific evidence is required on the use of 3D techniques in paediatric orthopaedic surgery. Despite the fact that the current literature shows promising results for various indications as discussed, randomized trials on 3D printing compared to conventional methods are still lacking. It is likely to expect that 3D printing will be mainly beneficial for complex surgical cases.

CONCLUSION

3D printing is a promising technique for numerous upper and lower limb surgical applications in paediatric orthopaedics. In upper limb surgery, 3D has been most frequently used in posttraumatic deformities. In lower limb surgery, 3D-printed models are mostly used to correct congenital and developmental deformities of the hip. Other applications of 3D-printed models include limb prostheses and non-surgical treatment of fractures. Future possibilities of this exciting technique are numerous.

The affordability of 3D printers has increased over the years, and literature shows that using 3D-printed models for PSI or intraoperative guiding reduces the operating time and radiation exposure. Moreover, an improved accuracy of deformity correction is attained. However, most studies have a low level of evidence. Moreover, using 3D-printed models in pediatric orthopaedic surgery is complex due to growth of children and therefore, the moment of planning *vs* the timing of the surgery is also a challenge to overcome. All in all, more research, preferably randomized controlled studies, is required to compare conventional approaches and the intraoperative use of 3D-printed models. Nevertheless, the use of 3D-printed models as an intraoperative tool seems to have great future potential in complex pediatric orthopaedic surgical procedures.

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REVIEW

Regional anesthesia for orthopedic procedures: What orthopedic surgeons need to know

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Abstract

Regional anesthesia is an integral component of successful orthopedic surgery. Neuraxial anesthesia is commonly used for surgical anesthesia while peripheral nerve blocks are often used for postoperative analgesia. Patient evaluation for regional anesthesia should include neurological, pulmonary, cardiovascular, and hematological assessments. Neuraxial blocks include spinal, epidural, and combined spinal epidural. Upper extremity peripheral nerve blocks include interscalene, supraclavicular, infraclavicular, and axillary. Lower extremity peripheral nerve blocks include femoral nerve block, saphenous nerve block, sciatic nerve block, iPACK block, ankle block and lumbar plexus block. The choice of regional anesthesia is a unanimous decision made by the surgeon, the anesthesiologist, and the patient based on a risk-benefit assessment. The choice of the regional block depends on patient cooperation, patient positing, operative structures, operative manipulation, tourniquet use and the impact of post-operative motor blockade on initiation of physical therapy. Regional anesthesia is safe but has an inherent risk of failure and a relatively low incidence of complications such as local anesthetic systemic toxicity (LAST), nerve injury, falls, hematoma, infection and allergic reactions. Ultrasound should be used for regional anesthesia procedures to improve the efficacy and minimize complications. LAST treatment guidelines and rescue medications (intralipid) should be readily available during the regional anesthesia administration.

Key Words: Orthopedic surgery; Regional anesthesia; Spinal; Epidural; Combined spinal epidural; Peripheral nerve blocks; Neuraxial blocks; Upper extremity; Lower extremity; Interscalene; Supraclavicular; Infraclavicular; Axillary; Femoral; Fascia iliaca; Popliteal; Sciatic; Saphenous; Adductor canal; Lumbar plexus; Brachial plexus; Ankle; iPACK; Complication; Local anesthetic systemic toxicity; Nerve injury; Block failure; Continuous nerve block catheters

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Core Tip: Understanding the fundamentals of regional anesthesia techniques for orthopedic surgery is essential for superior clinical outcomes and optimal patient safety. The choice of a regional technique requires a well-informed shared decision making process that encompass the anatomical coverage of the block, density of the block, duration of the block, patient positioning considerations, existing comorbidities, side effects, complications, advantages, disadvantages, positioning and impact on postoperative recovery. A risk-benefit analysis that achieves superior clinical outcomes can be only performed if the perioperative team has a profound understanding of the fundamentals of regional anesthesia administration.

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INTRODUCTION

Orthopedic surgery is one of the most rapidly growing surgical specialties in the world. A total of 22.3 million orthopedic surgical procedures were performed worldwide in 2017. The number of annual orthopedic procedures is forecasted to increase 4.9% annually, approaching 28.3 million surgeries by the year 2022[1]. Anesthetic techniques for orthopedic surgical procedures include general and regional anesthesia techniques. Over the past decades, regional anesthesia has become the anesthetic technique of choice for many orthopedic procedures. Regional anesthesia entails the injection of local anesthetic solution to interrupt signal transmission in peripheral nerves or spinal nerve roots that provide sensory and motor supply to operative structures.

The use of regional anesthesia for orthopedic procedures mitigates some of the complications associated with general anesthesia such as nausea, vomiting, airway trauma, hypoxia, respiratory depression, and the risk of pulmonary aspiration[2,3]. Advantages of regional anesthesia for orthopedic surgeries include superior postoperative pain control, reduction in opioid consumption, reduced opioid-associated side effects[4-12], shorter hospital stay[7,8,11-13], early initiation of physical therapy[7,11], reduced hospital readmission rate[14], higher patient satisfaction[4,11], faster recovery[15], reduced unanticipated admissions due to uncontrolled pain[16], improved intraoperative muscle relaxation, decreased intraoperative blood loss[11,12], and a reduction in postoperative urinary retention and ileus formation[8].

Although regional blocks are often administered by the anesthesiologist, it is important for the orthopedic surgeon to have an understanding of the relevant clinical aspects of the blocks in order to optimize patient safety, maximize perioperative efficiency, and improve clinical outcomes. In this article, we review the techniques of regional anesthesia used for orthopedic procedures.

TYPES OF REGIONAL ANESTHESIA

Regional anesthesia can be broadly divided into two categories: neuraxial anesthesia [spinal, epidural, combined spinal epidural (CSE)], and peripheral nerve blocks (upper and lower extremity blocks).

Neuraxial anesthesia

Neuraxial anesthesia (NA) is the process of placing a needle or a catheter between the vertebrae and injecting medications into the epidural (epidural anesthesia) or subarachnoid space (spinal anesthesia). The target of NA is the spinal nerve root. Medication injected neuraxially is primarily local anesthetics with adjuncts such as preservative free opioids. NA is commonly used for abdominal and lower extremity surgeries. The sensory level required for a specific surgery is determined by the extent

of surgical incision and surgical manipulation. Total hip arthroplasty (THA), open reduction and internal fixation of femur, and hip fractures require a sensory level of T10, whereas knee procedures require a sensory level of L1.

Spinal anesthesia is typically administered as a single injection, while epidural anesthesia is usually administered *via* an indwelling catheter for continuous infusion. CSE anesthesia is administered as a combination of both techniques. Anesthetic duration associated with the single shot approach used in the spinal technique is limited to the duration of action of the injected medication. The extent of spinal blockade (level) depends on the total dose of local anesthetic mixture, baricity of the injected solution, and patient position after the block. An epidural catheter allows for the continuous infusion of medications prolonging the duration of anesthesia. The spinal anesthesia needle is typically inserted at the level of L2-L3 interspace or below, to avoid trauma to the termination of the conus medullaris. The needle insertion point for epidural anesthesia depends on the extent of the dermatomes required to be anesthetized for the procedure. For orthopedic procedures, it is usually placed in the mid to low lumbar region. The extent of epidural blockade is determined by the volume of local anesthetic injected while density of the block is determined by the concentration of the local anesthetic. Compared to epidural anesthesia, spinal anesthesia produces a denser and more reliable block with lower incidence of block failure.

Peripheral nerve blocks

Peripheral nerve blocks (PNB) entails injecting a local anesthetic (LA) solution in proximity to a specific nerve or nerve bundle to produce a sensory and motor blockade of a specific region of the body. The LA blocks the transmission of painful impulse to the central nervous system. PNB can be used for surgical anesthesia or postoperative analgesia. It is commonly administered as a single shot, but a continuous infusion catheter can be placed to prolong the postoperative analgesic effect. PNB is commonly performed under ultrasound guidance to reduce the risks of intraneural and intravascular injection of LA, avoid peripheral nerve trauma, and to ensure proper delivery of the LA for a successful block. Upper extremity nerve blocks are performed at the level of the brachial plexus. Depending on the surgical site, various nerve blocks can be performed at different levels of the plexus. These blocks include interscalene block, supraclavicular block, infraclavicular block, and axillary block. Lower extremity nerve blocks include femoral nerve block, saphenous nerve block, Sciatic nerve block, iPACK (Infiltration between the Popliteral Artery and Capsule of the Knee) block, ankle block, and lumbar plexus block.

EVALUATING THE ORTHOPEDIC PATIENT FOR REGIONAL ANESTHESIA

Prior to considering a regional anesthetic for a patient, a thorough history and targeted physical examination should be performed to identify risk factors related to the nervous, pulmonary, cardiovascular, and hematologic systems that may affect the safety and efficacy of the nerve block. Certain patient factors may increase the potential for block failure, such as patient obesity[17]. Local skin infection, or systemic infection, may preclude a patient from receiving a regional anesthetic. The decision to proceed with a regional anesthesia block should be collectively agreed upon by the patient, the surgeon, and the anesthesiologist. For patients on anticoagulation / antiplatelet medications receiving superficial peripheral nerve blocks, the decision to proceed is largely dependent on a careful analysis of factors including site compressibility, vascularity, and consequences of bleeding, should it occur. This is often determined on a case-by-case basis.

The nervous system

A comprehensive neurological evaluation should be performed to assess for any pre-existing nervous system condition or nerve injury in the region of the block. Patients with multiple sclerosis may experience a flare up of symptoms with spinal anesthesia. Thus, epidural or general anesthesia may be preferable for these patients. Neuraxial anesthesia in patients with a history of extensive spine surgery with instrumentation may be technically difficult and may result in an inadequate anesthetic level. Scoliosis may increase the difficulty of placing a neuraxial anesthetic. Potential postoperative motor and sensory weakness after a regional anesthetic should be considered. For example, lower extremity motor weakness following a femoral nerve block may limit the patient's ability to participate in therapy post-operatively; as such, an alternative

motor-sparing technique should be considered[18].

The respiratory system

Patients who have a history of severe reactive or obstructive airway disease may benefit from the use of regional anesthesia to avoid airway manipulation and respiratory depression associated with general anesthesia. Pre-operative pulmonary function should be assessed, especially during the performance of upper extremity blocks that may anesthetize the phrenic nerve potentially causing respiratory distress. This may have significant impact on the respiratory function in patients with asthma, chronic obstructive pulmonary disease, or pre-existing diaphragmatic dysfunction [19]. An alternative regional anesthetic approach, such as the axillary block, may be performed in these patients[19].

The cardiovascular system

Patients with a history of severe cardiovascular disease often have an elevated risk of major complications after receiving general anesthesia. Regional anesthesia remains an excellent alternative for these patients and can be associated with lower rates of major cardiac complications[20]. It is important to consider cardiac contraindications for certain regional techniques. Neuraxial anesthesia has widely been contraindicated in the case of severe aortic stenosis and congestive heart failure, due to the sudden decrease in vascular tone and cardiac output. However, a carefully managed neuraxial anesthetic may be appropriate for some of these patients[21,22]. Patients with significant cardiac disease benefit from the gradual onset of epidural anesthesia allowing for careful and slow titration of LA rather than the rapid onset block induced by a single-shot spinal anesthetic.

The hematologic system

Patients who have a history of bleeding disorders or are currently receiving anticoagulants or antiplatelet medications are at an increased risk of bleeding complications after receiving a regional anesthetic. It is important to perform a thorough review of the patient's current medications prior to proceeding with a neuraxial anesthetic or peripheral nerve block. With the advent of novel anticoagulants, perioperative guidelines for regional anesthesia should consistently be adhered to[23].

Laboratory findings consistent with thrombocytopenia or coagulopathy may preclude the administration of regional anesthesia, due to the increased risk of bleeding. Excessive bleeding in neuraxial anesthesia may lead to a spinal hematoma and subsequent adverse neurological consequences. The American Society of Regional Anesthesia (ASRA) has published guidelines for the management of patients receiving antithrombotic or antiplatelet medications[23]. The ASRA guidelines are reviewed in Table 1. Patients who are on certain antiplatelet medications, such as low dose aspirin, may be candidates for peripheral nerve blockade or neuraxial anesthesia[23]. This decision is based on a risk-benefit assessment, taking into account considerations such as site compressibility and underlying bleeding disorders.

BLOCKS FOR UPPER EXTREMITY ORTHOPEDIC PROCEDURES

Understanding upper extremity peripheral nerve blockade requires a detailed knowledge of the brachial plexus anatomy. The muscular and the cutaneous nerve supply of the upper extremity derives mostly from the brachial plexus. The brachial plexus is comprised of ventral nerve roots (rami) of 5 spinal nerve (C5-T1) giving rise to trunks, divisions, cords and terminal branches. The nerve roots merge to form upper, middle and lower trunks. The 3 trunks split to form 6 divisions which merge to form 3 cords; lateral, posterior and medial cords. The nerves supplying most of the upper extremity are the terminal branches of the 3 cords. The cutaneous portion of the shoulder and upper arm is supplemented by nerves that are not part of the brachial plexus[24]. The superior aspect of the shoulder receives sensory innervation by the superficial cervical plexus (C3-C4) *via* the supraclavicular nerve. Seventy percent of the sensory innervation to the shoulder comes from the superior trunk *via* the suprascapular nerve with most of the contributions being from the C5 and C6 nerve roots [25]. The axilla is innervated by the second thoracic nerve root. The brachial plexus is blocked at four different levels: At the level of roots-trunks *via* the interscalene block, at the level of trunks-divisions *via* the supraclavicular block, at the level of cords *via* the infraclavicular block, and at the level of the terminal branches *via* the axillary block. A summary of upper extremity peripheral nerve blocks is included in Table 2.

Table 1 American Society of Regional Anesthesia guidelines for anticoagulant and antiplatelet drugs

Medication	Minimum time between last dose of medication and neuraxial injection or catheter placement	Minimum time after nerve/neuraxial cathether placement and administration of drug	Minimum time between last dose of drug and cathether removal	Minimum time between neuraxial injection or cathether removal and administration of drug
Anticoagulants for venous thromboembolism prophylaxis				
Enoxaparin (Lovenox); prophylaxis, once daily	12 h	≥ 12 h	≥ 12 h	4 h
Enoxaparin (Lovenox); prophylaxis, b.i.d.	12 h	Contraindicated while catheter in place		4 h
Heparin SQ; prophylaxis; low-dose, b.i.d. and t.i.d.	4-6 h	Immediately	4-6 h	Immediately
Heparin SQ; prophylaxis; higher-dose, b.i.d. and t.i.d.	12 h and assessment of coagulation status	Safety of indwelling catheters has not been established for doses > 5000 Units SQ or total daily dose > 15000 Units SQ. Risk/benefit assessment required		Immediately
Dalteparin (Fragmin); prophylaxis, once daily	12 h	≥ 12 h	12 h	4 h
Anticoagulants at therapeutic doses				
Heparin IV; full Dose	4-6 h and normal coagulation status	1 h, with close monitoring	4-6 h and normal coagulation status	1 h
Heparin SQ; therapeutic dose	24 h and assessment of coagulation status	Contraindicated while catheter in place		Immediately
Enoxaparin (Lovenox); therapeutic dose	24 h, consider checking anti-factor Xa level	Contraindicated while catheter in place		4 h
Apixaban (Eliquis)	72 h	Contraindicated while catheter in place		6 h
Rivaroxaban (Xarelto)	72 h	Contraindicated while catheter in place		6 h
Warfarin (Coumadin)	5 d and normal INR	Variable instructions regarding management of catheter		Immediately
Anti-platelet medications				
NSAID's	No restrictions, may increase risk of bleeding			
Aspirin	No restrictions, may increase risk of bleeding			
Plavix	5-7 d	24 h postoperatively; catheter may be maintained for 1-2 d due to delayed antiplatelet effect		Immediately if no loading dose given
Ticlodipine (Ticlid)	10 days	24 h postoperatively; catheter may be maintained for 1-2 d due to delayed antiplatelet effect		Immediately if no loading dose given
Ticagrelor (Brillinta)	5-7 d	Contraindicated while catheter in place		Immediately if no loading dose given

NSAID: Non-steroidal anti-inflammatory drug.

Table 2 Summary of upper extremity peripheral nerve blocks

Block	Clinical application	Nerves blocked	Anatomical landmarks	Advantages	Disadvantages	Complications
Interscalene nerve block	Surgeries involving the shoulder, proximal aspect of humerus and the distal aspect of the clavicle	(1) Brachial plexus:C5 to C7; and (2) Cervical plexus: Supraclavicular nerve (C3 and C4)	LA injected between anterior and middle scalene muscles lateral to carotid artery and internal jugular vein	(1) Easy to perform; and (2) Comfortable for the patient	(1) Hemidiaphragmatic paralysis leading to respiratory compromise in patients with severe COPD; and (2) Not sufficient for elbow, forearm or hand surgeries	(1) Phrenic nerve palsy (100%); (2) Horner syndrome; and (3) Hoarseness
Supraclavicular nerve block	Surgery of the arm, elbow, forearm and hand. Extension into the interscalene area can cover shoulder procedures	C5-T1	LA injected above the clavicle between anterior and middle scalene muscles at the level of the first rib, where the subclavian artery crosses over it	(1) Fast onset; (2) Easier to perform; and (3) Comfortable for the patient	Relatively higher incidence of pneumothorax	(1) Pneumothorax; (2) Phrenic nerve palsy; and (3) Hoarseness
Infraclavicular nerve block	Surgery of the arm, elbow, forearm and hand	C5-T1	LA injected around the axillary artery below the clavicle, medial to coracoid process	Good choice for catheter placement	(1) Deeper block to perform; and (2) Greater discomfort during block placement	Pneumothorax (relatively low incidence)
Axillary nerve block	Surgery of the elbow, forearm and hand	Median nerve, ulnar nerve, radial nerve, and musculocutaneous nerve	LA injected around the axillary artery at the medial aspect of proximal arm	(1) Easy to perform; and (2) Low complication rate	(1) Often spares the musculocutaneous nerve; and (2) Requires arm abduction	(1) Hematoma formation; and (2) Intravascular injection

COPD: Chronic obstructive pulmonary disease.

Interscalene block

The interscalene block is performed at the level of roots-trunks of the brachial plexus. The interscalene block results in anesthesia of C5 through C8, and also blocks the supraclavicular branches of the cervical plexus C3 and C4, which supplies the skin over the acromion and the clavicle. The inferior trunk (C8-T1) is usually spared; an effect referred to as ulnar sparing. Thus, if this block is performed for procedures at or distal to the elbow, an additional ulnar nerve block is required. The coverage of this nerve block makes it effective for procedures involving the shoulder, proximal aspect of humerus and the distal aspect of the clavicle[25].

The interscalene block targets the brachial plexus between the anterior and middle scalene muscle, lateral to the carotid artery and internal jugular vein, directly above the clavicle. Complications associated with the interscalene block include phrenic nerve blockade with an incidence near 100 percent[26,27], sympathetic chain blockade causing Horner's syndrome, inadvertent injection in the vertebral artery, recurrent laryngeal nerve blockade causing hoarseness, and peripheral neuropathy[28]. Rare complications include pneumothorax, epidural injection, intrathecal injection leading to total spinal anesthesia, spinal cord damage, and dorsal scapular or long thoracic nerve injury. Due to the high incidence of phrenic nerve blockade, the interscalene

block is contraindicated in patients with severe pulmonary disease due to elevated risk of respiratory compromise. In an otherwise healthy individual, respiratory compromise is uncommon and the block is well-tolerated.

Supraclavicular block

The supraclavicular block targets the brachial plexus superior to the clavicle at the level of the trunks and divisions. It involves the C5-C7 distribution from the more superficial and lateral branches which supply the shoulder, lateral aspect of arm, and forearm, as well as the deeper and more medial contingent branches of C8 and T1 which supply the hand and medial aspect of forearm. Adequate spread of local anesthetic in both areas is necessary for successful nerve block of the arm and hand [25]. The supraclavicular block involves injection of local anesthetic between anterior and middle scalene muscles at the level of the first rib, where the subclavian artery crosses posterior to the midpoint of the clavicle.

The supraclavicular block results in anesthesia of the upper limb that includes the shoulder because all the trunks and divisions of the brachial plexus are tightly packed and can be anesthetized at this location. Due to the density and extent of the supraclavicular block, it is colloquially known as the "spinal of the arm". Indications of this nerve block include surgery of the hand, forearm, elbow, and arm. The proximal medial side of upper arm is spared since that is supplied by the intercostobrachial nerve (T2), which can be anesthetized separately.

Complications associated with supraclavicular block include pneumothorax (0.6% to 6.1%) as the apical pleural is in close proximity to the nerve block. The prevalence of pneumothorax can reach 0% with proper ultrasound usage[29]. Other complications of the supraclavicular block include phrenic nerve blockade resulting in hemidiaghragmatic paresis (17% to 50%) and recurrent laryngeal nerve blockade leading to hoarseness in (22 %)[30,31].

Infraclavicular block

The infraclavicular block targets the brachial plexus at level of the cords before the branching of the axillary and the musculocutaneous nerves. It results in anesthesia of the upper limb below the shoulder, including the arm, elbow, forearm and hand, sparing the medial proximal upper arm, which is supplied by intercostobrachial nerve (T2)[25].

The infraclavicular block involves the injection of local anesthetic surrounding the axillary artery below the clavicle. Under ultrasound guidance, the local anesthetic is injected surrounding the axillary artery in a U-shaped pattern covering the all three cords of the brachial plexus. The infraclavicular block has a low prevalence of pneumothorax at 0.7%[32].

Axillary block

The axillary block is performed at the level of the branches of the brachial plexus. It anesthetizes the median nerve, the ulnar nerve, the radial nerve, and the musculocutaneous nerve, resulting in anesthesia of the upper limb from mid-arm extending distally to the elbow, forearm, and hand. It is to note that this block does not block the axillary nerve; rather the name of this regional technique is derived from the approach. In order to perform this block, the patient is positioned supine with the arm abducted to 90 degrees. Under ultrasound guidance the median, ulnar and radial nerve are identified surrounding the axillary artery. The nerve bundles are surrounded by three muscles-the biceps is located anterior and superficial, the coracobrachialis is located anterior and deep and the conjoined tendon of the teres major and latissimus dorsi is located medial and posterior. The musculocutaneous nerve is located between the fascial layers of coracobrachialis and biceps muscles. If required, the medial side of upper arm can be blocked separately. The axillary nerve block carries the risk of hematoma formation and intravascular injection, due to its close proximity to the axillary artery and vein. The need to abduct the arm to perform this block may be difficult with certain upper extremity injuries. In such case, other upper extremity blocks such as supraclavicular block can be utilized.

BLOCKS FOR LOWER EXTREMITY ORTHOPEDIC PROCEDURES

Neuraxial blocks for lower extremity procedures

Neruraxial anesthesia results in the blockade of sympathetic, motor, and sensory

nerves, which leads to unopposed parasympathetic tone. Major physiologic effects of neuraxial anesthesia include hypotension, bradycardia, hypothermia, nausea and vomiting, and high neuraxial blockade leading to respiratory depression[33,34]. There are several benefits to using neuraxial anesthesia for lower extremity orthopedic surgery that include reduced incidence of deep venous thrombosis in patients undergoing hip and knee replacement surgery, decreased intraoperative blood loss and transfusion requirements, and improved postoperative cognition[2,3,35,36] .Decreased intraoperative blood loss is likely due to a reduction in venous pressure from the sympathetic blockade. Multiple studies have showed that neuraxial anesthesia reduces the risk of postoperative deep venous thrombosis by at least 50% [36].

Spinal anesthesia

Spinal anesthesia is used for orthopedic procedures including total knee arthroplasty (TKA) and THA. Spinal anesthesia is usually performed with the patient in the sitting position while being continuously monitored. Also, it can be performed in the lateral decubitus position when the patient's condition does not permit sitting.

The complications and adverse effects associated with spinal anesthesia include: high spinal anesthesia, inadequate or failed spinal anesthesia, nerve injury, urinary retention, postdural puncture headache, transient neurologic symptoms, infection, and spinal-epidural hematoma

Epidural anesthesia

Epidural anesthesia and analgesia can be utilized as an effective technique to either supplement general anesthesia or as the primary anesthetic approach for lower extremity orthopedic surgical procedures. Moreover, epidural anesthesia may be supplemented with peripheral nerve blockade to decrease postoperative pain. Common indications for epidural anesthesia in orthopedic surgery include THA, TKA, foot/ankle surgery, and major knee surgery.

Epidural anesthesia is better suited for elderly patients with cardiac comorbidities that limit their ability to tolerate the sudden sympathetic blockade and the resulting hypotension associated with spinal anesthesia[37,38]. An epidural catheter may be incrementally dosed to slowly obtain an adequate surgical anesthetic level, thereby decreasing major rapid fluctuations in blood pressure[39]. Additionally, the epidural catheter can be continuously dosed during the surgery and may remain in place postoperatively for analgesic purposes[39].

With the advent of peripheral nerve blockade, the role of epidural analgesia strictly for postoperative pain has been decreasing in use. When comparing epidural analgesia with peripheral nerve blockade in patients who underwent TKA, a meta-analysis showed equivalent pain scores and morphine consumption between both groups up to 48 h postoperatively (Fowler, SJ 2008)[40]. Additionally, the use of epidural analgesia was associated with a higher incidence of urinary retention and hypotension, suggesting that peripheral nerve blockade provides equivalent postoperative analgesia with a favorable side-effect profile[40,41].

Serious complications of epidural anesthesia are extremely rare (0.03%), but can be potentially devastating[42]. These complications include epidural hematomas, epidural abscesses, nerve damage, infection, and cardiovascular instability[42]. Absolute contraindications to epidural anesthesia include patient refusal, local infection at puncture site, and severe coagulation disorders. Relative contraindications include sepsis, elevated intracranial pressure, anticoagulant use, bleeding disorders, fever, aortic stenosis, pre-existing neurologic injury, prior spine surgery, and placement in anesthetized individuals[43].

COMBINED SPINAL-EPIDURAL

The CSE anesthetic is a technique which combines many of the benefits of epidural and spinal anesthetics in a single approach. It may be utilized in patients undergoing lower extremity orthopedic procedures who require surgical anesthesia with the added ability to add epidural anesthetics for intraoperative or postoperative uses[44]. As with alternative neuraxial techniques, the CSE may be utilized for patients undergoing hip and knee arthroplasty, femur fractures, major knee surgery, and foot/ankle surgery[45].

This technique is performed by injecting an anesthetic solution in the subarachnoid space (coaxial needle placement *via* epidural needle), followed by placing an

indwelling epidural catheter. The CSE technique provides the rapid onset of spinal anesthesia with the prolonged and flexible duration of an epidural catheter[46]. With the CSE technique, surgical anesthesia is achieved rapidly, saving 15-20 min compared to epidural anesthesia[44]. The epidural catheter may be left in place to supplement inadequate spinal anesthesia, prolong surgical anesthesia, and to provide postoperative pain control[44].

The CSE can be used in high-risk patients, in order to facilitate careful titration of epidural anesthetics after surgical anesthesia is initiated with a reduced dose of intrathecal local anesthetic[44]. This can prevent sudden decreases in systemic blood pressure.

Caution should be exercised when intrathecal or epidural long-acting opioids are administered, due to the risk of delayed respiratory depression[47]. The success rate of CSE is higher than has been demonstrated with epidural anesthesia alone[44]. There is a theoretical risk that the epidural catheter may migrate or is non-functioning, which will only be discovered once the spinal blockade begins to diminish, thereby necessitating conversation to general anesthesia[44]. Overall, the CSE remains an excellent anesthetic and analgesic technique in patients undergoing lower extremity orthopedic surgery. While the combined spinal-epidural approach has several benefits over spinal or epidural anesthesia, there is a risk that the epidural may become dislodged during patient positioning. This may not be detected until later in the case, as the spinal anesthetic will provide reliable anesthesia for the first portion of the case, and may mask a poorly-functioning epidural. This may necessitate the administration of sedatives or the conversion to general anesthesia depending on the surgical case. Patients should be considered fall-risks until their neuraxial anesthetic has completely worn off. Moreover, return of motor function often occurs prior to the recovery of functional balance. As such, the first ambulation following neuraxial anesthesia should be performed with caution.

LOWER EXTREMITY PERIPHERAL NERVE BLOCKS

Peripheral nerve blocks may be utilized either as the primary anesthetic modality or as adjuncts to general or neuraxial anesthesia. Due to anatomical limitations in successfully achieving adequate surgical anesthesia through peripheral nerve blockade, lower extremity nerve blocks are typically utilized as an adjunct to general or neuraxial anesthesia. Advances in regional anesthesia have allowed for increased applications of peripheral nerve blocks while minimizing potential side effects such as undesirable motor blockade[16]. A summary of lower extremity peripheral nerve blocks is included in in Table 3.

Femoral nerve block

The femoral nerve block is indicated for lower extremity procedures involving the anterior aspect of the thigh and medial aspect of the leg below the knee. Common uses of the femoral nerve block include providing analgesia for TKA, anterior cruciate ligament reconstruction, quadriceps tendon repair, surgery to the foot, and surgery to the ankle. The femoral nerve block may be combined with other regional anesthetic techniques, such as the sciatic nerve block, to expand the distribution of the anesthetic block, particularly below the knee[16].

The femoral nerve block has been reported to effectively reduce pain and assist with rehabilitation after TKA[48,49]. Patients who received femoral nerve block for knee surgery had fewer unplanned hospital admissions during outpatient surgery [50]. At one major academic center, patients who underwent anterior cruciate ligament (ACL) repair with the assistance of regional anesthesia for postoperative pain control were able to bypass the PACU 82% of the time and were able to avoid hospital admission 96% of the time; both of these values translated into significant hospital cost savings [51].

Absolute contraindications to femoral nerve block include patient refusal and allergy to local anesthetics. Relative contraindications to femoral nerve block include concurrent anticoagulation use, coagulopathy, previous ilioinguinal surgery, local infection, preexisting femoral neuropathy, or large inguinal lymph nodes[16].

Anatomically, the femoral nerve is the largest branch of the lumbar plexus and arises from the ventral rami of the L2-L4 spinal nerve roots[16]. It enters the femoral triangle directly inferior to the inguinal ligament and lies lateral to the femoral artery [52]. The femoral nerve splits distally to the anterior and posterior divisions. The anterior division, gives rise to the medial femoral cutaneous nerve while the posterior

Table 3 Summary of lower extremity peripheral nerve blocks

Block	Clinical application	Nerves blocked	Anatomical landmarks	Advantages	Disadvantages	Complications
Femoral nerve(Femoral nerve block)	Surgeries involving anterior aspect of the thigh and medial aspect of the leg below the knee	Femoral nerve	Inguinal crease; located lateral to femoral artery	(1) Broad coverage; and (2) Easily identifiable landmarks	Causes quadriceps weakness which may lead to falls	(1) LE weakness and falls; (2) Bleeding; (3) Infection; and (4) Nerve damage
Femoral nerve (Fascia Iliaca block)	Surgeries involving anterior aspect of the thigh and medial aspect of the leg below the knee	(1) Femoral nerve; and (2) Lateral femoral cutaneous nerve of the thigh	Inguinal crease, LA injected under fascia iliaca	(1) Easily identifiable landmarks; and (2) Assist in optimal patient positioning for spinal anesthesia	(1) Causes quadriceps weakness which may lead to falls; and (2) Large volume of local anesthetic required	(1) LE weakness and falls; (2) Bleeding; (3) Infection; and (4) Nerve damage
Sciatic nerve (Anterior, transgluteal, and subgluteal approaches)	Surgeries involving foot, ankle, and posterior knee	Sciatic nerve	Variable, based on injection site	(1) Broad lower extremity coverage; and (2) Easilyidentifiable landmarks	Motor blockade	(1) Bleeding; (2) Infection; and (3) Nerve damage, persistent foot drop and heel ulcers
Sciatic nerve (Popliteal Block)	Surgeries involving foot, ankle, posterior knee	Sciatic nerve	Popliteal fossa, located cephalad to the knee near popliteal artery	(1) Broad lower extremity coverage; and (2) Easilyidentifiable landmarks	Motor blockade	(1) Bleeding; (2) Infection; and (3) Nerve damage, persistent foot drop and heel ulcers
Saphenous nerve (Femoral triangle, medial femoral condyle, tibial tuberosity approaches)	Surgeries involving medial aspect of knee, foot, and ankle	Saphenous nerve	Variable, based on injection site	Motor-sparing	Does not provide anesthesia and analgesia to the posterior capsule of knee	(1) Bleeding; (2) Infection; and (3) Nerve damage - Potential lower extremity weakness at high doses
Saphenous nerve (Adductor Canal block)	Surgeries involving medial aspect of knee, foot, and ankle	(1) Saphenous nerve; and (2) Nerve to vastus medialis (branch of femoral nerve)	Medial thigh, located deep to the sartorius muscle, adjacent to the femoral artery and vein.	Motor-sparing	(1) Does not provide anesthesia and analgesia to the posterior capsule of knee; and (2) Compared to femoral nerve block, it is less efficacious for analgesia after ACL reconstruction surgery	(1) Bleeding; (2) Infection; (3) Nerve damage; and (4) Potential lower extremity weakness at high doses
iPACK	Surgeries involving the posterior knee capsule	Articular branches of the tibial, common peroneal, and obturator nerve to the posterior aspect of the knee	Popliteal crease, located cephalad to femoral condyles	Motor-sparing, increased posterior knee coverage	Coverage only to posterior knee; useful as an adjunct to alternative blocks	Inadvertent motor block due to local anesthetic spread to sciatic nerve branches
Ankle	Foot surgery	Saphenous, sural, posterior tibial, superficial peroneal, and deep peroneal nerves	Ankle and foot bony landmarks	Injection based on surface landmarks, no requirement for ultrasound	Limited efficacy for surgery proximal to the foot, potential higher failure rate due to blind technique	(1) Bleeding; (2) Infection; and (3) Nerve damage
Lumbar plexus	Hip surgery	Lumbar plexus, providing blockade to femoral, obturator, and lateral femoral cutaneous nerves	Lateral to lumbar spine, located cephalad to iliac crest	Coverage of multiple nerves with a single block	High potential for complications and block failure, technically challenging block to perform	(1) Bleeding and hematoma; (2) Infection; (3) Nerve damage; (4) Epidural spread resulting in high neuraxial anesthesia; (5) Hypotension, and (6) LAST

ACL: anterior cruciate ligament; LAST: local anesthetic systemic toxicity.

division gives rise to the saphenous nerve.

The femoral nerve provides sensory innervation to the anterior thigh and medial aspects of the calf, foot, and ankle[16]. The femoral nerve additionally provides motor innervation to muscles of the lower extremity, including the quadriceps, sartorius, and pectineus muscles. As such, the femoral nerve block will cause weakness of the quadriceps muscles[53-55]. This may result in decreased patient mobility and may potentially increase the risk of falls. Thus, patients should not be ambulating without assistance after a femoral nerve block[18].

The quadriceps weakness associated with the femoral nerve block has decreased its clinical use for providing post-operative analgesia for patients undergoing TKR. Motor-sparing regional anesthesia techniques are often favored for these patients, such as blocks targeting the saphenous nerve which provides sensory innervation to the anterior and medial aspects of the knee[56,57].Weakness induced by a femoral nerve block may be assessed by manual muscle testing[58]. Recommendations to minimize post-operative falls in patients receiving this block include utilizing ambulation-assistive devices, patient and staff education, and considering post-operative immobilization until muscle strength is regained[16]. Data supports the use of femoral nerve block over adductor canal block for ACL reconstruction, despite the increased risk of quadriceps weakness[59,60].

The femoral nerve block is often well-tolerated by patients, as the needle only traverses through the skin and adipose tissue of the inguinal region. Complications associated with the femoral nerve block are rare, and include nerve injury, intravascular injection, and quadriceps weakness[61]. The femoral nerve block is performed by positioning the patient in a supine position with the targeted limb placed slightly abducted and externally rotated. The femoral nerve is identified lateral to the femoral artery. The femoral nerve is located deep to the fascia lata and fascia iliacia, and superficial to the iliopsoas muscles.

Fascia iliaca block

The fascia iliaca block is a regional anesthetic technique which provides anesthesia to the femoral nerve and lateral femoral cutaneous nerve[62]. It is used in patients who have sustained traumatic hip fractures or for analgesia following hip surgery. This block may be performed pre-operatively while the patient is awaiting their surgery, and has been shown to provide rapid analgesic benefit[63]. Moreover, patients reported improvements with passive hip flexion, which allowed them to sit up in bed pre-operatively[64]. Faster time to fascia iliaca block has been shown to reduce opioid use, pain, and hospital length-of-stay in patients with hip fractures[65]. Pain relief after fascia iliaca block has been shown to be superior to systemic intravenous opioid therapy and this block can be performed upon presentation to the emergency department[66]. The fascia iliaca block may also assist with optimally positioning these patients for spinal anesthetic placement for surgical femur fracture repair[67,68].

The fascia iliaca block is performed by injecting a relatively large volume of local anesthetic (20-30 cc) under the fascia iliaca above the level of the inguinal crease. The goal of this block is to spread local anesthetic laterally to the iliac spine and medially to the femoral nerve, and is typically performed under ultrasound-guidance[62]. The femoral nerve and lateral femoral cutaneous nerve lie deep to the fascia iliaca, and as such, are blocked during this injection[69-71]. The femoral nerve component provides blockade to the anterior and medial thigh, and the lateral femoral cutaneous nerve component provides anesthesia to the anterolateral thigh.

Saphenous nerve block

The saphenous nerve block is indicated for various lower extremity orthopedic procedures involving the knee, foot, or ankle. It may be used as a sole nerve block, or in conjunction with the sciatic nerve block to provide increased anatomical coverage for surgery to the medial aspect of the foot and ankle[16]. The saphenous nerve block results in sensory anesthesia of the medial aspect of the leg down to the foot and ankle.

There are various approaches to performing a block of the saphenous nerve. With the use of ultrasonography, the saphenous nerve block is often performed subsartorially at the adductor canal; hence, this block is referred to as the "adductor canal block". Alternative locations to perform a saphenous nerve block include the femoral triangle, the medial femoral condyle, or the level of the tibial tuberosity.

Adductor canal block

The adductor canal block provides effective analgesia for surgery to the knee and medial aspect of the lower extremity. It may be used as part of a multimodal analgesic

pathway for patients undergoing TKA to facilitate earlier ambulation, improve patient comfort, and enhance patient satisfaction[72]. Over half of the patient's undergoing TKA will likely experience moderate-to-severe post-operative pain which can subsequently result in increased length-of-stay, immobility-related complications, and decreased patient satisfaction[73]. As a result, safe and effective regional anesthetic techniques are of paramount importance to these patients[73,74].

While the femoral nerve block can provide effective analgesia for patients undergoing total knee arthroplasty, it can be associated with quadriceps muscle weakness which may increase the risk of falls[18]. As a result, the adductor canal block is often a favorable alternative used for post-operative analgesia for patients undergoing TKR[56,57]. Compared to the femoral nerve block, the adductor canal block results in significant quadriceps motor sparing and significantly preserved balance while still maintaining a similar degree of postoperative pain relief[53-55]. This allows for effective pain control with the ability to promote early mobilization and ambulation post-operatively[75].

The adductor canal block has been evaluated for its potential analgesic use in patients undergoing ACL reconstruction. The adductor canal block has theoretical advantages for this patient population, including preserved quadriceps strength fulfilling the requirements of short hospital stay and immediate mobilization for outpatient ACL reconstruction. Currently, the data has been inconsistent in supporting the routine use of the adductor canal block over the femoral nerve block for ACL reconstruction with regards to analgesic equivalence; as such, the femoral nerve block for ACL reconstruction remains an appropriate option[60,76-78].

The adductor canal block can be combined with various other regional techniques to increase the overall distribution of analgesia[16]. A limitation of the adductor canal block as a sole nerve block is that it will only produce anesthesia to the anteromedial side of the knee[73]. Patients undergoing knee surgery report improved pain relief by combining the adductor canal block with periarticular injections of local anesthetic by the surgeon[79-81]. The addition of the iPACK block may offer patients improved pain relief and earlier ambulation by providing anesthesia to the posterior capsule of knee [82].

Complications from an adductor canal block are rare and potentially include bleeding, infection, and nerve damage[83]. It is important to note that while the saphenous nerve block is a sensory nerve block, an injection of a large volume of local anesthetic into the adductor canal may result in a partial motor block of the vastus medialis due to a blockade of the femoral nerve's branch to the vastus medialis[84]. As a result, caution must be exercised with patients ambulating without support after receiving an adductor canal block.

The adductor canal block has widely become the standard of care for analgesia for total knee arthroplasty. The downside to the adductor canal block is that often times direct sonographic visualization of the saphenous nerve is not achieved; rather, local anesthetic is deposited within the anatomic region of the adductor canal. It is likely that motor-sparing blocks will increase in their use for a wide array of lower extremity surgical procedures, especially in the ambulatory surgical setting.

iPACK block

The iPACK block has been increasingly utilized in TKA to provide analgesia to the posterior compartment of the knee without compromising lower extremity strength. It targets the medial and lateral superior genicular nerves to provide adequate posterior knee capsule analgesia[85]. The combination of the iPACK block with the ACB provides a larger distribution of anesthetic coverage, by ensuring both anteromedial and posterior joint coverage[73,86].

Recent data indicates the iPACK block, used in conjunction with the adductor canal block and periarticular injection for TKA, substantially decreased pain at rest and on ambulation postoperatively[82,87]. This resulted in earlier hospital discharge, decreased opioid requirements, and earlier ambulation[82].

To perform iPACK block the needle is inserted in the medial thigh under ultrasound guidance. Typically, a total volume of 15-20 cc of a local anesthetic solution is utilized for this block. During the performance of this block, it is important to avoid inadvertent local anesthetic spread to the tibial or common peroneal nerve, which may result in undesirable motor weakness[88].

The IPACK block can be quite uncomfortable for awake patients to undergo, given the needle positioning and needle depth. As such, in certain patients, this block may be performed after the patient has been sedated in order to facilitate proper needle placement. It is likely that in the future the IPACK block will be utilized in combination with the adductor canal block as the standard of care for providing

"circumferential" analgesic coverage for knee surgery. That being said, caution should be exercised to the total volume of local anesthetic utilized in order to avoid inadvertent local anesthetic systemic toxicity.

Sciatic nerve block

The sciatic nerve block is indicated for lower extremity orthopedic procedures involving the foot, ankle, and posterior knee. The sciatic nerve block may be used as a singular block, as in the case of an achilles tendon repair, or in conjunction with the femoral or saphenous nerve block to obtain anesthetic coverage for knee surgery or foot/ankle surgery, respectively[16]. The sciatic nerve is formed from the anterior rami of L4 to S3 and is the largest nerve in the body[89]. The terminal branches of the sciatic nerve are the tibial nerve and common peroneal nerve. The sciatic nerve block provides anesthesia to the posterior aspect of the knee, hamstrings, and the entire limb below the knee (motor and sensory innervation), with the exception of medial lower extremity and foot, which is supplied by the saphenous nerve.

The sciatic nerve may be blocked in several locations, depending upon the region of the limb requiring anesthetic blockade. The anterior approach of the sciatic nerve block is performed on the proximal medial thigh. The transgluteal approach is performed on the posterior buttock, between the ischial tuberosity and greater trochanter. The subgluteal approach is performed posteriorly on the gluteal crease. Commonly, the sciatic nerve block is performed at the level of the popliteal fossa, known as the "popliteal block".

Popliteal block

The popliteal block is performed in conjunction with the saphenous nerve block for surgery involving the foot and ankle[16]. The popliteal fossa is the region where the sciatic nerve divides into its two major terminal branches, the tibial nerve and common peroneal nerve[89]. The popliteal block is often performed proximal to the bifurcation of the tibial and common peroneal nerves; however, a recent study suggests that a popliteal block distal to the sciatic nerve bifurcation may result in 30% faster onset of the blockade while still achieving blockade of the terminal branches[90]. Additionally, injection of local anesthetic distal to the bifurcation of the sciatic nerve provides superior sensory block of the lower extremity[91].

Potential complications from the sciatic nerve block are rare, and include nerve injury, bleeding, and intravascular injection[92]. Nerve injury may be manifested as a persistent foot drop with potential pressure necrosis[16].

The popliteal sciatic nerve block is performed with the patient in the supine position with the affected limb placed in an elevated position with the assistance of blankets or towels for positioning. The knee joint is slightly flexed, and the ultrasound transducer is placed on the posterior aspect of the knee within the popliteal crease. Caution should be exercised to avoid entering the nerve bundle or inadvertently injecting the popliteal artery.

Ankle block

The ankle block can be performed to provide anesthesia to the foot. All types of foot surgery can be performed with the ankle block, including forefoot reconstruction, bunionectomy, osteotomy, and amputation. The ankle block is effective for providing pain relief for foot fractures, soft tissue injuries, and gout. The ankle block has several benefits over alternative regional techniques. It is performed through anatomic landmarks, and does not require ultrasonography to perform; however, data suggests that the addition of ultrasound-guidance may improve the clinical efficacy of the ankle block[93].The ankle block is motor-sparing; however, the ankle block may result in mild impairment to ambulation.

The ankle block is performed by blocking the five peripheral nerves at the level of the ankle. The medial aspect of the foot is innervated by the saphenous nerve, which is a branch of the femoral nerve. The remainder of the foot is innervated by branches of the sciatic nerve—the sural nerve, the posterior tibial nerve, the superficial peroneal nerve, and the deep peroneal nerve[94].

Compared to the ankle block for forefoot surgery, the popliteal block provided improved analgesia and decreased opioid requirements in the immediate post-operative period[95].

Contraindications to the ankle block include local infection, burn, soft tissue injury, scarring, or distorted anatomy in the region of the block. Potential complications of the ankle block are rare, and include bleeding, infection, and nerve damage[96].

The ankle block is often underutilized as a technique to provide analgesia to the midfoot and forefoot. As it does not require ultrasound to perform, it can be reliably performed in settings which may not be equipped with an ultrasound. Moreover, it may be performed upon presentation to the emergency room for providing pain relief for foot fractures or soft tissue injury, as part of a multimodal analgesic plan. The ankle block may also be performed by the surgeon intraoperatively for post-operative analgesia.

Lumbar plexus block

The lumbar plexus block is indicated for lower extremity procedures and has been shown to be useful for hip surgery, including arthroplasty and fracture repair. By performing this regional anesthetic, blockade of the femoral, obturator, and lateral femoral cutaneous nerve can be achieved. Various techniques have been described for this block. The ultrasound-guided shamrock technique, first described in 2013, provides sufficient sonographic visibility of the target plexus[97]. In this technique, an ultrasound-probe is placed in an axial orientation cephalad to the iliac crest approximately along the posterior axillary line. The lumbar plexus block can be combined with the sacral plexus block to provide effective anesthesia for hip surgery; this provides for an alternative to spinal anesthesia which may cause prolonged periods of hypotension[98].

With the advent of alternative regional anesthesia techniques, the lumbar plexus block has seen a decrease in clinical use. These peripheral blocks are often performed with greater ease and reliability by most anesthesiologists, and are better tolerated by patients. Moreover, the potential for serious complications is higher for the lumbar plexus block when compared to alternative peripheral nerve blocks. The fascia iliaca block can be utilized as an alternative for analgesia after hip surgery and has been shown to provide non-inferior pain relief[99,100]. In Addition, the fascia iliaca block is often easier to perform from a technical perspective, which may lead to its increased use[99]. Studies have shown that peripheral nerve blocks for patients who have sustained a traumatic hip fracture can reduce pain on movement and decrease the risk of developing pneumonia[101]. As such, it is important to perform a technique, such as the fascia iliaca block, which can be mastered by most clinicians without advanced specialized regional anesthesia training. However, because of the decreasing utility of the lumbar plexus block, residency training programs often do not emphasize the teaching of this block.

The lumbar plexus block has the potential for causing serious complications, including inadvertent epidural spread resulting in high neuraxial anesthesia, hypotension, local anesthetic toxicity, bleeding, hematoma formation, infection, and nerve damage. In order to minimize these complications, large volumes of local anesthetic should be avoided in patients with multiple comorbidities. During performance of this block, patients should be continuously monitored for unilateral sympathectomy or hypotension due to epidural spread[102]. Deformation or degeneration of spinal anatomy and musculature may result in poor ultrasound image quality, potentially leading to failed blockade[103].

COMPLICATIONS OF REGIONAL ANESTHESIA

Local anesthetic systemic toxicity

Local anesthetic systemic toxicity (LAST), is a potentially life-threatening complication that may result from unintentional intravascular injection of local anesthetic or slow absorption of an inappropriately high dose of local anesthetic injected perineurally. The ASRA publishes practice advisories for the management of patients who experience LAST[104].

The clinical presentation and speed of onset of LAST are extremely variable. Signs and symptoms of toxicity may immediately become apparent; however, they may take as long as 30 min or more to occur[105]. Symptoms typically present as a continuum; neurologic toxicity occurs at lower concentrations followed by cardiac toxicity at higher concentrations.

Early clinical signs of neurotoxicity are subjective, and include dizziness, drowsiness, perioral numbness, and tinnitus[105]. These signs may be missed if the patient is sedated or under general anesthesia. Following this, with increasing plasma concentrations, muscle twitching and tremors are observed. As blood and brain levels of local anesthetic continue to increase, generalized tonic-clonic seizures occur. Finally, generalized central nervous system (CNS) depression occurs leading to a reduced level

of consciousness and coma[106].

Cardiotoxicity follows a two-step pathway[107]. In early cardiotoxicity, activation of the sympathetic nervous system results in hypertension and tachycardia. Following this, myocardial depression occurs leading to ventricular arrhythmias, conduction delays, contractile dysfunction, and eventual cardiovascular collapse. Inhibition of myocardial voltage-dependent sodium channels by local anesthetics may lead to a noticeable increase in the PR interval and QRS duration, as well as the presence of subtle T wave abnormalities[107].

Treatment of LAST begins with the recognition of the early signs and symptoms of toxicity, followed by immediate intervention including early administration of intravenous Intralipid emulsion. Intravenous Intralipid emulsion has been postulated to function by acting as a lipid sink to extract lipophilic local anesthetic from plasma and tissues[108]. It additionally functions directly on myocardial tissue by improving cardiac output[109]. Intralipid should be administered as a weight-dependent bolus followed immediately by an infusion[106]. Boluses may be repeated, and the infusion rate may be doubled if the patient continues to remain unstable[104]. The infusion should be continued for at least 15 min after obtaining hemodynamic stability[104].

CNS instability such as seizures should be appropriately managed with intravenous benzodiazepine administration or low doses of propofol[104]. Cardiovascular collapse should be managed with careful titration of intravenous epinephrine. Individual boluses of less than 1 mcg/kg should be administered to avoid ventricular fibrillation or tachycardia[104]. ACLS dosing of epinephrine (1 mg) may result in poor long-term outcomes due to the increased risk of arrhythmogenicity. A summary of the clinical presentation and treatment of LAST is presented in Table 4.

Risk factors for LAST include extremes of age, low muscle mass, female gender, and patients with cardiac, liver, and metabolic comorbidities[110]. The ASRA recommendations for preventing LAST include the use of ultrasound, use of the lowest effective dose, incremental injections, aspiration before each injection, and the addition of epinephrine when employing potentially toxic doses of local anesthetic[110]. The presence of epinephrine within the local anesthetic solution may cause a transient increase in heart rate if injected intravascularly, thus alerting the clinician of inadvertent intravascular injection. The risk of LAST increases with the administration of large volumes of local anesthetic to perform multiple nerve blocks at the same time. For example, patients who undergo blockade of the saphenous (adductor canal block) and sciatic (popliteal block) nerves may receive a large combined total volume of local anesthetic. As such, extreme caution should be administered to the individual and combined doses of local anesthetic, especially when there are plans to administer further local anesthetic within the surgical field intraoperatively by the surgeon. It is important to utilize the minimum effective dose of local anesthetic required to perform the nerve block.

Prevention of LAST remains a cornerstone of safe administration of regional anesthesia. Checklists and treatment algorithms of LAST should be prominently displayed in any area where regional anesthesia nerve blocks are performed, and resuscitation equipment and medications should be immediately available if required [111,112]. Due to the life-threatening nature of LAST, prompt diagnosis and management of LAST should be frequently reviewed and reinforced with the use of simulation[111]. All personnel, including surgical staff, nursing staff, and anesthesia staff should be trained in recognizing and treating LAST if they work in a perioperative setting where peripheral nerve blocks are performed. Moreover, resuscitative medications should be well-marked and easily accessible by all members of the treatment team.

Block failure

Regional anesthesia is often effectively utilized as the primary anesthetic or as an adjunct for postoperative analgesia; however, despite these benefits, it has an inherent failure risk even in the most experienced hands. Block failure is manifested as inadequate anesthesia or analgesia in the targeted region. This may result in poorly-controlled pain, delayed surgical schedule, subjecting the patients to repeated block attempts, or unanticipated conversion to general anesthesia.

Certain technical variables have been found to be the cause of certain block failures. Injection of anesthetics outside of the neurovascular sheath prevents appropriate spread to the target nerve. Additionally, the utilization of a high threshold for stimulation when using a nerve stimulator technique may lead to an increased rate of failed blocks[17].The experience level of the anesthesiologist performing the block has been reported to impact the performance of a regional anesthetic[113]. It is important to optimize all patient variables for increasing the rate of success. This can be achieved

Table 4 Clinical presentation and management of local anesthetic systemic toxicity

Local anesthetic systemic toxicity (LAST)
Clinical presentation of LAST
1 Dizziness, drowsiness, tinnitus, perioral numbness
2 Muscle twitching and tremors
3 Seizures
4 CNS depression, coma
5 Hypertension, tachycardia
6 Myocardial depression, ventricular arrhythmias, conduction delays
7 EKG changes: Prolonged PR, QRS; T-wave changes
8 Cardiovascular collapse
Management of LAST
1 Call for help
2 Call for LAST rescue kit
3 Consider early lipid emulsion administration
(1) Under 70 kg: Bolus 1.5 mL/kg over 2-3 min, Infuse 0.25 mL/kg/min. Repeat bolus or double the infusion rate if the patient remains unstable
(2) Over 70 kg: Bolus approximately 100 mL over 2-3 min, infuse approximately 250 mL over 15-20 min. Repeat bolus or double the infusion rate if the patient remains unstable
(3) If the patient is stable, continue lipid emulsion ≥ 15 min after hemodynamic stability. Maximum lipid dose: 12 mL/kg
4 Seizure
(1) Airway management
(2) Benzodiazepine
(3) Consider low dose propofol
5 Arrhythmia or cardiovascular Instability
(1) Epinephrine: Administered at lower dose than ACLS dosing, start with ≤ 1 mcg/kg
(2) Avoid local anesthetics, beta-blockers, vasopressin, calcium channel blockers
(3) Consider alerting cardiopulmonary bypass team
6 Close monitoring
Once stable, continue close monitoring: 2 h after seizure, 4-6 h after cardiovascular instability, and as clinically appropriate after cardiac arrest

EKG: Electrocardiogram; CNS: Central nervous system.

by proactively taking measures to optimize patient positioning with towels or pillows, using ultrasonography if available, and to take into account anatomic variation. Current graduating anesthesiology residents are receiving advanced training in peripheral nerve blockade, and are likely to be well-versed in the use of peripheral nerve blockade, which will likely decrease the rate of block failure.

One study noted that regardless of block type, patients with a body mass index (BMI) greater than 25 kg/m^2 are more likely than those with lower BMI to experience non-surgical anesthesia; moreover, the rate of block failure increased incrementally with BMI[17]. This is likely due to the difficulty in identifying anatomical landmarks in these patients. Additionally, patients who were an American Society of Anesthesiologists class IV physical status experienced a higher degree of block failure[17].

Block failure may also occur in patients who undergo placement of continuous peripheral nerve block (CPNB) catheters. One study noted the incidence of failure for continuous peripheral nerve block with the supraclavicular approach to be 26%, the highest among the blocks evaluated[114]. The infraclavicular approach was noted to have a lower failure rate, likely due to anatomical characteristics which allow for a more stable catheter placement with a lower rate of dislodgement[114]. Areas with more stable anatomy, with limited range of motion, may minimize the amount of undue traction placed on catheters resulting in lower rates of catheter dislodgement.

Several mechanisms have been implicated in CPNB failure, including catheter insertion techniques, anatomic variation, and equipment malfunction. The CPNB catheter may have initially been incorrectly placed in relationship to the target nerve, or the catheter can migrate post-placement[115,116]. Other causes of CPNB failure include dislodgement or obstruction of the of the catheter tubing[117]. Leakage of local anesthetic solution after dislodgement may potentially increase the risk of LAST or rarely may even cause myonecrosis[114]. Further upstream, the infusion pump may malfunction or disconnect, causing leakage of local anesthetic solution[118]. Genetic variations in certain patients may result in abnormal metabolism of local anesthetic, which may cause inadequate sensory blockade[119]. Lastly, pain is a subjective multifactorial entity. Thus perception of pain may be affected by psychological factors including anxiety and pain-sensitivity, especially in the perioperative period[114].

The advent and increased clinical use of ultrasound-guidance has been shown to increase success rates and improve the quality of sensory blockade[120]. Also, ultrasound-guidance has been shown to shorten block procedural times by reducing the number of needle passes required to localize the target nerve[121].

The overall success of any regional anesthesia technique relies on the ability to correctly identify the nerves or nerve plexus involved in the surgery and place an adequate dose of local anesthetic surrounding the nerve structures. Advances in the field of regional anesthesiology have led to an increase in the use of regional anesthesia with the addition of novel block techniques, especially with the use of ultrasound-guidance[110]. Given the increasing use of peripheral nerve blockade, anesthesiology training programs have drastically increased their emphasis on mastering regional anesthesia skills, leading to the development of anesthesiologists with a strong skillset of performing safe and effective peripheral nerve blocks[122]. The risk of block failure should be discussed with the patient prior to performing the nerve block, so they are aware of this potential occurrence. As part of this discussion, it is beneficial to review alternative analgesics (*e.g.*, alternative blocks, intravenous, and oral medication) that may be administered if the block provides limited pain relief. It is important to utilize alternative methods of analgesia for patients who experience block failure. Consideration should be given to performing an alternative nerve block, if the first block technique fails while considering the total dose of local anesthetic used.

Nerve injury

Peripheral nerve injury is rare following regional anesthesia. Although the definition of injury varies between studies, the incidence of persistent symptoms of nerve dysfunction may be as high as 8 to 10 percent in the days following the block[123,124]. The majority are transient, lasting days to months. Major complications resulting in permanent (greater than six months) nerve damage ranges between 0.015 and 0.09 percent[125-127]. Incidence of nerve injury associated with continuous catheters is around 0.21 percent[118,128]. Most nerve injuries are believed to occur secondary to intraneural injection. Intrafascicular injections, particularly at high pressure, are felt to result in greater risk of nerve damage[129,130]. To minimize the incidence of intrafascicular injection, injection of anesthetic should be halted if the patient feels a paresthesia (shooting pain), or if the pressure required for injection is greater than usual. Appropriate spread of the anesthetic should be observed when ultrasound-guidance is used. Preexisting nerve pathology (including diabetes) may make a nerve more susceptible to injury. Continuous visualization of the block needle using ultrasound is presumed to decrease the risk of intrafascicular injection, but does not decrease the risk of nerve injury. Also, nerve injury can also occur as a direct effect of certain LA medications[131].

Symptoms of nerve injury are primarily sensory (pain, tingling, or paresthesias), but can include any combination of motor or sensory deficits depending on the nerve involved and severity of the injury. Most symptoms resolve within six months; if symptoms are either severe or persistent, the patient should be referred to a specialist for further evaluation and testing.

Hematoma

Inadvertent puncture of nearby vascular structures can lead to hematoma formation. It is important to avoid performing PNB's in patients with an abnormal coagulation status in anatomic locations in which application of pressure to the puncture site is not possible. The vast majority of hematomas may be controlled with direct pressure to the needle puncture site; rarely, surgical decompression may be required.

Allergic reaction

Most adverse reactions to LAs are non-allergic. However, two different types of allergic reactions to LAs have been described: allergic contact dermatitis and delayed swelling at the site of administration within 72 h, and rarely anaphylaxis.

Infection

Infection risk for single-shot peripheral nerve block is negligible and for peripheral catheters is low (0 to 3.2 percent)[132]. Risk of infection is increased in critically ill patients, admission, trauma patients, immune compromised patients, males, and the absence of antibiotics. The risk of infection may be minimized by removing the catheter within 48 to 72 h of placement.

Fall risk

Certain lower extremity nerve blocks may result in muscle weakness which can secondarily increase the risk of post-operative falls[133].

Local anesthetic-induced central nervous system toxicity (toxic left hemispheric syndrome)

Recently, severe stroke-like symptoms following intrascelene block has been reported after interscalene block. Patients had typical hemispheric symptoms in the absence of cerebral vessel occlusion. Hemispheric syndrome in the reported cases occurred in the ipsilateral side of the interscalene block. The proposed mechanism of injury in these cases was apoptotic cell death due to local anesthetic neurotoxic effects. Patient presented with impaired consciousness, slow-wave EEG activity in the affected hemisphere, epilepsy, global aphasia, dysphagia, dysarthria, facial palsy, hemiparesis, pyramidal tract signs, and complex behavioral manifestations. No abnormal computed tomography or magnetic resonance imaging (MRI) imaging was observed in the immediate postoperative period. MRI imaging abnormalities were appreciated postoperative days 1 through 5 in some patients which included hyperintensity of cortical grey matter and basal ganglia. Hospital stay ranged from 9 to 19 d with patient requiring mechanical ventilation for airway protection. Most patients experienced gradual improvement of the functional outcome after a prolonged course of rehabilitation but still has residual symtpoms[134].

CONCLUSION

Regional anesthesia is one of the cornerstones of successful perioperative orthopedic management. In addition to providing superior anesthesia for orthopedic procedures, regional anesthesia provides superior analgesia with relatively fewer side effects compared to systemic analgesia modalities. Perioperative team awareness of regional anesthesia fundamentals is one essential step towards improving clinical outcomes, lowering health care costs, and sustaining higher patient satisfaction scores.

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REVIEW

Management of proximal biceps tendon pathology

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Abstract

The long head of the biceps tendon is widely recognized as an important pain generator, especially in anterior shoulder pain and dysfunction with athletes and working individuals. The purpose of this review is to provide a current understanding of the long head of the biceps tendon anatomy and its surrounding structures, function, and relevant clinical information such as evaluation, treatment options, and complications in hopes of helping orthopaedic surgeons counsel their patients. An understanding of the long head of the biceps tendon anatomy and its surrounding structures is helpful to determine normal function as well as pathologic injuries that stem proximally. The biceps-labral complex has been identified and broken down into different regions that can further enhance a physician's knowledge of common anterior shoulder pain etiologies. Although various physical examination maneuvers exist meant to localize the anterior shoulder pain, the lack of specificity requires orthopaedic surgeons to rely on patient history, advanced imaging, and diagnostic injections in order to determine the patient's next steps. Nonsurgical treatment options such as anti-inflammatory medications, physical therapy, and ultrasound-guided corticosteroid injections should be utilized before entertaining surgical treatment options. If surgery is needed, the three options include biceps tenotomy, biceps tenodesis, or superior labrum anterior to posterior repair. Specifically for biceps tenodesis, recent studies have analyzed open *vs* arthroscopic techniques, the ideal location of tenodesis with intra-articular, suprapectoral, subpectoral, extra-articular top of groove, and extra-articular bottom of groove approaches, and the best method of fixation using interference screws, suture anchors, or cortical buttons. Orthopaedic surgeons should be aware of the complications of each procedure and respond accordingly for each patient. Once treated, patients often have good to excellent clinical outcomes and low rates of complications.

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Key Words: Shoulder pathology; Long head of the biceps tendon; Biceps-labral complex; Biceps tenotomy; Biceps tenodesis; Superior labrum anterior to posterior lesions

Core Tip: Management of proximal pathologies involving the long head of the biceps tendon is evolving. While biceps tenotomy, biceps tenodesis, and superior labrum anterior to posterior repair can be used to treat these pathologic injuries, no consensus exists with regard to which procedure is best. This clinical review provides a current understanding of the long head of the biceps tendon anatomy and its surrounding structures, function, and relevant clinical information such as evaluation, treatment options, and complications in hopes of helping orthopaedic surgeons counsel their patients.

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INTRODUCTION

While the role of the long head of the biceps tendon (LHBT) in shoulder pathology has been studied extensively, the management of such pathology has evolved. Recently, studies have demonstrated that biceps tenodesis can be used to treat individuals with symptomatic superior labrum anterior to posterior (SLAP) lesions[1-3]. As a result, the number of biceps tenodesis procedures performed each year has increased[4]. Despite this rise in volume, there is no consensus on which procedure-biceps tenotomy, biceps tenodesis, or SLAP repair is superior in terms of clinical outcomes. Typically, orthopaedic surgeons use their preference and specific patient factors to determine which procedure is ideal for each patient. Furthermore, in patients who undergo biceps tenodesis, there is controversy as to whether orthopaedic surgeons should utilize open *vs* arthroscopic techniques, the best method of fixation with interference screws, suture anchors, or cortical buttons, and the ideal location of tenodesis with intra-articular, suprapectoral, subpectoral, extra-articular top of groove, or extra-articular bottom of groove approaches. Regardless of this debate, researchers can agree that the LHBT is widely recognized as an important pain generator, especially in anterior shoulder pain and dysfunction[5-8].

The purpose of this review is to provide a current understanding of LHBT anatomy, function, and clinical information such as evaluation, nonsurgical management, surgical management, and complications in hopes of helping orthopaedic surgeons counsel their patients.

ANATOMY AND FUNCTION

An appreciation of the LHBT anatomy and its surrounding structures is helpful to understand normal function as well as proximal pathologic injuries (Figures 1 and 2)[9,10]. The LHBT originates from the supraglenoid tubercle and the superior glenoid labrum and exits the glenohumeral joint through the bicipital groove[11]. The attachment point of the LHBT on the superior labrum is variable amongst patients: equal anterior and posterior attachment is the most common (37%), predominantly anterior is the least common (8%), and other variations such as entirely posterior (22%) or mostly posterior (33%) also exist[12,13]. As it exits the glenohumeral joint and before it enters the bicipital groove, the LHBT is stabilized by a capsule-ligamentous complex referred to as the biceps pulley, which consists of the subscapularis tendon, the supraspinatus tendon, the coracohumeral ligament, the pectoralis major tendon insertion, and the falciform ligament (Figure 1)[14,15]. The LHBT then travels distally into the bicipital groove along the anterior surface of the humerus through the osteoligamentous sheath which is formed by the transverse humeral ligament as well

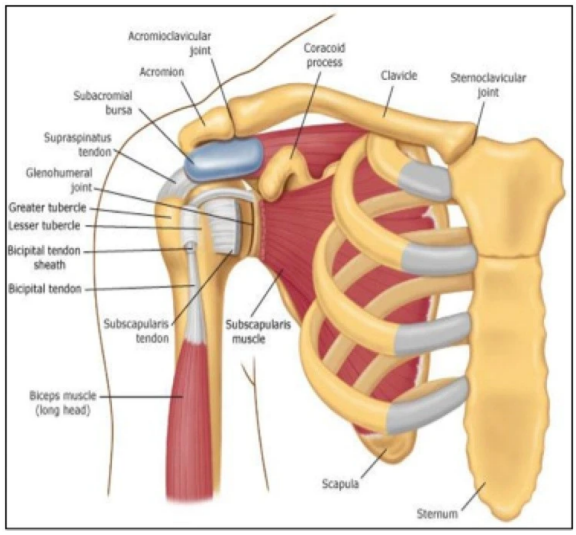

Figure 1 Schematic illustration of anterior shoulder anatomy from Blum *et al*[9]. Citation: Blum K, Chen AL, Chen TJ, Waite RL, Downs BW, Braverman ER, Kerner MM, Savarimuthu SM, DiNubile N. Repetitive H-wave device stimulation and program induces significant increases in the range of motion of post operative rotator cuff reconstruction in a double-blinded randomized placebo controlled human study. BMC Musculoskelet Disord 2009; 10: 132. Copyright© The Authors 2009. Published by BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons CC BY license, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

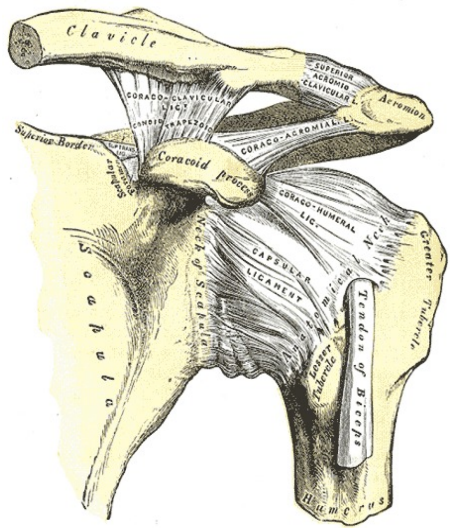

Figure 2 Anterior view of the left shoulder joint depicting tendons and ligaments from Miniato *et al*[10]. Citation: Miniato MA, Anand P, Varacallo M. Anatomy, Shoulder and Upper Limb, Shoulder. [Updated 2020 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536933/. Copyright© The Authors 2021. Published by StatPearls Publishing LLC. This book is distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits use, duplication, adaptation, distribution, and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, a link is provided to the Creative Commons license, and any changes made are indicated.

as the greater and lesser tuberosities (Figures 1 and 2)[16]. The LHBT and the short head of the biceps tendon, which originates from the coracoid process with the coraco-brachialis, give rise to the muscle belly of the biceps brachii which externally rotates 90° before the tendons attach as a single tendinous insertion on the ulnar aspect of the bicipital tuberosity of the radius[6].

Furthermore, the long head of the biceps (LHB) and glenoid labrum have collectively been described as the "biceps-labral complex" (BLC) which can be categorized into three main parts: (1) The inside, which includes the superior labrum and the LHBT anchor at the supraglenoid tubercle; (2) The junction, which includes the intra-articular LHBT and its stabilizing pulley system; and (3) The bicipital tunnel, which includes the LHBT beginning at the articular margin of the humeral head adjacent to the pulley and extending to the subpectoral region (Figure 3)[17-19]. The bicipital tunnel, which houses the extra-articular biceps, is further divided into three

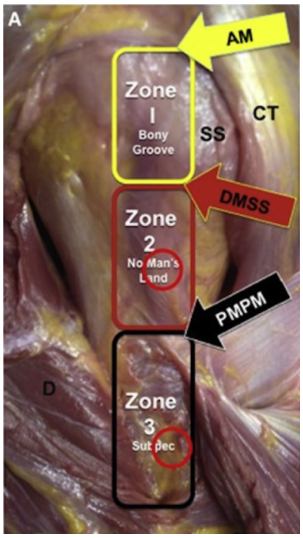

Figure 3 Visual depiction of biceps-labral complex with zone 2 red circle as site for arthroscopic suprapectoral tenodesis and zone 3 red circle as open subpectoral tenodesis location from Forsythe *et al*[120]. Citation: Forsythe B, Zuke WA, Agarwalla A, Puzzitiello RN, Garcia GH, Cvetanovich GL, Yanke AB, Verma NN, Romeo AA. Arthroscopic Suprapectoral and Open Subpectoral Biceps Tenodeses Produce Similar Outcomes: A Randomized Prospective Analysis. Arthroscopy 2020; 36: 23-32. Copyright© The Authors 2020. Published by Elsevier. The authors have obtained the permission for figure (Supplementary material). AM: Articular margin; CT: Conjoined tendon; d: Deltoid; DMSS: Distal margin of subscapularis tendon; PMPM: Proximal margin of pectoralis major; SS: Subscapularis.

clinically relevant zones. Zone 1 stretches from the articular margin to the distal margin of the subscapularis. Zone 2 extends from the distal margin of the subscapularis to the proximal margin of the pectoralis major. Lastly, zone 3 is the subpectoralis region[20].

The function of the LHBT still remains highly debated. Prior cadaveric studies have shown it may serve as a humeral head depressor, a stabilizer of the glenohumeral joint, or a stabilizer of the humeral head particularly in the anterosuperior and anterior directions of shoulder abduction[21-23]. Other authors consider the LHBT to be a vestigial structure that is not active during isolated shoulder movements and may have a larger role in proprioception of the shoulder[24,25]. Anatomically, there is consensus that the LHBT mainly functions as a forearm supinator while the short head of the biceps tendon mostly functions as an elbow flexor[6].

PROXIMAL BICEPS TENDON PATHOLOGY

The pathologic entities involving the LHBT can be classified into three general categories: inflammatory, instability, and traumatic[8]. Inflammation of the biceps tendon is commonly attributed to degenerative tendinopathy and overuse injuries. Additionally, rotator cuff tears and subacromial impingement can also lead to or be associated with bicipital tendinitis[26-30]. Some studies have found a prevalence as high as 93% in the association of LHBT inflammatory injuries and rotator cuff tears [31]. Instability of the tendon can create mechanical symptoms such as popping and clicking with range of motion. If the LHBT is unstable, the physician should highly suspect an associated subscapularis tendon tear or tears of the coracohumeral and/or superior glenohumeral complex[6,8]. Lastly, the LHBT is susceptible to traumatic injury, most commonly a complete rupture of the tendon, where pain resolves over time and function is typically reserved. These injury categories have been associated with other various shoulder conditions such as glenohumeral arthritis, labral lesions, and anterior or anterosuperior rotator cuff tears[1,32-35].

Anatomically, the three main parts of the BLC are associated with specific pathologic entities[17]. Injuries to the inside, which is predominantly associated with SLAP lesions, can be caused by superior migration of the humeral head, biceps tension, or peelback as a result of internal impingement[36]. Injuries to the junction include LHBT tears, LHBT incarceration, biceps chondromalacia, hourglass biceps, and pulley lesions[37-39]. The bicipital tunnel, specifically zones one and two, encompass LHBT tears, loose bodies, and tenosynovitis[18,40].

Evaluation

An in-depth history and physical examination must be done to differentiate biceps pain from other causes of referred shoulder pain[41]. This can be difficult because individuals with biceps pain can also have concomitant pathologies such as rotator cuff tears and may even have similar symptoms to patients with SLAP lesions[42-44]. As a result, physicians should utilize patient history, physical examination results, and imaging modalities to consider multiple differential diagnoses and help determine appropriate management.

A comprehensive history should be acquired when evaluating patients with LHBT injuries. A thorough history that documents the mechanism of injury can help the physician differentiate between various shoulder pathologies[45]. Obtaining information such as hand dominance, history of injury/trauma to the shoulder area, symptom exacerbation with overhead activities, pain at rest and/or pain at night, history or current overhead sport participation, history of current manual labor occupation or employment status, and any relevant surgical history can be incredibly useful in conjunction with the physical examination to determine the etiology of the pain[45].

Physical examination should start with assessment of range of motion as well as neurovascular examination that includes strength testing of all rotator cuff muscles. Common LHBT conditions that should be differentiated with an in depth physical examination include inflammatory injuries, instability, and rupture. LHBT inflammatory changes such as tenosynovitis or tendinitis often presents with pain in the anterior aspect of the shoulder that radiates to the anterior biceps[46]. Symptoms can be exacerbated by overhead activity or elbow flexion. LHBT instability will often present with reproducible clicking or tendon subluxation on physical examination[6]. For this type of injury, the physician should pay special attention to the subscapularis muscle as LHBT instability is associated with rotator cuff tears, especially those of the upper border of the subscapularis[17]. Therefore, physicians should also perform passive external rotation, lift-off, belly-press, and bear hug test for the subscapularis (Figure 4)[8,17,47]. LHBT rupture often occurs with a tearing sensation anteriorly and presents with swelling and ecchymosis. Some patients may have a Popeye deformity or sagging biceps muscle belly which can be exaggerated by having the patient flex his biceps (Figure 5)[6,17,48]. For these patients, muscle belly cramping has also been reported[49]. In patients with symptomatic proximal biceps pathology, pain will often be localized to the bicipital groove. This pain can be elicited on direct palpation of the area 7 cm below the acromion with the arm adducted, internally rotated 10°, and the elbow flexed[50]. To assist in proper palpation and pain elicitation, the shoulder should be internally and externally rotated in this position.

While specific examinations in patients with biceps-related pathology and SLAP tears can be utilized to differentiate etiologies of shoulder pain, these maneuvers often lack specificity[51,52]. For example, the Speed test, which is used to elicit anterior shoulder pain with resisted elbow flexion has overall sensitivity of 57% and specificity of 52% in diagnosing biceps tendon disorders and SLAP lesions (Figure 6)[47,52-55]. Similarly, the Yergason test, which is used to elicit anterior shoulder pain with resisted forearm supination, has been shown to be an unreliable predictor of biceps pathology or SLAP tears with a reported sensitivity of 43% and specificity of 79%[54-56]. Physical examination maneuvers specific for SLAP pathology, such as the O'Brien active compression test and the O'Driscoll dynamic labral shear test, have demonstrated reasonable diagnostic utility, but are still controversial (Figure 7)[57]. While some studies initially reported excellent results for the diagnostic utility of the O'Brien active compression test, recent meta-analyses have suggested that it is not diagnostic of SLAP tears[58,59]. The O'Driscoll dynamic labral shear test was also found to have excellent initial results in terms of diagnostic utility for SLAP tears, but was questioned by further studies[60-62]. Furthermore, examination maneuvers for SLAP pathology are limited by shoulder pathology that is often observed in individuals with SLAP tears, such as Bankart lesions and partial-thickness rotator cuff tears[63-65].

Imaging and diagnostic injections

With the lack of specificity in physical examination maneuvers, imaging studies are often used to differentiate LHBT pathology. Unfortunately, this too has its faults. While radiographs can be useful in assessing bony anomalies and ruling out concomitant osseous disorders, they often appear normal[7,52]. Advanced imaging studies such as MRI demonstrate reasonable sensitivity and specificity for the diagnosis of SLAP tears, LHBT rupture, and other inside lesions of the BLC; however, junctional and bicipital tunnel lesions are poorly identified[66-70]. Additionally,

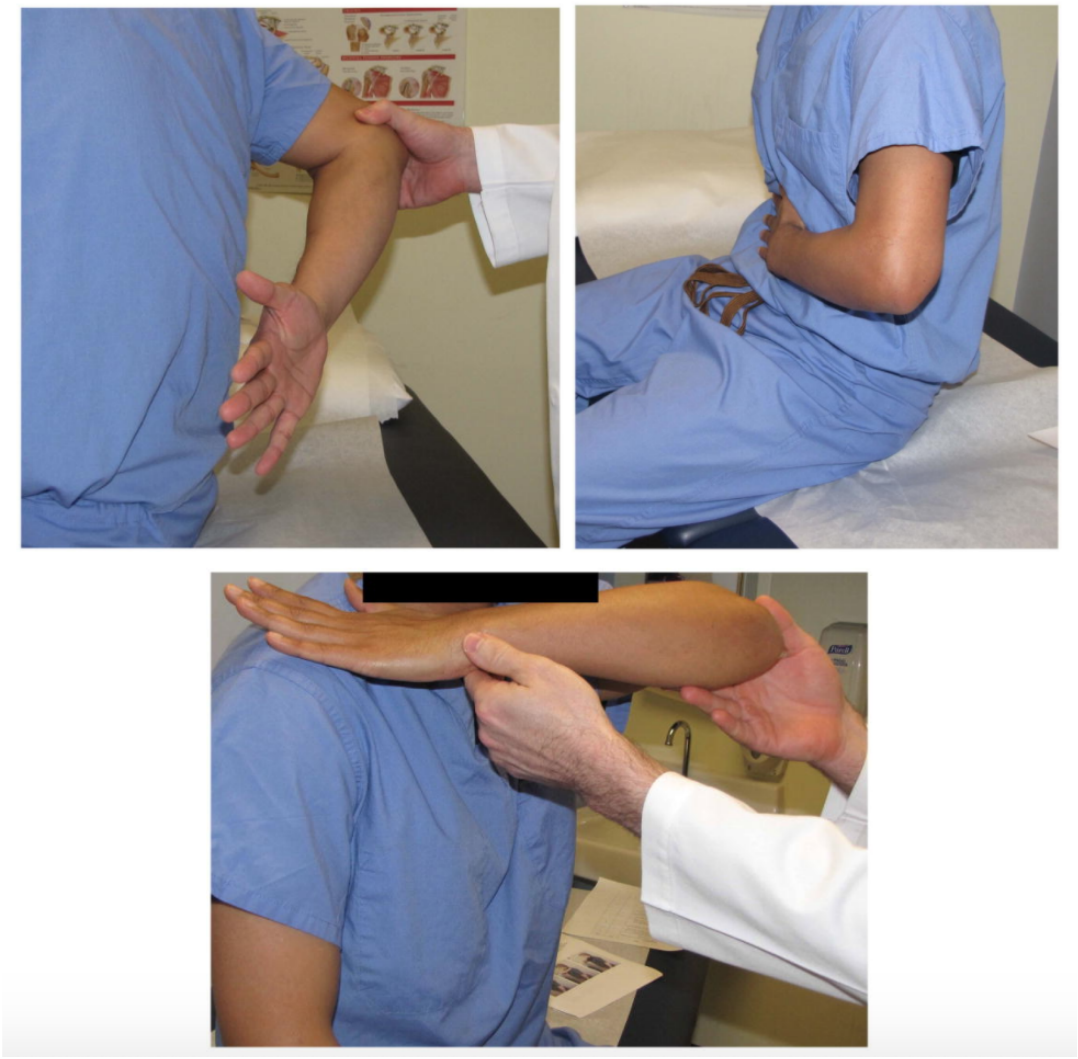

Figure 4 Special tests for subscapularis from Jain *et al*[47]. Citation: Jain NB, Wilcox RB 3rd, Katz JN, Higgins LD. Clinical examination of the rotator cuff. PM R 2013; 5: 45-56. Copyright© The Authors 2013. Published by John Wiley and Sons. The authors have obtained the permission for figure (Supplementary material). Top left: Lift-off test; Top right: Belly-press test; Bottom: Bear hug test.

ultrasonography is a fast, cost-effective, and radiation-free diagnostic method for shoulder and has been used for LHBT instability, dynamic examination of the tendon, examination of hypoechogenic areas, and increased tendon diameter[71,72]. While ultrasound techniques are useful in detecting LHBT pathology with a sensitivity between 50%-96% and a sensitivity of 98%-100%, it is less helpful in diagnosing partial-thickness tears[71,73,74]. Regardless of its faults, ultrasonography techniques should be used in conjunction with MRI when examining LHBT pathology.

Diagnostic injections could also be utilized in patients with anterior shoulder pain as peritendinous or sheath injections are often used to clinically diagnose and treat biceps tendinopathy[75,76]. Injections into the tendon sheath can be diagnostic and therapeutic by providing the physician information about the patient's pathology based on their pain response post-treatment[77,78]. It is important to note that injections should not be directly inserted into tendons as it can lead to tendon rupture [79]. Improved injection accuracy through ultrasound guidance has proven to be effective compared to blind injection techniques. In a recent study by Hashiuchi *et al* [80], ultrasound-guided injections resulted in 87% accuracy while blind injections were accurate only 27% of the time.

TREATMENT OPTIONS

The treatment of LHBT pathology can be separated into nonsurgical and surgical management. Initially, LHBT injuries should be treated conservatively followed by

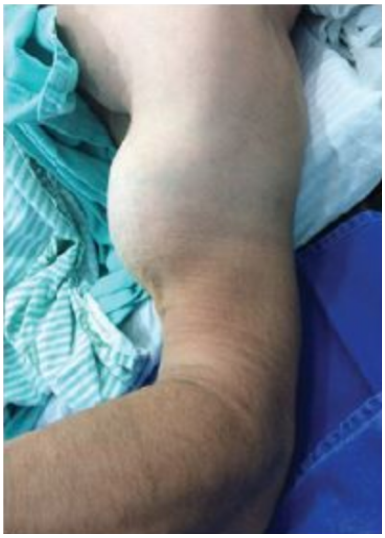

Figure 5 Lateral view showing Popeye deformity from José *et al*[48]. Citation: José AG, Luís Felipe HFS, Gabriel RSM, Fernando MI. Treatment of the Distal Biceps Brachii Tendon Rupture Using the Three Mini-Incisions Technique: Evaluation through MEPS and DASH. Ortho Rheum Open Access J. 2019; 14: 555888. Copyright© The Authors 2019. Published by Juniper Publishers INC. This work is licensed under Creative Commons Attribution 4.0 License.

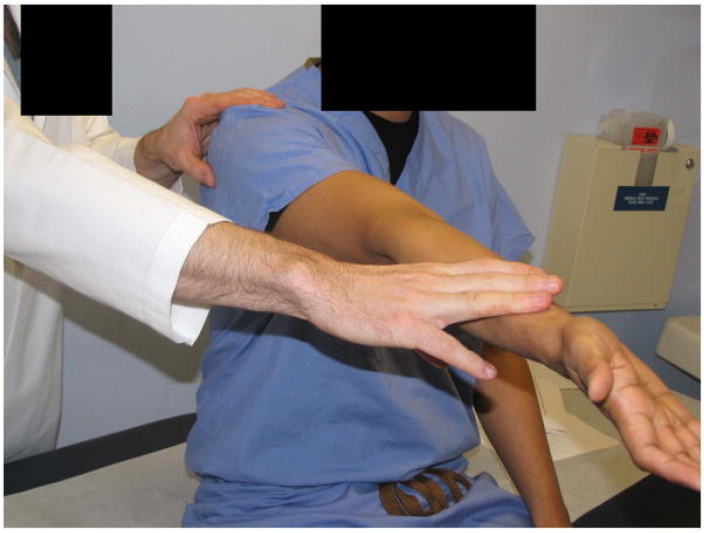

Figure 6 Speed test from Jain *et al*[47]. Citation: Jain NB, Wilcox RB 3rd, Katz JN, Higgins LD. Clinical examination of the rotator cuff. PM R 2013; 5: 45-56. Copyright© The Authors 2013. Published by John Wiley and Sons. The authors have obtained the permission for figure (Supplementary material).

surgery when all conservative treatments fail.

Nonsurgical management

Nonsurgical management of LHBT disorders is largely driven by individual surgeon experience. Typically, management begins with nonsteroidal anti-inflammatory drugs, physical activity, activity modifications, and ultrasound-guided corticosteroid injections into the biceps sheath[56,80,81]. Although physical therapy improves overall shoulder strength, range of motion, and function, limited research has been done that analyzes the outcomes of physical therapy as a nonoperative management option for LHBT pathologies. As mentioned earlier, the corticosteroid injection should be carefully placed as accidentally guiding the injection into the biceps tendon may cause rupture[82]. If correctly placed, ultrasound-guided corticosteroid injections have shown to cause lower patient discomfort as well as superior accuracy compared to palpated and blind injections[83]. Unfortunately, corticosteroid injections were found only to be beneficial in the short term, but may be worse than other treatment options in the intermediate and long terms[84]. Regardless of technique, research on the effectiveness of corticosteroid injections is inconclusive[85].

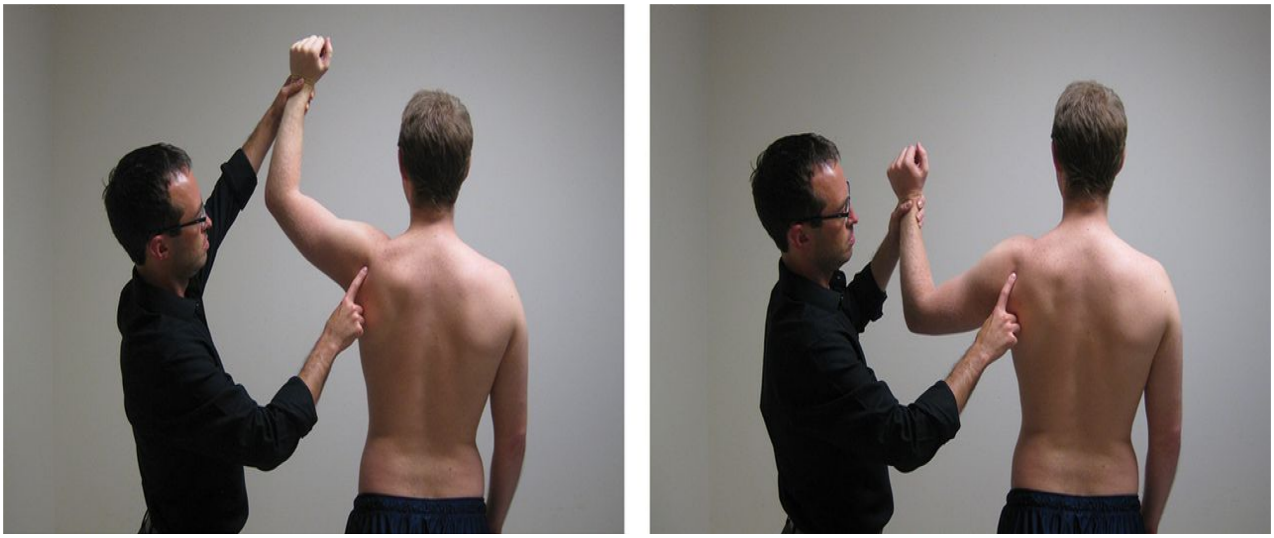

Figure 7 O'Driscoll dynamic labral shear test from Myer *et al*[57]. Citation: Myer CA, Hegedus EJ, Tarara DT, Myer DM. A user's guide to performance of the best shoulder physical examination tests. Br J Sports Med 2013; 47: 903-907. Copyright© The Authors 2013. Published by BMJ Publishing Group Ltd. The authors have obtained the permission for figure (Supplementary material).

Other options for nonsurgical management include iontophoresis, phonophoresis, ultrasonography, extracorporeal shock wave therapy, and laser therapy. Unfortunately, these have shown conflicting results in the literature[86,87]. Furthermore, promising yet inconclusive clinical outcomes have been shown for treatment options such as regenerative injection therapy which includes platelet-rich plasma[88,89]. If all nonsurgical treatment options fail, then patients should consider surgical treatment options.

Surgical management

While surgical management of LHBT pathologies is reserved for individuals who have failed all previously performed nonsurgical treatment options or individuals with acute injuries, the optimal surgical treatment is still up for debate[17]. The three options include biceps tenotomy, biceps tenodesis, and SLAP repair.

Biceps tenotomy: Biceps tenotomy is a viable option to surgically manage LHBT pathology and involves cutting the LHBT at its origin and maintaining the integrity of the labrum (Table 1)[49]. While numerous studies have shown excellent outcomes, pain relief, and improved patient-reported outcomes in individuals who undergo biceps tenotomy, there are a few complications shown in Table 1[46,90-92]. Other cited complications include stiffness, infection, transient nerve injuries, complex regional pain syndrome, and stroke secondary to cerebral hypoperfusion[93]. In recent studies, surgeons have tried to address some of these complications by testing arthroscopic techniques to limit distal migration of the LHB after tenotomy to minimize and even eliminate the occurrence of the Popeye deformity[94-97]. Other studies have reported ways to improve the efficiency of arthroscopic biceps tenotomy by using a biceps squeeze maneuver[98]. This is a simple method that entails manually squeezing the biceps muscle belly while performing the arthroscopic biceps tenotomy in order to shorten and tension the intra-articular portion of the tendon. In doing so, this technique improves the efficiency and safety of the procedure without adding additional cost.

Biceps tenodesis: Biceps tenodesis is increasingly used to treat individuals with LHBT pathology (Table 1). It involves releasing the LHBT from its origin and attaching it at one of four locations: (1) Within the glenohumeral joint to the intact rotator cuff; (2) To the conjoint tendon or the transverse humeral ligament; (3) Proximal to or within the bicipital groove in a suprapectoral fashion; or (4) Distally in a subpectoral fashion (mini-open approach)[6]. Current areas of debate include whether orthopaedic surgeons should perform biceps tenodesis open or arthroscopically, the best method of fixation (interference screw, suture anchor, or cortical button), and the ideal location of tenodesis (intra-articular, suprapectoral, subpectoral, and other positions such as extra-articular top of groove or extra-articular bottom of groove)[99].

Table 1 Comparison of biceps tenotomy *versus* biceps tenodesis

	Biceps tenotomy	Biceps tenodesis
Timing and cost	Quicker, shorter procedure with a lower cost	Technically more challenging with a longer surgical and rehabilitation time as well as a higher cost
Patient population	Symptomatic patients with biceps tenosynovitis > 60 yr of age, individuals with lower demand occupations, those with minimal cosmesis concerns	Symptomatic athletic patients, individuals with higher demand occupations, those with cosmesis concerns
Complications	Postoperative Popeye deformity, muscle belly cramping, discomfort and fatigue	Risk of infection, loss of fixation and recurrence of Popeye deformity, implant failure

Open *vs* arthroscopic: Biceps tenodesis can be performed *via* an open or arthroscopic approach; both methods have excellent clinical outcomes[100,101]. While a comparison between approaches is difficult due to concomitant pathology and different types of fixation, a comparison highlighting timing and cost, functional outcomes, range of motion, and complications can be seen in Table 2[102-105]. With no consensus over which method is superior, surgeons should take into account their own preference and technical experience when deciding on the proper approach for their patients.

A number of studies have analyzed open biceps tenodesis procedures in patients without rotator cuff tears and demonstrated improved patient reported outcome measures as well as pain and functional outcome scores[106-110]. Even though fewer studies have been identified for arthroscopic biceps tenodesis procedures in isolated LHB pathology, the patient reported outcome measures, pain scores, and objective outcomes are satisfactory in 98%-99% of patients with low rates of revision (0.4%) for biceps related problems[111-113].

Some studies have compared open LHB tenodesis to arthroscopic LHB tenodesis in order to determine which is superior. Abraham *et al*[100] and Green *et al*[114] found excellent outcomes with both methods and low complication rates. Gombera *et al*[115] compared forty-six patients who underwent arthroscopic or open biceps tenodesis and found no significant differences in American Shoulder and Elbow Surgeons (ASES) scores, patient satisfaction scores, return to sports activity, pain levels at night, pain levels with heavy activity, or Popeye deformities. In terms of complications, arthroscopic biceps tenodesis mirrors open biceps tenodesis. Complications following arthroscopic biceps tenodesis include residual postoperative groove pain, injury to the surrounding neurovascular structures, and increased risk of early postoperative stiffness[116]. Additionally, complications can be dependent on the fixation strategy. For example, open biceps tenodesis can be associated with fracture when using an interference screw and can also cause neurovascular injury in the subpectoralis region due to association with brachial plexus palsy and musculocutaneous nerve injury[117-119]. From these studies, no difference in outcomes can be found between open and arthroscopic biceps tenodesis.

Tenodesis placement: Biceps tenodesis is mainly done with intra-articular, suprapectoral, or subpectoral placement; other possible positions include extra-articular top of the groove and extra-articular bottom of the groove placement. In the intra-articular approach, the LHBT is cut and reattached within the intertubercular groove. While the clinical outcomes of this approach are excellent, patients may have persistent bicipital groove pain and tendinopathy with a portion of the tendon within the bicipital groove[120,121]. In the suprapectoral approach, the LHBT is cut and reattached distally to the bicipital groove and proximally the pectoralis major tendon. Even though this approach avoids the inflammation from the tendon remaining in the bicipital groove and sheath, it may be a longer and thus more costly approach compared to the subpectoral method and has thinner bone stock for hardware fixation [120,122,123]. Furthermore, in intra-articular and suprapectoral approaches, residual pain has been described[100,124].

In patients with significant inflammation in the biceps groove or patients where the suprapectoral part of the biceps is of poor quality or significantly injured, the subpectoral approach is the preferred method[125]. Subpectoral tenodesis is advantageous because it eliminates the pain created from reattachment within the groove, it is associated with stronger bone for fixation in the humerus, and it can potentially lead to a quicker recovery[126-128]. Like the other approaches, the subpectoral method has its disadvantages. The main disadvantages include scar formation, elongation of the biceps, biceps asymmetry, and partial detaching and reattaching of the pectoralis major to the humerus[126,128,129]. Compared to the suprapectoral approach, the

Table 2 Comparison of open biceps tenodesis *versus* arthroscopic biceps tenodesis

	Open approach	Arthroscopic approach
Timing and cost	Lower cost with slightly longer operation time	Higher cost with slightly lower operation time
Functional outcomes	No significant difference found between ASES, Constant, UCLA, DASH, or SST scores	
Range of motion	Similar in both approaches, forward range of motion slightly higher in arthroscopic approach	
Complications	Higher overall rate of complications such as wound healing issues, hematoma/seroma formation, nerve injury, deep vein thrombosis, and general anesthetic complications	Lower overall rate of complications, but higher incidence of postoperative stiffness and bicipital groove tenderness in early stages of recovery

ASES: American shoulder and elbow surgeons; DASH: Disabilities of the arm, shoulder and hand; SST: Simple shoulder test.

subpectoral approach has more residual tenderness and spasm initially following the procedure[120]. Furthermore, fracture has been described as a complication particularly with the use of interference screws[130,131].

In a study by Godshaw *et al*[121], authors compared forty-three patients who had undergone intra-articular tenodesis to fifty-six patients who had undergone suprapectoral tenodesis. While both groups showed improvement in all outcome measures, there was no difference between the groups in functional outcomes for physical and mental component scores as well as ASES scores. Werner *et al*[128] compared arthroscopic suprapectoral biceps tenodesis in nine cadavers to open subpectoral biceps tenodesis in nine cadavers. They found that the arthroscopic suprapectoral biceps tenodesis group had a significantly decreased load to failure compared to the open subpectoral biceps tenodesis group. Additionally, the arthroscopic suprapectoral technique over-tensioned the biceps tendon. Despite these findings, other individuals did not know if there would be similar results in live patients. To further test this idea, Werner *et al*[132] compared thirty-two patients who underwent arthroscopic suprapectoral biceps tenodesis to fifty patients who underwent open subpectoral biceps tenodesis patients. There was no significant difference reported in Constant, ASES, Single Assessment Numeric Evaluation, Simple Shoulder Test (SST), LHB, and Veterans RAND 36-Item Health Survey scores. Furthermore, there were no range of motion or strength deficits in either group. These studies prove that regardless of associated complications for intra-articular, suprapectoral, and subpectoral biceps tenodesis placement, all three approaches have excellent and similar clinical outcomes.

Fixation strategies: The two types of fixations that can be used in intra-articular, suprapectoral, and subpectoral approaches include inlay and onlay. With inlay fixation, the biceps tendon is inserted perpendicularly into the bicipital groove. This technique is less technically challenging to perform, but can result in tenodesis failure in patients with poor tendon quality or osteoporosis at the screw insertion site[133,134]. For the onlay technique, the biceps tendon lays parallel to the bicipital groove. Onlay fixation with a suture anchor may be technically challenging and require longer operative times, but may have superior clinical and functional outcomes compared to the inlay technique[135,136].

Within inlay and onlay strategies, the different fixation techniques include interference screw and suture anchor, which are the most common, as well as cortical button and all-suture suture anchor constructs. Arthroscopic intra-articular biceps tenodesis has historically utilized an inlay technique in which the tendon is docked into a bone socket perpendicular to the bicipital groove and secured with an interference screw[113,137]. In open subpectoral tenodesis, the onlay technique is used with a suture anchor meant to heal the tendon to the cortical surface of the humerus [138-141].

The various types of interference screws include titanium, polyether ether ketone (PEEK), and bioresorbable screws. Titanium interference screws are infrequently used as they have an increased risk of tendon laceration during screw insertion and can make postoperative assessment challenging due to significant artifact on MRI[142,143]. PEEK interference screws have become more popular for several reasons: (1) They are chemically inert and insoluble; (2) They have a modulus of elasticity similar to human cortical bone; and (3) They are compatible with MRI and have a higher resistance to radiation[144,145]. Suture anchors require a smaller bone socket compared to interference screws and as previously mentioned secure the tendon to the

humeral cortex. Furthermore, all-suture suture anchors allow for even less violation of the cortex.

While all constructs have been studied and proven to be effective, there is no consensus on which fixation strategy provides the most superior fixation[141,146-148]. In a study by Buchholz *et al*[147], researchers compared intramedullary cortical button fixation to interference screw usage and found similar results in regard to stiffness and ultimate failure loads. In Chiang *et al*[149], interference screws and all-suture suture anchors were found to have similar failure loads and stiffness which correlates to an increased likelihood of tenodesis failure. Likewise, Tashjian *et al*[141] found failure loads to be similar when comparing interference screws to dual-anchor all-suture suture anchors. Despite these results, additional studies have concluded contrary findings. In Richards *et al*[148], authors analyzed eleven cadaveric humerus specimens in which biceps tenodesis was performed with interference screw fixation or double suture anchor fixation. Authors reported consistent failure at the anchor or anchor eyelet in the suture anchor cadaver models and concluded that interference screw fixation had superior fixation strength. On the other hand, Golish *et al*[133] found interference screws to have a higher failure load and stiffness compared to all-suture suture anchors. With mixed results from these studies, there is no consensus on which fixation strategy provides the greatest advantage.

Supporters of the interference screw technique argue that it creates more surface area contact between the tendon and cancellous bone and thus results in greater exposure to marrow-derived endogenous stem cells[150-153]. However, this comes at a cost, as securing the tendon within a bone socket can result in local deformations in the tendon[140,154]. In Tan *et al*[150], researchers used a rabbit model of bicep tenodesis and compared tendon healing within the bone socket to healing on the cortical surface. Histologic analysis showed similar healing profiles between the two groups which allowed authors to conclude that the creation of large bone sockets with interference screws, which can lead to increased fracture risk, may be unnecessary. Furthermore, the interference screw technique has been associated with additional complications such as persistent pain and bioabsorbable screw reactions[119,155,156].

In contrast, all-suture suture anchors provide the benefits of conventional interference screws while being less traumatic to the bone and thus having a lower risk of fracture[157,158]. Frank *et al*[157] compared torsional energy in humeri that underwent biceps tenodesis with all-suture suture anchors to humeri that underwent biceps tenodesis with interference screws. They found that humeri in the all-suture suture anchor group required greater torsional energy to fracture suggesting that this construct creates less of a stress riser than the interference screw construct.

Although many studies have compared the biomechanical qualities of these constructs, few have compared differences in clinical outcomes. Park *et al*[140] compared clinical and anatomic outcomes of the interference screw and suture anchor fixation techniques for biceps tenodesis and found that both methods improved functional outcomes. Additionally, there was no difference in patient-reported outcomes measured by the visual analog scale (VAS) for pain, ASES score, SST, Constant score, Korean shoulder score, and LHB score between the two groups. With that said, the authors did find interference screw fixation and more physically demanding work levels to be associated with tenodesis failure. In another study by Millett *et al*[159], no statistically significant differences were reported at thirteen months postoperatively in VAS, ASES, and modified Constant scores between individuals who underwent biceps tenodesis with interference screw fixation and individuals who underwent biceps tenodesis with all-suture suture anchor fixation.

From the various biomechanical studies described above, the decision on which fixation strategy to utilize can be rather nuanced. While some studies have cited no differences in regards to stiffness or ultimate failure load between fixation strategies, other studies have contradicted these findings declaring interference screw fixation as more superior in terms of fixation strength and more inferior in regards to failure load and stiffness[133,141,147-149]. Despite the lack of consensus amongst the ideal fixation technique regarding biomechanical data, there appears to be no difference between fixation techniques in terms of clinical outcomes.

Biceps tenotomy *vs* biceps tenodesis: Several studies have investigated the differences between biceps tenotomy and biceps tenodesis, but mainly for LHB tendinopathy with rotator cuff tears, which makes it difficult to determine the extent to which biceps management influences outcomes[160-162]. A comparison of the techniques can be found in Table 1. In a systematic review by Leroux *et al*[160], authors analyzed patients who underwent rotator cuff repair in combination with either biceps tenotomy or biceps tenodesis. They reported that patients who underwent biceps

tenodesis had better Constant assessment scores (92.8 [tenodesis] *vs* 90.6 [tenotomy], $P < 0.01$) and decreased rates of biceps deformity compared to patients who underwent biceps tenotomy (3.8% [tenodesis] *vs* 15.5% [tenotomy], $P < 0.01$).

Another study compared the clinical results of biceps tenotomy and biceps tenodesis based on technique. In Shank *et al*[163], seventeen patients underwent biceps tenotomy, nineteen patients underwent suprapectoral biceps tenodesis with a double-loaded anchor fixation, and thirty-one control patients did not have any biceps surgery performed. Analysis showed no significant difference in either forearm supination nor elbow flexion strength among patients in all three groups.

One theory that has been challenged recently is the duration of postoperative rehabilitation. Zabrzyński *et al*[164] attempted to test different rehabilitation protocols in tenotomy *vs* tenodesis groups with the tenotomy group undergoing a personalized postoperative rehabilitation protocol. They found that patients who underwent tenotomy with a shortened postoperative rehabilitation protocol were able to achieve better clinical outcomes and ensure faster return to sports activity compared to those who underwent tenodesis[164].

The results described above demonstrate how challenging it can be to make direct comparisons between tenotomy and tenodesis in hopes of determining which is superior. Furthermore, the concern for cosmesis plays a role in determining whether a patient should undergo tenotomy or tenodesis. Typically, tenotomy is indicated in older patients as cosmesis is of minimal concern whereas tenodesis is indicated in younger more active patients where cosmesis tends to play a more significant role. Recent systematic reviews and meta-analyses by MacDonald *et al*[165], Zhou *et al*[166], and Kooistra *et al*[167] confirm the findings that there is no evidence-based difference in LHB tenodesis *vs* tenotomy when evaluating shoulder function, pain, or biceps-related strength.

SLAP lesion: Treatment recommendations for SLAP lesions are based on patient age as well as activity level and include nonsurgical management, arthroscopic debridement, arthroscopic repair, and biceps tenodesis. Over the last five years, orthopaedic literature has documented the growing trend to move away from SLAP repair due to an increased incidence of subsequent revision surgery[168,169]. Instead, literature has shown an increase in the frequency of biceps tenodesis, particularly in patients over the age of forty and athletes as return to activity after biceps tenodesis was significantly higher than the rate after revision SLAP repair[170,171].

SLAP tears are often categorized into Type I through Type X[172]. In a type II SLAP lesion, there is detachment of the superior labrum and the origin of the LHBT insertion from the glenoid[173,174]. Surgical techniques that can be used to repair a standard type II SLAP lesion include the use of a single suture anchor placed posterior to the biceps anchor or the use of two suture anchors with one suture anchor placed anterior and the other placed posterior to the biceps anchor[17]. A few studies have reported on outcomes regarding type II SLAP repair. Sayde *et al* included 506 patients who underwent repair of type II SLAP tear and reported excellent satisfaction in 83% of patients and return to previous level of play in 73% of patients; however, in the 198 patients who were overhead athletes, inferior outcomes were reported with only 63% able to return to previous level of play. Similar studies have assessed the outcomes of overhead athletes who have undergone arthroscopic SLAP lesion repair and report a return to preinjury level of sports activity between 22% and 85%[175-178]. In Frank *et al*[179], sixty-two patients underwent arthroscopic repair of a type II SLAP tear. Authors reported that patients aged twenty years and younger as well as overhead throwers were more likely to require revision surgery than patients greater than twenty years of age and non-overhead throwers. Furthermore, they concluded that patients greater than forty years of age were more likely to have inferior postoperative ASES scores compared to patients aged less than forty years of age.

An increasingly popular alternative to arthroscopic repair of SLAP lesions is biceps tenodesis as it has a significantly higher rate of return to activity following surgery [170,171]. Some studies have performed biceps tenodesis in combination with SLAP repair or performed biceps tenodesis in place of SLAP repair. For example, Boileau *et al*[1] compared ten patients with an isolated type II SLAP lesion who underwent repair with the use of suture anchors to fifteen patients with an isolated type II SLAP lesion who underwent arthroscopic biceps tenodesis with the use of an absorbable interference screw. Patients in the SLAP repair group had inferior outcomes including lower mean Constant assessment scores, lower satisfaction, and lower return to previous level of sports activity. On the other hand, some studies have reported similar outcomes in patients with a type II SLAP tear who undergo biceps tenodesis. In

Denard *et al*[2], thirty-seven patients greater than thirty-five years of age with an isolated type II SLAP tear underwent arthroscopic biceps tenodesis or SLAP repair. Authors demonstrated that patients in the biceps tenodesis group had shorter postoperative recovery, higher satisfaction rates, and higher rates of return to normal activity. Similarly, Ek *et al*[3] compared twenty-five patients with an isolated type II SLAP lesion who underwent biceps tenodesis or SLAP repair and found that both groups had improved clinical outcomes with low failure rates and similar rates of return to sports. These studies demonstrate that patients who undergo biceps tenodesis for SLAP lesions experience a shorter postoperative recovery time, higher Constant assessment scores, higher satisfaction rates, higher rates of return to normal sports activity, and lower failure rates compared to patients who undergo SLAP repair.

While type II SLAP tears have seen an increase in biceps tenodesis as treatment, type III and type IV SLAP tears can be adequately treated with SLAP repair depending on the extent of the injury[172]. In a type III SLAP tear, a bucket-handle tear of the superior labrum occurs with potential displacement of the mobile labral fragment into the glenohumeral joint. In this case, the attachment of LHBT remains intact. Typically, type III SLAP lesions require resection of the unstable bucket-handle fragment with no further stabilization of the biceps anchor[172,180]. Some authors have also recommended refixation of the torn flap analogous to meniscal tears if the lesion is caused by trauma and located within a specific part of the shoulder[181]. For a type IV SLAP tear, there is a bucket-handle tear of the superior labrum that extends to the biceps tendon in a variable degree. Type IV SLAP lesion repair is reliant on biceps tendon stability after resection of the torn flap as at least half of the tendon should be intact to preserve stability of the labro-bicipital complex[172]. In an unstable biceps tendon where more than 50% of the tendon is affected, a tenotomy or tenodesis is preferred over a SLAP repair. With SLAP repairs demonstrating a wide variability in outcomes, specifically in rates of return to play and failure rates for older individuals, biceps tenodesis has shown a significant improvement in ASES scores and VAS scores [182].

The excellent outcomes and low rate of complications of biceps tenodesis for SLAP lesions have led to an increase in frequency of biceps tenodesis[119,183]. In a study by Patterson *et al*[4], trends in the management of SLAP lesions were reviewed and the proportion of SLAP repairs between 2002 and 2011 decreased from 69.3% to 44.8%, whereas the proportion of biceps tenodesis procedures increased from 1.9% to 18.8%. Furthermore, the proportion of SLAP repairs used to manage SLAP lesions in combination with rotator cuff repair decreased from 60.2% to 15.3%, whereas the proportion of biceps tenodesis or tenotomy procedures increased from 6% to 28%. In a more recent study by Cvetanovich *et al*[171], there was a 69.3% decrease in isolated SLAP repair from 2007 to 2016 and an increase of 370% in biceps tenodesis for the diagnosis of an isolated SLAP tear over the same period. With this knowledge, Chalmers *et al*[184] conducted a study with three groups: (1) Forty-five patients with a SLAP tear who underwent isolated SLAP repair; (2) Twenty-three patients with a SLAP tear who underwent isolated biceps tenodesis; and (3) Eighteen patients with a SLAP tear who underwent SLAP repair in combination with biceps tenodesis. Authors reported substantially worse postoperative ASES scores and visual analog scale pain scores in patients who underwent SLAP repair in combination with biceps tenodesis compared to either of the other categories. These studies demonstrate the utility and improved clinical outcomes in patients with SLAP lesions who undergo biceps tenodesis compared to patients with SLAP lesions who undergo arthroscopic repair. Furthermore, improved outcomes seen in biceps tenodesis for SLAP tears is supported by the increase in volume of biceps tenodesis procedures over the last five years or so.

CONCLUSION

LHBT is a common source of disease and shoulder pain with etiologies including inflammation, instability, and trauma. Although the anatomy can be easily digested, the decision to operate is a little more nuanced. Despite various physical examination maneuvers, the lack of specificity requires orthopaedic surgeons to rely on patient history as well as advanced imaging in order to best manage the patient's condition. Nonsurgical treatment typically includes physical therapy, anti-inflammatory medications, and ultrasound-guided corticosteroid injections. If nonsurgical treatment fails, surgical techniques such as biceps tenotomy, biceps tenodesis, or SLAP repair can be used. In biceps tenodesis, differences between arthroscopic and open biceps

tenodesis, type of fixation system, and location of tenodesis should be discussed with patients keeping in mind that no functional differences have been established. Furthermore, SLAP lesions can be treated with SLAP repair or biceps tenodesis depending on the categorization. While debridement has been used as the standard of treatment in the past for SLAP lesions, the increase in volume of biceps tenodesis for SLAP lesions indicates a transition to a treatment option with better functional and clinical outcomes.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Should we use similar perioperative protocols in patients undergoing unilateral and bilateral one-stage total knee arthroplasty?

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Abstract

BACKGROUND

Bilateral one-stage total knee arthroplasty (BTKA) is now in greater use as an alternative option for patients with bilateral end-stage knee arthropathy. However, postoperative pain and disablement during convalescence from BTKA, and procedure-related complications have been concerning issues for patients and surgeons. Although some studies reported that BTKA in selected patients is as safe as the staged procedure, well-defined guidelines for patient screening, and perioperative care and monitoring to avoid procedure-related complications are still controversial.

AIM

To compare the perioperative outcomes including perioperative blood loss (PBL), cardiac biomarkers, pain intensity, functional recovery, and complications between unilateral total knee arthroplasty (UTKA) and BTKA performed with a similar perioperative protocol.

METHODS

We conducted a retrospective study on consecutive patients undergoing UTKA and BTKA that had been performed by a single surgeon with identical perioperative protocols. The exclusion criteria of this study included patients with an American Society of Anesthesiologists score > 3, and known cardiopulmonary comorbidity or high-sensitivity Troponin-T (hs-TnT) > 14 ng/L. Outcome

study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: The authors declare that they have no competing interests related to the study design, data collection, and interpretation of results presented in this manuscript.

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measures included visual analogue scale (VAS) score of postoperative pain, morphine consumption, range of knee motion, straight leg raise (SLR), length of stay (LOS), and serum hemoglobin (Hb) and hs-TnT monitored during hospitalization.

RESULTS

Of 210 UTKA and 137 BTKA patients, those in the BTKA group were younger and more predominately female. The PBL of the UTKA *vs* BTKA group was 646.45 ± 272.26 mL *vs* 1012.40 ± 391.95 mL ($P < 0.01$), and blood transfusion rates were 10.48% and 40.88% ($P < 0.01$), respectively. Preoperative Hb and body mass index were predictive factors for blood transfusion in BTKA, whereas preoperative Hb was only a determinant in UTKA patients. The BTKA group had significantly higher VAS scores than the UTKA group at 48, 72, and 96 h after surgery, and also had a significantly lower degree of SLR at 72 h. The BTKA group also had a significantly longer LOS than the UTKA group. Of the patients who had undergone the procedure, 5.71% of the UTKA patients and 12.41% of the BTKA patients ($P = 0.04$) had hs-TnT > 14 ng/L during the first 72 h postoperatively. However, there was no difference in other outcome measures and complications.

CONCLUSION

Following similar perioperative management, the blood transfusion rate in BTKA is 4-fold that required in UTKA. Also, BTKA is associated with higher pain intensity at 48 h postoperatively and prolonged LOS when compared to the UTKA. Hence, BTKA patients may require more extensive perioperative management for blood loss and pain, even if having no higher risk of complications than UTKA.

Key Words: Bilateral one-stage total knee arthroplasty; Unilateral total knee arthroplasty; Blood loss; Postoperative pain; High-sensitivity Troponin-T; Cardiovascular events

Core Tip: The safety of bilateral one-stage total knee arthroplasty (BTKA) is still debated because of greater blood loss, higher risk of cardiovascular events, increased postoperative pain, and longer disablement period than unilateral total knee arthroplasty (UTKA). After comparing consecutive patients underwent BTKA and UTKA with similar perioperative management, we found that the blood transfusion rate in the BTKA is 4-fold than UTKA. Moreover, BTKA is associated with significantly higher pain intensity at 48 h postoperatively and prolonged hospitalization. Although our study demonstrated that BTKA is a safe procedure in selected patients, extensive perioperative management for blood loss and pain is mandatory for BTKA patients.

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INTRODUCTION

Total knee arthroplasty (TKA) is widely accepted as one of the most effective and safe surgical procedures for treating severe osteoarthritis (OA) of the knee. Currently, advances in anesthesia, surgical techniques, and perioperative care, including multimodal pain management and accelerated rehabilitation, have improved functional recovery and shortened the length of the hospital stay for patients undergoing unilateral total knee arthroplasty (UTKA)[1]. There have also been contemporary blood-conserving methods published that substantially decrease the

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rate of postoperative blood transfusions when kept below 10%[2-4].

Approximately 25% of patients undergoing UTKA have bilateral OA knees[5] and subsequently will undergo contralateral TKA within 1 year[6]. Thus, bilateral one-stage total knee arthroplasty (BTKA) is now in greater use as an alternative option for patients with bilateral OA knees because of the potential advantages that include single anesthesia, reduction in total hospitalization and rehabilitation time, as well as overall costs[7]. However, the safety of BTKA is still debated because of perioperative morbidity that is associated with greater blood loss and a higher risk of cardiovascular adverse events than UTKA[8,9]. Various blood-conserving strategies including regional anesthesia, tourniquet use and deflation after wound closure, femoral canal occlusion, and use of tranexamic acid (TXA) are commonly implemented in patients having BTKA with documented efficacy[10]. However, recently published studies revealed that blood loss after BTKA ranged between 874 and 1067 mL, and blood transfusion rate ranged between 24% and 44% even if TXA was administered[11-13].

The substantial blood loss related to BTKA may subsequently cause occult hypoperfusion of vital organs such as the heart and kidneys. Conversely, requirements for blood transfusions may also increase the risk of complications such as allergic reaction, cardiovascular volume overload, and subsequent heart failure or pulmonary edema [14,15]. The risk of myocardial infarction (MI) has been reported to significantly increase among the TKA group during the immediate postoperative phase when compared to the non-surgical group[16,17]. Taking data from the National Hospital Discharge database, 1.1% of patients were diagnosed with cardiac complications in the 90 d after TKA, and BTKA had a higher rate than UTKA (2.0% *vs* 1.7%)[18]. Therefore, these findings may emphasize the need for extensive perioperative care and monitoring to avoid such complications in BTKA.

Furthermore, significant pain after UTKA has been noted and inadequate pain control has been demonstrated to be associated with inferior functional outcomes at 2 years after TKA[19]. Thus, postoperative pain has been an issue frequently concerning patients as to whether the intensity of pain and disablement during convalescence from BTKA are worse than that following UTKA. Nevertheless, there has been limited evidence comparing postoperative pain and functional recovery after BTKA and UTKA, and the known results are still equivocal[20,21]. Therefore, the objective of the present study was to compare the perioperative outcomes including perioperative blood loss (PBL), cardiac biomarkers, pain intensity and functional recovery, and complications between patients undergoing UTKA and BTKA with a similar perioperative protocol. The authors hypothesized that patients undergoing BTKA may require additional perioperative care and monitoring to improve outcomes.

MATERIALS AND METHODS

The study received institutional review board approval for retrospective analysis of data recorded prior to initiation and has been registered as TCTR20181220001. The authors' criteria for BTKA were painful bilateral end-stage OA knees, and therefore the selection of BTKA or UTKA was based upon patient preference. Consecutive patients who had undergone UTKA and BTKA for primary OA, performed by a single surgeon between January 2016 and December 2019, were enrolled in the study. The exclusion criteria of this study were patients with a history of prior knee surgery or previous knee infection. Participants with an American Society of Anesthesiologists (ASA) score > 3, known cardiopulmonary comorbidity or high-sensitivity Troponin-T (hs-TnT) > 14 ng/L, CKD stage ≥ 3, or significant renal impairment (serum creatinine > 1.5 mg/dL) were also excluded.

All the UTKA and BTKA were performed by a single surgeon with identical pre-, peri-, and postoperative protocols. Regional anesthesia, prophylactic intravenous antibiotics (ATB), and tourniquet control at 250 mmHg were applied for all patients. A medial parapatellar approach was performed through an approximately 10 cm midline skin incision, the cruciate ligaments were excised, and conventional instruments were then used to prepare the proximal tibial and distal femoral bone cuts by using extramedullary and intramedullary reference guides, respectively. A bone plug was applied to occlude the opening hole of the distal femur after finishing all the bone cuts. Soft tissue balancing was performed to achieve appropriate flexion and extension gaps. The patella was selectively resurfaced. Before prosthesis implantation, local infiltration anesthesia (LIA) was induced by injecting Bupivacaine (0.5% Marcaine; AstraZeneca, Sweden), 30 mg of ketorolac tromethamine (ketorolac tromethamine 1 mL; SiuGuan, Taiwan), and sterile normal saline solution into the

anterior and posterior compartment of the knee with the 2:1 ratio technique. All the patients received a fixed bearing, posterior stabilized prosthesis which was implanted with bone cement. A vacuum drain was then applied, and 15 mg/kg of topical tranexamic acid was poured into the knee joint before closure of the arthrotomy. The drain was clamped for 3 h and subsequently removed at 24 h after the surgery.

For postoperative management, intravenous patient-controlled analgesia morphine (100 mL solution containing 50 mg of morphine sulphate) was injected as an on-demand bolus of 1 mL with a 5 min lockout period, 30 mg of ketorolac was given intravenously every 8 h, and 500 mg of oral acetaminophen was administered three times a day. After 48 h, all the catheters were discarded, and 2 mg of morphine were injected every 8 h with an additional 2 mg of morphine used for a breakthrough pain throughout hospitalization. Also, oral medications including 250 mg of naproxen twice a day and 500 mg of acetaminophen three times a day were given. All patients were administered with low molecular weight heparin for the first 48 h and combined with oral warfarin for 10 d. Rehabilitation including active ankle pump was started after the surgery, and a continuous passive motion device was utilized on the day after surgery. Every patient was encouraged to attempt early ambulation with gait aids as able to be tolerated.

Data collected for analysis were patient demography, visual analogue scale (VAS) scores of postoperative pain, morphine consumption, range of knee motion (ROM), straight leg raise (SLR), length of stay (LOS), and laboratory evaluation comprising serum hemoglobin (Hb), blood transfusion rate, creatine phosphokinase (CPK), and hs-TnT preoperatively and at 24, 48, and 72 h after the surgery.

The patient's total blood volume (TBV) was calculated by the equation of Nadler *et al*[22]. The difference between preoperative and lowest postoperative Hb was applied with the Hb balance method to determine PBL[2].

Males: TBV (mL) = [0.0003669 × height^3 (cm)] + [32.19 × body weight (kg)] + 604

Females: TBV (mL) = [0.0003561 × height^3 (cm)] + [33.08 × body weight (kg)] + 183

PBL (mL) = TBV (mL) × (Hb_i – Hb_e)/Hb_i + sum of blood products transfused (mL), where Hb_i (g/dL) is the preoperative Hb, and Hb_e (g/dL) is the postoperative Hb.

Serum Hb level that drops below 9.0 g/dL is indicated for blood transfusion for both the UTKA and BTKA at our institution. A hs-TnT level > 14 ng/L is considered as possible for MI in our laboratory system. Any complications and readmission rates at 90 d after the index surgery were recorded.

Statistical analysis

All demographic data and measured outcomes are summarized with descriptive statistics. Continuous data are presented as the mean and standard deviation, and Student's *t*-test was used to compare between the UTKA and BTKA groups. Categorical data which are presented as counts and percentages were compared by using Chi-square or Fisher's exact test. Repeated-measures analysis of variance was applied to compare the time-dependent variables including VAS, ROM, SLR, Hb, CPK, and hs-TnT between groups. The *post hoc* comparisons of all pairwise points in time were applied to account for multiple testing with Bonferroni adjustments. A multiple logistic regression analysis was performed to determine which of these variables, including age, gender, body mass index (BMI), ASA physical status classification, and preoperative Hb, were the predictive factors for allogeneic blood transfusion. The sample size of the UTKA and BTKA groups had 99.5% power to detect a difference of 200 mL in PBL, which could significantly impact on blood transfusion rate, with standard deviation (SD) of 400 mL, and 95.4% power to ascertain a difference of 1.0 for VAS with SD of 2.5, with type I error of 5%. Stata/MP 15.0 software (StataCorp LP, College Station, TX, United States) was used for all statistical analyses. Statistical significance was defined as $P < 0.05$.

RESULTS

There were 210 UTKA and 137 BTKA included for analysis. The demographic and perioperative characteristics are briefly summarized in Table 1. Patients in the BTKA group were younger and more predominately female, and had a longer total duration of operation (TDO).

Blood loss

The postoperative Hb level of both groups gradually dropped and reached the lowest point at 72 h after the surgery. BTKA was associated with a significantly lower level of

Table 1 Demographic and perioperative characteristics

	UTKA	BTKA	*P* value
Age (yr)	65.00 ± 7.48	63.10 ± 6.83	0.02[a]
Gender (female/male)	178/32	129/8	0.01[a]
BMI (kg/m^2)	26.99 ± 3.49	26.54 ± 3.89	0.20
ASA (1/2/3)	4/134/72	5/101/31	0.05
Preop. VAS pain score	6.89 ± 2.33	6.77 ± 1.89	0.44
Preop. ROM	113.86 ± 13.55	111.16 ± 14.26	0.13
Preop. Hb (g/dL)	12.60 ± 1.19	12.44 ± 1.08	0.21
Preop. CPK (u/L)	125.05 ± 84.64	116.05 ± 65.12	0.41
Preop. TnT (ng/dL)	6.77 ± 3.04	6.46 ± 3.18	0.79
TDO (min)	62.21 ± 9.86	125.12 ± 16.30	< 0.01[a]

[a]$P < 0.05$ indicates statistical significance. All parameters are presented as the mean ± standard deviation, except for gender and American Society of Anesthesiologists score.

BMI: Body mass index; ASA: American Society of Anesthesiologists; Preop.: Preoperative; VAS: Visual analog scale; TDO: Total duration of operation; Hb: Hemoglobin; sCr: Serum creatinine; TnT: Troponin-T; CPK: Creatine Phosphokinase; UTKA: Unilateral total knee arthroplasty; BTKA: Bilateral one-stage total knee arthroplasty.

Hb than UTKA at 24, 48, and 72 h postoperatively (Figure 1). The PBL of the UTKA *vs* BTKA group was 646.45 ± 272.26 mL *vs* 1012.40 ± 391.95 mL ($P < 0.01$), respectively.

Blood transfusion rates in UTKA and BTKA were 10.48% (22/210) and 40.88% (56/137), ($P < 0.01$), respectively. For UTKA, 18 of 69 (26.09%) patients with preoperative anemia (defined as preoperative Hb < 12 g/dL in females and < 13 g/dL in males) received blood transfusion compared to 6 of 141 (4.26%) patients without anemia ($P < 0.01$). Twenty-eight of 43 (65.12%) patients with preoperative anemia in the BTKA group required a transfusion, whereas patients without anemia had a transfusion rate of approximately 1 in 4 (26/94, 27.67%; $P < 0.01$). The multivariate analysis demonstrated that preoperative Hb [odd ratio (OR): 0.33, 95% confidence interval (CI): 0.22-0.50, $P < 0.01$] and BMI (OR: 0.90, 95%CI: 0.81-0.99, $P = 0.03$) were predictive factors for blood transfusion in the BTKA group, whereas preoperative Hb (OR: 0.21, 95%CI: 0.12-0.37, $P < 0.01$) was only a determinant in the UTKA group when using similar perioperative blood management and cut-off values for transfusion.

Postoperative pain and recovery

There was no difference between the UTKA and BTKA groups regarding VAS scores at 6, 12, and 24 h, but the BTKA group had significantly higher VAS scores than the UTKA group at 48, 72, and 96 h after surgery (Figure 2A). The BTKA group had a significantly lower degree of SLR than the UTKA group at 72 h; however, the ROM was comparable between groups throughout the study period (Figure 2B and C). Total morphine consumption in the UTKA *vs* BTKA group was 11.93 ± 9.20 *vs* 13.81 ± 10.81 ($P = 0.16$) at 24 h, and 16.78 ± 13.24 *vs* 19.51 ± 15.47 ($P = 0.15$) at 48 h postoperatively. The incidence of postoperative nausea and vomiting (PONV) during the first 24 h in the UTKA and BTKA groups was 38.79% (90/142) and 46.47% (112/129) ($P = 0.09$), respectively. The UTKA had an LOS of 4.01 ± 0.97 d, which was significantly shorter than that of the BTKA group (5.17 ± 1.32 d; $P < 0.01$).

Cardiac biomarkers

The BTKA group showed significantly higher CPK than the UTKA group at 24 h and 48 h after the surgery (Figure 3A). For the hs-TnT, it was gradually rising during 72 h after the UTKA and it was rising to a peak at 48 h after the BTKA, but the hs-TnT level was not significantly different between groups along the study period (Figure 3B). Nonetheless, there were 12 patients (5.71%) who had hs-TnT > 14 ng/L during the first 72 h after the UTKA compared to 17 patients (12.41%) following the BTKA ($P = 0.04$), but no patient presented cardiovascular symptoms and signs, or abnormal electrocardiogram indicating MI.

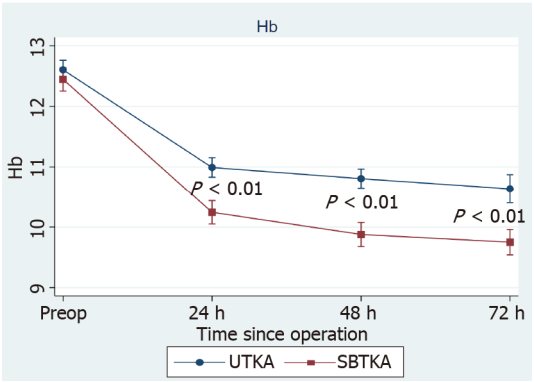

Figure 1 Serum hemoglobin levels preoperatively and at 24 h, 48 h and 72 h after the surgery. UTKA: Unilateral total knee arthroplasty; SBTKA: Safety of bilateral one-stage total knee arthroplasty.

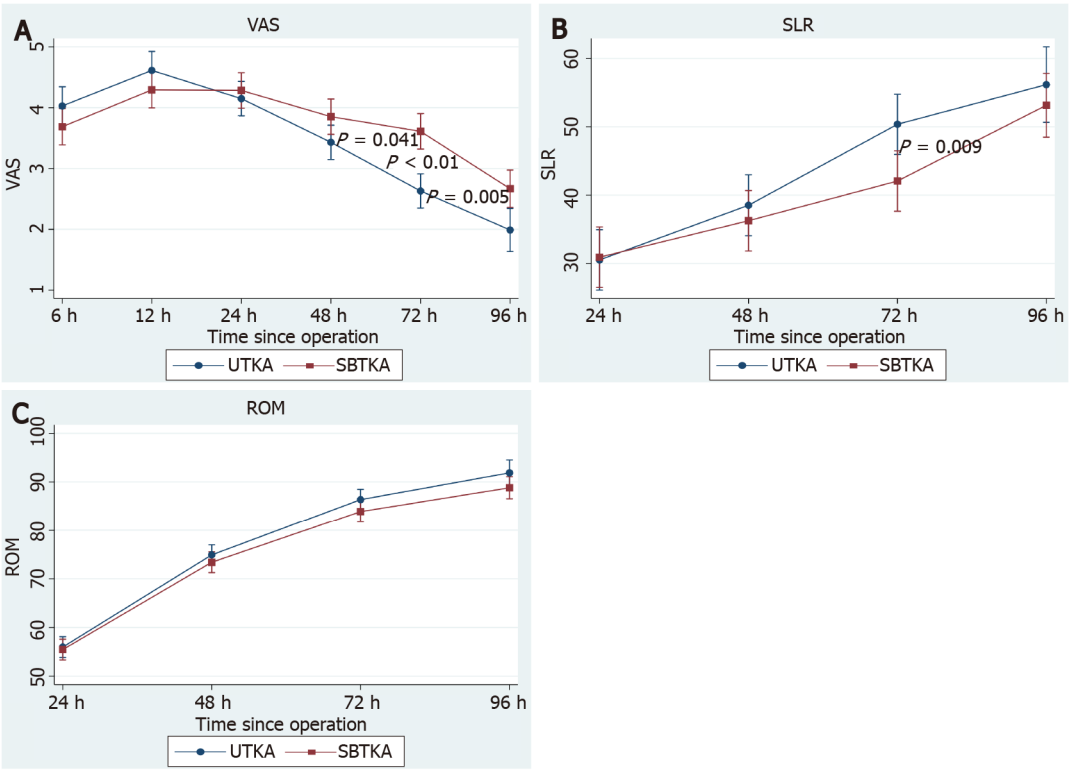

Figure 2 Index changes in different time periods after operation. A: Visual analog scale scores for pain intensity determined at 6 h, 12 h, 24 h, 48 h, and 72 h after the surgery; B: Straight leg raise assessed at 24 h, 48 h, and 72 h postoperatively; C: Range of knee motion measured at 24 h, 48 h, and 72 h after the surgery. VAS: Visual analogue scale; ROM: Range of knee motion; SLR: Straight leg raise; UTKA: Unilateral total knee arthroplasty; SBTKA: Safety of bilateral one-stage total knee arthroplasty.

Complications and readmission at 90 d

During the 90 d after the index surgery, there was one superficial infection, one cerebrovascular event, and two deep vein thromboses (DVT) in the UTKA group. For the BTKA group, one patient experienced peptic ulcer bleeding, one had DVT in the unilateral leg, and one had periprosthetic joint infection (PJI) which was successfully treated by two-stage revision TKA. Additionally, each group had one patient who required readmission due to severe pain at the surgical site.

DISCUSSION

Bilateral one-stage TKA potentially increases the rate of complications which are related to more soft tissue trauma, blood loss, postoperative pain, and cardiovascular

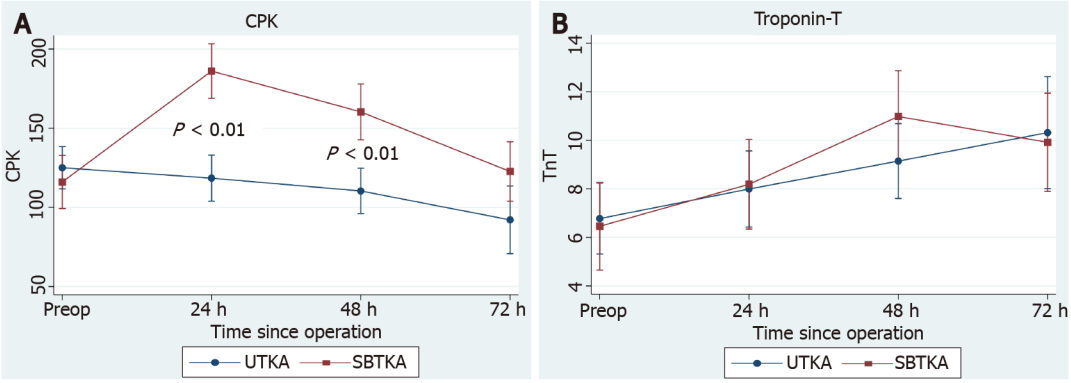

Figure 3 Changes in creatine phosphokinase and high-sensitivity Troponin-T before operation and at 24 h, 48 h, and 72 h after operation.
A: Creatine phosphokinase evaluated preoperatively and at 24 h, 48 h, and 72 h postoperatively; B: High-sensitivity Troponin-T preoperatively and at 24 h, 48 h, and 72 h postoperatively. CPK: Creatine phosphokinase; UTKA: Unilateral total knee arthroplasty; SBTKA: Safety of bilateral one-stage total knee arthroplasty.

adverse events, and therefore this is still a concerning issue for some patients and surgeons[8,9]. However, recent studies reported that BTKA in selected patients is as safe as the staged procedure, but proper patient screening, and perioperative care and monitoring to avoid complications and mortality are still controversial[23,24]. In the current study, BTKA was associated with significantly greater blood loss and higher allogeneic blood transfusion rates, as well as higher CPK levels, when compared to the UTKA group. The BTKA group tended to have higher hs-TnT levels at 48 h despite not reaching statistical significance. After 48 h, the BTKA group had a significantly higher VAS score than the UTKA group, and the SLR at 72 h after the BTKA was also worse than that after the UTKA. The LOS of the BTKA group was also significantly longer than that for the UTKA group. Nevertheless, the total morphine use, ROM, complications, and 90-d readmission rate were not different between the groups.

Generally, BTKA is known for its association with inevitably greater blood loss than UTKA. Advances in surgical techniques, use of TXA, and change in transfusion thresholds have substantially reduced postoperative transfusions following UTKA[3]. Recently, TXA is widely respected as an effective anti-fibrinolytic agent and has been demonstrated as having advantages when used in BTKA[25]. Although TXA is effective for reducing blood loss following BTKA, when it is applied either intravenously (IV) or intra-articularly (IA), the ideal regimen of TXA is still not well defined[13]. Arora *et al*[26] revealed no difference in average drop of Hb and blood transfusion rate between patients undergoing BTKA with IV-TXA or IA-TXA. Also, combined IA and IV TXA administration in BTKA did not show superior efficacy in blood loss reduction[27]. Therefore, the intraoperative IA-TXA use alone, in our study, should be sufficient to control blood loss, while avoiding potential complications related to systemic administration of TXA. However, our transfusion rate in BTKA is still quite high at 40.88%. Chalmers *et al*[28] retrospectively reviewed 475 patients who underwent BTKA and received double doses of TXA and contemporary blood management. They found that BTKA is still associated with a blood transfusion rate of approximately 1 in 5, and 50% of patients with a preoperative Hb < 12.5 required blood transfusion. Accordingly, we identified the preoperative Hb as a predictive factor for allogeneic transfusion in BTKA. Particularly, approximately 1 out of 3 patients in our study had preoperative anemia, and this finding may underline the opportunity for further improvement and for addressing this modifiable risk factor before BTKA. Delasotta *et al*[29] demonstrated that giving three preoperative doses of epoetin-α could significantly increase Hb levels and reduce blood transfusions in BTKA. Intravenous iron supplementation has also been reported for its efficacy in reducing the rate of transfusion in BTKA when combined with IA-TXA administration [30]. Other determinants including female gender, preoperative Hb level, operative time, and drain use have also been identified as risk factors for blood transfusion in BTKA[11,28]. In addition, soft tissue surface and intramedullary canal violation have been revealed as a possible significant source of bleeding[11,31-33]. Nevertheless, the efficacy of fibrin sealant applied to the bleeding soft tissue is unclear for blood loss reduction in BTKA[31], and also outcomes of emerging technologies such as computer-assisted or accelerometer-based navigation are still equivocal[13,34].

Significant pain after UTKA has been noted and this has been an issue frequently concerning patients as to whether the intensity of pain and disablement, during

convalescence from BTKA, is worse than that of UTKA. Shetty *et al*[20] reported that BTKA had significantly higher VAS pain scores than UTKA on the first postoperative day. However, the VAS, ROM, and SLR were equal in both groups at the time of discharge. Other researchers found a 1-point higher VAS in the BTKA group during day 1, with 20% more narcotic use for the first 48 h, and patients in the BTKA group lagged behind the UTKA group in ambulatory milestones by approximately 36 h[21]. In the present study, we found that the UTKA and BTKA group had comparable pain intensity, morphine consumption, and knee function during the first 24 h after the surgery by using the same multimodal pain management. The neuroaxial anesthesia, LIA that was induced by injecting with bupivacaine and ketorolac tromethamine, and opioid-sparing analgesia with a multidrug regimen may be an explanation of the effective pain control during the first 24 h after UTKA and BTKA. Despite that, patients in the BTKA gradually developed higher pain scores afterwards and had worse SLR at 72 h. Higher postoperative CPK levels might reflect the certainty of more muscle injury in the BTKA, and so may indicate the need for intensive pain control extended beyond 48 h after the surgery. Intravenous administration of non-steroidal anti-inflammatory drugs (NSAIDs) is commonly used because of their efficacy in controlling post-TKA pain and may be administered up to 72 h after the surgery. Recently, Parecoxib, which is a selective cyclooxygenase-2 (COX-2) inhibitor, has been demonstrated to be effective in the reduction of post-TKA pain with the additional advantage of having less platelet inhibition and is consequently associated with less blood loss when compared to conventional NSAIDs[2]. Furthermore, intravenous corticosteroid and acetaminophen were also revealed as useful adjuncts for mitigating pain after TKA[35,36].

The safety of BTKA is still debated. Chen *et al*[24] recently demonstrated that patients aged > 80 years with an ASA score ≥ 3 who received careful screening for cardiopulmonary disorder and contemporary perioperative management for BTKA, had significantly decreased incidences of major and minor complications. Gromov *et al*[37] reported a 0% incidence of mortality in 284 selected patients without cardiopulmonary compromise, and they also found that ASA score ≥ 3 was a risk factor for 90-d readmission and prolonged LOS whereas higher BMI was a weak predictive factor for readmission. Lindberg-Larsen *et al*[23] conducted a study to compare outcomes after simultaneous and staged bilateral TKA in propensity-scores matched patients from nine centers. Of 232 matched patients in each group, perioperative complications and re-operation rates were significantly higher after simultaneous bilateral TKA. However, there was no difference in the rate of readmission within 30 d as well as the mortality between groups. In the present study, the hs-TnT level, which is a biomarker for cardiac muscle injury, was not different between UTKA and BTKA when patients had an ASA score ≤ 3 and preoperative hs-TnT within normal values. Although there were 12 and 17 patients after the UTKA and BTKA who had hs-TnT > 14 ng/L, no patients in either group presented symptoms and signs of cardiovascular complications. Hence, serial testing of cardiac biomarkers may be indicated only when patients have suspected clinical presentation[38]. Additionally, Hb evaluation seems to be unnecessary for non-anemic patients who undergo UTKA, due to the very low risk for blood transfusion. However, we suspect that Hb testing at 48 h after BTKA may be appropriate as a reflection of ongoing blood loss that is possibly linked to cardiac stress because the hs-TnT was rising to a peak at 48 h after BTKA when the Hb level was dropping. For other complications, the risk of PJI and DVT was not different between BTKA and UTKA when similar prophylaxis ATB and anticoagulants were applied. Nevertheless, further investigation may be needed to develop well-defined guidelines for perioperative monitoring in patients undergoing BTKA to decrease potential morbidity and mortality.

Nonetheless, we realized some limitations of the present study. First, this investigation is retrospective with some limitations accorded by study design, even if the selection of BTKA or UTKA as patient preference might be better accommodated with our real-life practice. Second, both study groups comprised predominantly female patients. However, previous studies found that gender has no effect on blood loss and functional recovery following TKA[12,39]. Third, variation of thresholds or cut-off values for blood transfusion among individual institutions may result in a different transfused rate. Indeed, the incidence of patients with preoperative anemia in our study seems to be higher than previously reported[3] and thereby may be a reason for higher transfusion rates than those reported in other studies[4,28]. Lastly, our sample size might not be sufficient to assess the exact risk of cardiovascular events and thromboembolism after UTKA and BTKA.

CONCLUSION

Following similar perioperative management, the blood transfusion rate in BTKA is 4-fold that required in UTKA. Also, BTKA is associated with higher pain intensity at 48 h postoperatively and prolonged LOS when compared to UTKA. Hence, patients undergoing BTKA may require more extensive perioperative management for blood loss and pain, even if they have no higher risk of complications and 90-d readmission than those receiving UTKA.

ARTICLE HIGHLIGHTS

Research background

Bilateral one-stage total knee arthroplasty (BTKA) is a notable option for patients with bilateral end-stage knee arthropathy because of the potential advantages that include reduction in total hospitalization and rehabilitation time, as well as overall cost.

Research motivation

Despite previously acknowledged benefits, there is an issue frequently concerning patients as to whether the intensity of pain and disablement during convalescence from BTKA is worse than that following unilateral total knee arthroplasty (UTKA). Also, the risk of cardiovascular morbidity and other complications are subjects that lead some surgeons to refrain from BTKA. Thus, our objective was to identify what perioperative aspects of BTKA need to be improved and handled differently than for UTKA.

Research objectives

To compare the perioperative outcomes including perioperative blood loss (PBL), cardiac biomarkers, pain intensity, functional recovery, and complications between UTKA and BTKA by using an identical perioperative protocol.

Research methods

All patients who had undergone UTKA and BTKA for primary osteoarthritis that had been performed by a single surgeon with identical perioperative protocols between January 2016 and December 2019 were retrospectively reviewed. The exclusion criteria of this study included patients with an American Society of Anesthesiologists score > 3, known cardiopulmonary comorbidity or high-sensitivity Troponin-T (hs-TnT) > 14 ng/L, CKD stage ≥ 3 or significant renal impairment (serum creatinine > 1.5 mg/dL), prior knee surgery, and previous knee infection.

Research results

Patients who received BTKA had significantly higher PBL with a 4-fold greater transfusion rate. As well, the patients in the BTKA group had higher visual analogue scale scores at 48, 72, and 96 h after the surgery and a higher postoperative creatine phosphokinase level. Consequently, a longer length of hospital stays than those who had UTKA was required. However, there was no difference regarding the postoperative hs-TnT level and complications.

Research conclusions

Patients who undergo BTKA may require more extensive perioperative care for blood loss and pain than those patients who undergo UTKA.

Research perspectives

Future prospective studies may be required to develop a particular perioperative protocol in patients undergoing BTKA to decrease potential morbidity and mortality.

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ORIGINAL ARTICLE

Retrospective Study

Epidemiology and incidence of paediatric orthopaedic trauma workload during the COVID-19 pandemic: A multicenter cohort study of 3171 patients

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Institutional review board statement: This study was reviewed and approved by the Ethics Committee of the Aalborg University Hospital. The Danish Data Protection Agency approved the study.

Informed consent statement: This study was conducted in accordance with the ethical standards of the responsible committee and with the ethical principles of the 1975 Declaration of Helsinki.

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Abstract

BACKGROUND

Coronavirus disease 2019 (COVID-19) has a major influence on all parts of society.

AIM

To examine the consequences of the national lockdown and political initiatives during the first surge of the COVID-19 pandemic expressed by changes in incidences of musculoskeletal paediatric injuries.

METHODS

Study design was a retrospective multicenter cohort study. A 'pandemic' cohort was established from 16 March 2020 to 21 April 2020, where all institutions including day care and schools were closed. A 'pre-pandemic' cohort was established from the same period in 2019 for comparison. Included were all patients admitted at the emergency departments with paediatric musculoskeletal injuries (aged 0-15 years) identified by a relevant musculoskeletal ICD-10 diagnosis (DSxxx), concussions (DZ033D), or burns (DT2xx).

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RESULTS
The 'pre-pandemic' cohort consisted of 2101 patients, and the 'pandemic' cohort consisted of 1070 patients, indicating a decrease of paediatric musculoskeletal injuries of 51%. The incidence of paediatric injury in the 'pre-pandemic' cohort was 10460/100000/year. In the 'pandemic' cohort, the incidence was 5344/100000/year.

CONCLUSION
A resource re-allocation to help serve the COVID-19 patients might be possible without reducing the level of care for injury-related paediatric patients.

Key Words: COVID-19; SARS-CoV-2; Paediatric trauma; Paediatric emergency; Paediatric fracture

Core Tip: Coronavirus disease 2019 (COVID-19) has had a significant impact on all parts of society and medical services. Here we compare the epidemiology of paediatric trauma at major university hospitals and rural hospitals before and during COVID-19 lockdown in 3171 emergency department contacts.

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INTRODUCTION

From the first reported case of coronavirus disease 2019 (COVID-19) in December 2019 in Wuhan, China, the severe acute respiratory syndrome coronavirus 2 virus spread around the globe at a rapid pace. The World Health Organization declared it a global pandemic on 11 March 2020.

A national lockdown was issued on 11 March 2020 in Denmark, including prolonged closure of schools and the cessation of sporting activities, social activities, and other close-contact situations. The aetiology of paediatric injury is coherent to physical and sporting activities; hence a reduction in paediatric injuries and consultations at the emergency department was to be expected[1-4].

Several epidemiological studies before the COVID-19 pandemic have shown incidence rates of paediatric fracture of 1800-2000/100000/year[3-7]. However, a general overview of musculoskeletal injury treated at emergency departments is poorly reported[8]. To the authors' knowledge, only one former study examined musculoskeletal injuries seen at the emergency department using a population-based incidence rate and reported an incidence of 6300/100000/year[9].

Although current literature investigates the frequencies of paediatric injuries during the COVID-19 pandemic, no overview of the pandemic's consequences of the pandemic on population-based incidences of paediatric injuries and related trauma mechanisms is available[10-15].

The present study aimed to examine the consequences of the national lockdown from 16 March till 21 April 2020 and political initiatives during the first surge of the COVID-19 pandemic expressed by changes in incidences of musculoskeletal paediatric injuries at the emergency departments across multiple hospitals. Furthermore, the aim was to examine changes in the mode of injury and related trauma mechanisms observed.

MATERIALS AND METHODS

The study design was a retrospective cohort study investigating the incidence of paediatric musculoskeletal injuries in patients aged 0–15 years, before and during the national COVID-19 pandemic lockdown in the northern and middle parts of Denmark.

A 'pandemic' cohort was established from 16 March 2020 to 21 April 2020, where all institutions including day care and schools were closed. A 'pre-pandemic' cohort was established from the same period in 2019 for comparison.

Included were five regional hospitals and two university hospitals. The hospitals serve rural and suburban areas with a population of 198138 citizens between 0–15 years of age during the study period in 2019, representing the 'pre-pandemic cohort'. The 'pandemic' cohort includes a population of 197516 citizens during the study period.

In Denmark, a unique possibility of performing population-based studies is present since Danish law requires all patient contact with hospitals and clinics to be registered in the Danish National Patient Register (DNPR)[16]. All Danish residents receive a civil registration number that is registered in the Civil Registration System. Hospital identification, date and time of hospitalization, and municipality are registered. Therefore, a complete registry of all health-related issues, both individual and population-based, is obtainable.

Based on the DNPR, the 'pandemic' and the 'pre-pandemic' cohorts were established for comparison.

Included were all patients admitted at the emergency departments with paediatric musculoskeletal injuries identified by a relevant musculoskeletal ICD-10 diagnosis (DSxxx), concussions (DZ033D), or burns (DT2xx).

Clinical information about diagnosis, age, gender, date, and mode of injury was obtained. Manual chart and X-ray review of 50% of the medical charts (n = 1546) was performed for validating the register data.

This study was conducted in accordance with the ethical standards of the responsible committee and with the ethical principles of the 1975 Declaration of Helsinki. The Danish Data Protection Agency approved the study. The reporting of the study complies with the Strengthening the Reporting of Observational Studies in Epidemiology Statement[17].

RESULTS

In total, 3171 paediatric injuries leading to an emergency department visit at one of the five hospitals were included in the study. The 'pre-pandemic' cohort consisted of 2101 patients, and the 'pandemic' cohort consisted of 1070 patients, indicating a decrease of paediatric musculoskeletal injuries in patients aged 0–15 years of 51% during the COVID-19 pandemic.

Primary outcome

The overall incidence of paediatric injury in the 'pre-pandemic' cohort was 10460/100000/year. In the 'pandemic' cohort, the overall incidence was 5344/100000/year, indicating a twofold decrease in paediatric emergency patients during the COVID19 pandemic.

Secondary outcomes

Gender-divided and age-specific incidence rates are depicted in Figure 1A and B. The incidence rates showed a similar bimodal trend for both genders. Before the pandemic the incidence rates were significantly higher in the age group from 9-15 years compared with the incidence during lockdown of the society (Figure 1A).

No differences were found in the proportion of the various diagnoses, with fractures being the most common in both cohorts. A higher proportion of injuries were found on school days in the 'pre-pandemic' cohort than the 'pandemic' cohort (Supplementary Table 1).

A proportional increase in bicycle (51%), skateboard, scooter, rollerblade (36 %), and trampoline injuries (98%) between the 'pre-pandemic' and the 'pandemic' cohorts was observed. A marked decrease in sports-related injuries and collisions with objects was observed in the 'pandemic period' compared to the pre-pandemic period. (Supplementary Table 2) In the age group 9–15 years of age (Figure 2A and B), a similar distribution was observed, indicating a shift in sporting activities to home-based activities.

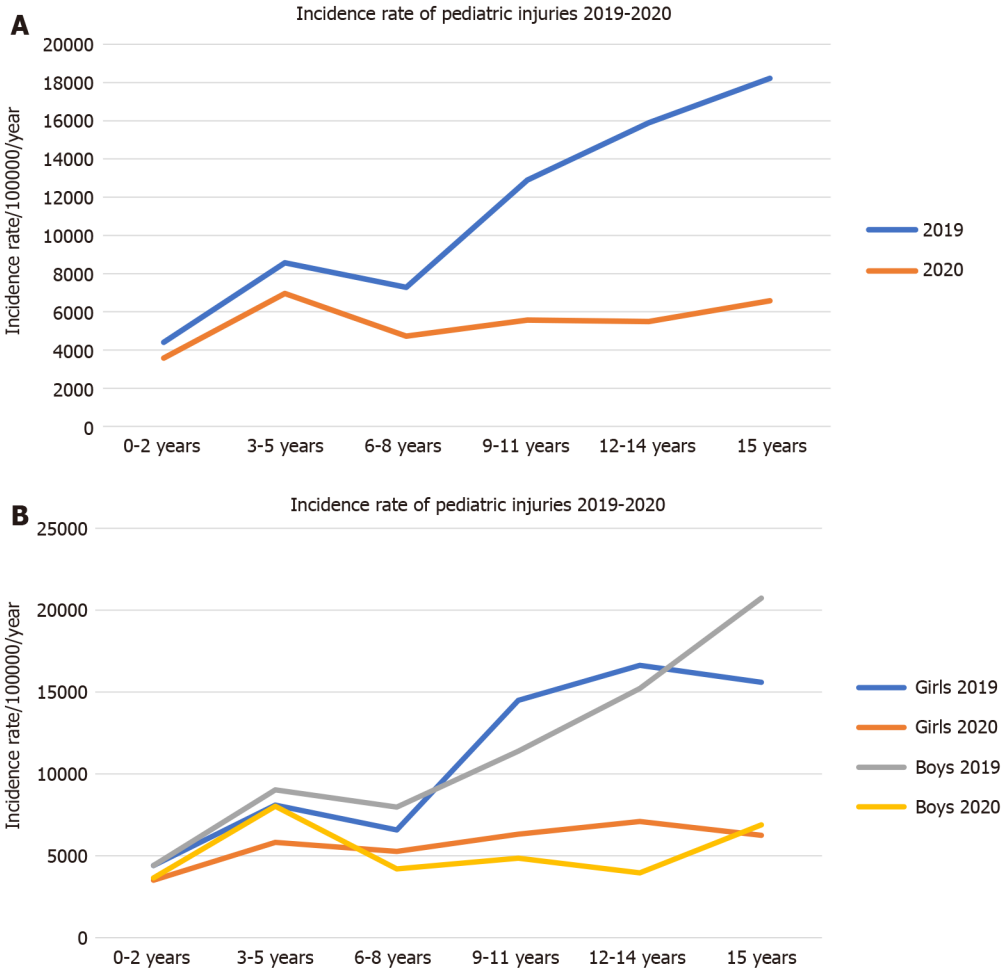

Figure 1 Incidence rates of pediatric injuries 2019 and 2020. A: Divided by year; B: divided by gender.

The manual review of 50% of all contacts showed a high level of accuracy of both diagnosis (< 99%) and trauma mechanism (< 99%), indicating that register data are of very high quality.

DISCUSSION

The overall incidence rate for paediatric injury decreased two-fold during the COVID-19 national lockdown from 16 March 2020 – 21 April 2020 compared with the same weeks in 2019. The overall incidence was 10460/100000/year in 2019 and 5344/100000/year during the lockdown in 2020.

Results from the present study are supported by Sheridan *et al*[18], examining the effect of COVID-19 regulations using the incidence rate for paediatric trauma admissions in Ireland. A reduction of paediatric admissions from 0.146 admissions/person-year to 0.139 admissions/person-year in the pandemic period was reported. Sheridan *et al*[18] reported on relatively small numbers, with only 28 paediatric patients included in the pandemic group. Most other studies evaluating the effect of the COVID-19 pandemic did not report on the incidence, making a further comparison of results from the present study difficult.

Several studies examined the effect of the COVID-19 Lockdown with regards to the prevalence and found a decrease between 33%-68% of paediatric fractures[10-13]. These results align with the present study reporting a decrease of paediatric musculoskeletal injuries in patients aged 0–15 years of 51% during the COVID-19 pandemic.

The age-specific incidence rates showed a bimodal distribution. Children below nine years of age showed similar distributions between the 'pandemic' and the 'pre-pandemic' cohorts. In contrast, children above nine years of age in the 'pandemic' cohort showed a marked decrease in the incidence rates during the COVID-19 Lockdown. This pattern was similar for both genders.

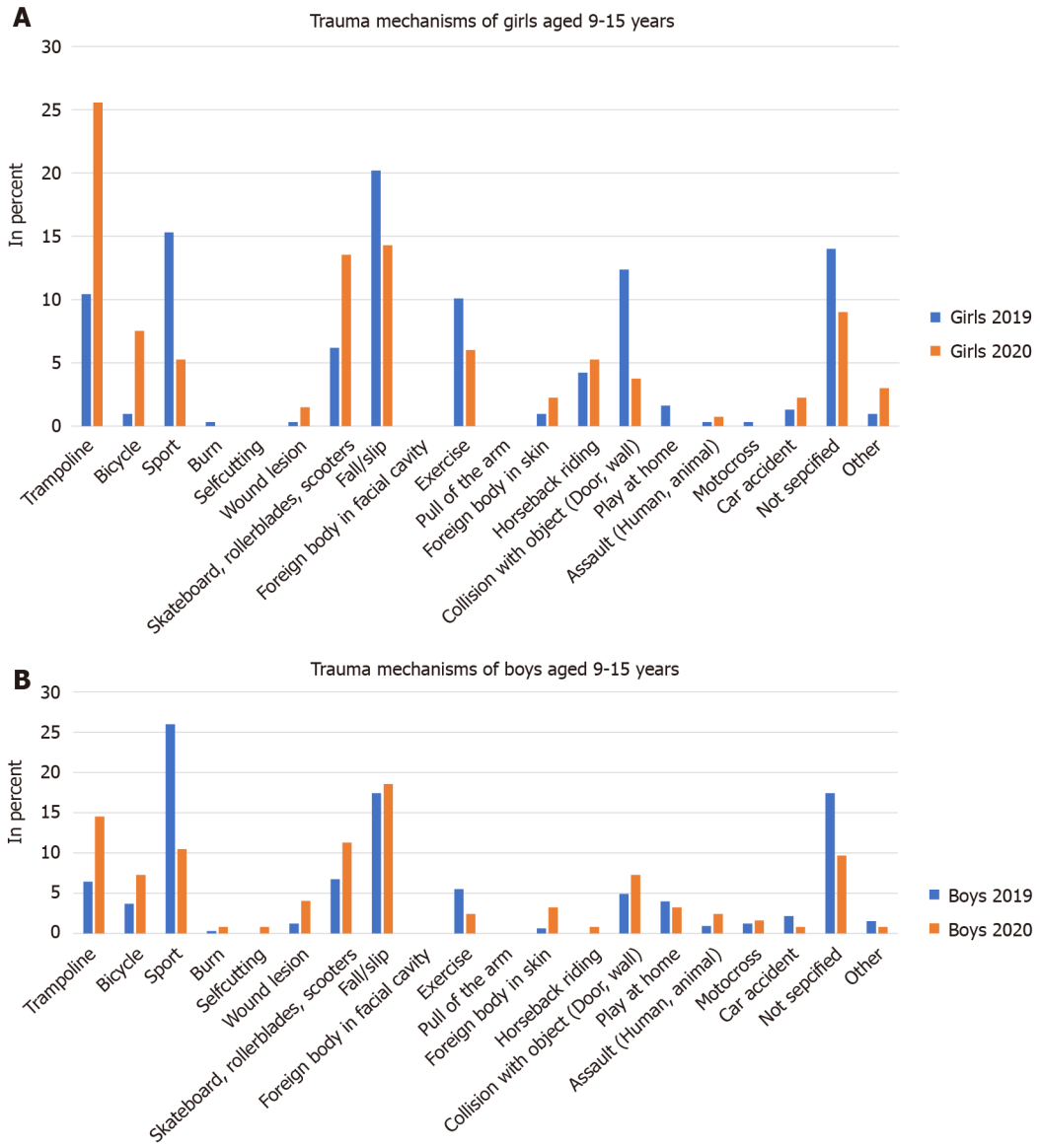

Figure 2 Trauma mechanisms of girls and boys aged 9-15 years. A: Girls; B: Boys.

These findings are corroborated by Bram *et al*[10] and Keays *et al*[14], reporting that the prevalence of paediatric fracture and injury-related emergency department visits decreased the most in children above 12 years of age during the COVID-19 pandemic. The observed decrease in the incidence in the adolescent populations during the COVID-19 pandemic may be due to a reduction in sporting activities and social activities compared to the younger children.

The distribution of paediatric musculoskeletal injuries in patients aged 0–15 years was almost comparable between the 'pre-pandemic' and the 'pandemic' cohorts. The most common diagnose was fracture (2019: 34.0%, 2020: 33.9%) followed by contusion (2019: 19.2%, 2020: 16.2%) and distortion (2019: 18.5%, 2020: 14.3%).

Several studies report change in the distribution of trauma mechanisms during the COVID-19 pandemic[10-12,14]. The present study showed that a higher proportion of injuries in the 'pandemic' cohort was caused by trampoline, bicycling, skateboarding, scooters, and rollerblades compared to the 'pre-pandemic' cohort. Furthermore, a lower proportion of injuries was due to other sporting activities and exercise. Keays *et al*[14] reported a proportional rise in bicycling injuries in the pandemic period, but no change in injuries caused by trampoline, skateboarding, and scootering. Bram *et al*[10] reported an increase in the proportion of injuries during the COVID-19 pandemic occurring at home or on bicycles and a decrease in those related to sports. Other studies reported a reduction of injuries related to sports during the pandemic period [11-12]. These observed small differences between studies may be explained by differences in lockdown procedures in the different countries, influencing the closure

of schools, cessation of sporting activities, social activities, and other close contact situations. Furthermore, regardless of the COVID-19 pandemic, differences in trauma mechanisms between different countries are well-known.

At present, the health care system worldwide is strained due to a large number of patients with COVID-19. A simultaneous reduction in paediatric injuries is observed and well reported. A resource re-allocation to help serve the COVID-19 patients might be possible without reducing the level of care for injury-related paediatric patients. This knowledge could benefit the health care system in a future pandemic. Conversely, when reopening schools and returning to sports, an increase in emergency department visits by paediatric patients is to be expected.

The significant drop in incidence of pediatric injuries during the COVID-19 pandemic may indicates that safety priority issues and the development of prevention strategies may be needed. Guardians may help children to adhere to safety recommendations at play grounds, such as a maximum of one child per trampoline. However, most pediatric musculoskeletal injuries are minor and not complicated. The impact of COVID-19 on children and young people's mental health and well-being has been reported to weigh heavily[19]. The disruption to routines, education, recreation, as well as concern for family income and health, is leaving many young people with significant consequences due to the lock down. Furthermore, the lock down has been reported to significant decrease the level of children's physical activity[20]. Regular physical activity is well-known to improve cardiorespiratory fitness, build strong bones and muscles, control weight, reduce symptoms of depression, and reduce the risk of developing serious health conditions[21].

The present study has several limitations. A limitation may be the use of register data from the DNPR. However, reporting to the DNPR is required by law in Denmark, and allocation of cost to the health providers is partly based on the register. The DNPR is reported with an overall high quality of data, and the positive predictive value of orthopaedic diseases is reported to be 89%–91%[22]. Furthermore, a manual review of 50% of the data for validation showed high data completeness. Another potential limitation is a difference in coding between the different hospitals. However, variation among the various hospitals is of less importance as a difference in coding practice between the 'pandemic' and 'pre-pandemic' cohorts is expected to be comparable. Importantly, the manual check of 50% of the data did not reveal any signs of increase in non-accidental injuries, *i.e.* physical child abuse. However, health care workers should be aware that there may be an increased incidence during the pandemic[23].

CONCLUSION

The overall incidence rate for paediatric injury in the 'pre-pandemic' cohort was 10460/100000 persons/year. The overall incidence rate decreased to 5344/100000 persons/year in the 'pandemic' cohort. The primary decrease in incidence between the 'pandemic' and 'pre-pandemic' cohorts was observed in the adolescents.

ARTICLE HIGHLIGHTS

Research background

Coronavirus disease 2019 (COVID-19) had a major influence on all parts of society. During the total lockdown of the Danish society, we noticed a substantial change in the pediatric and adolescent trauma.

Research motivation

We aimed to quantify the change in workload and estimate the incidence rates.

Research objectives

The aim was to examine the consequences of the national lockdown and political initiatives during the first surge of the COVID-19 pandemic expressed by changes in incidences of musculoskeletal paediatric injuries.

Research methods

We compared the epidemiology of pediatric and adolescent trauma during the lockdown period of approximately one month with the same period of the previous

year.

Research results

The 'pre-pandemic' cohort consisted of 2101 patients, and the 'pandemic' cohort consisted of 1070 patients, indicating a decrease of paediatric musculoskeletal injuries of 51%. The incidence of paediatric injury in the 'pre-pandemic' cohort was 10460/100000/year. In the 'pandemic' cohort, the incidence was 5344/100000/year.

Research conclusions

A resource re-allocation to help serve the COVID-19 patients might be possible without reducing the level of care for injury-related paediatric patients.

Research perspectives

If new lockdowns are enforced, hospitals and emergency and orthopedic departments in particular may be able to redistribute workforce without compromising patient care.

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ORIGINAL ARTICLE

Clinical Trials Study

Can bedside needle arthroscopy of the ankle be an accurate option for intra-articular delivery of injectable agents?

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Clinical trial registration statement: Prior to the first inclusion, the study was registered at ToetsingOnline.nl with reference NL71185.018.19.

Informed consent statement: All patients provided written consent for their participation in the study prior to enrollment.

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Abstract

BACKGROUND

Bedside needle arthroscopy of the ankle under local anesthesia has been proposed for intra-articular delivery of injectable agents. Accuracy and tolerability of this approach in the clinical setting–including patients with end-stage ankle pathology and/or a history of prior surgery–is not known.

AIM

To assess clinical accuracy and tolerability of bedside needle arthroscopy as a delivery system for injectable agents into the tibiotalar joint.

METHODS

This was a prospective study that included adult patients who were scheduled for an injection with hyaluronic acid to the tibiotalar joint. In our center, these injections are used as a last resort prior to extensive surgery. The primary outcome was injection accuracy, which was defined as injecting through the arthroscopic cannula with intra-articular positioning confirmed by a clear arthroscopic view of the joint space. Secondary outcome measures included a patient-reported numeric rating scale (NRS, 0-10) of pain during the procedure and willingness of patients to return for the same procedure. NRS of ankle pain at rest

Conflict-of-interest statement: Dr. Kennedy reports consultancy fees from Arthrex, outside the submitted work.

Data sharing statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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

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Country/Territory of origin: Netherlands

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Peer-review model: Single blind

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

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and during walking was collected at baseline and at 2-wk follow-up. Complications were monitored from inclusion up to a 2-wk control visit.

RESULTS
We performed 24 inspection-injections. Eleven (46%) participants were male, and mean age was 46.8 ± 14.5 years. Osteoarthritis was the indication for injection in 20 (83%) cases, of which 8 (33%) patients suffered from osteoarthritis Kellgren-Lawrence grade IV, and 10 (42%) patients from Kellgren-Lawrence grade III. An osteochondral defect was the indication for injection in 4 (17%) cases. A history of ankle surgery was present in 14 (58%) participants and a history of multiple ankle surgeries in 11 (46%) participants. It was possible to confirm accuracy in 21 (88%) procedures. The 3 (12%) participants where needle arthroscopy did not reach a clear view of the joint space all suffered from Kellgren-Lawrence grade IV osteoarthritis. Pain during the procedure was reported with a median of 1 [interquartile ranges (IQR): 0–2]. Willingness to return was 100%. Pain in rest decreased from a median NRS of 4 (IQR: 2–7) at baseline to a median of 3 (IQR: 1–5) at follow-up ($P < 0.01$). Pain during walking decreased from a median NRS of 8 (IQR: 6–9) to a median of 7 (IQR: 4–8) ($P < 0.01$). Infections or other complications were not encountered.

CONCLUSION
Clinical accuracy and tolerability of bedside needle arthroscopy of the ankle as a delivery system for injectable agents are excellent. Accuracy was 100% in patients without total ventral joint obliteration.

Key Words: Ankle arthroscopy; NanoScope; Needle arthroscopy; Injections; Proof of concept; Patient experience

Core Tip: Needle arthroscopy is rapidly attracting the interest of the orthopedic field, as recent technical innovation has increased image quality and improved surgical handling. Bedside needle arthroscopy under local anesthesia has been proposed as a possible use. In this study, we performed needle arthroscopic inspection-injections of the tibiotalar joint in the procedure room and using only local anesthesia. We found high accuracy of these guided injections, and excellent patient tolerability of the procedure. The results of this study may form the groundwork for further expansion of indications that merit needle arthroscopy of the ankle under local anesthesia, including operative procedures.

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INTRODUCTION

Intra-articular injections play an important role in orthopedic surgery[1], and innovative injectable agents promise to further increase their importance as minimally invasive treatment[2,3]. Yet, accuracy of articular injections is often limited, which lowers the chance of a positive treatment effect[4]. In the tibiotalar joint, accuracy of injections ranges between a mere 67% and 77% when guided by palpation[4]. The effect of ultrasound guidance is highly variable, and often does not improve injection accuracy at all[5]. Inaccurate injections may be especially unacceptable in case of expensive biologic augments, slowly releasing delivery systems, or for injections that have a detrimental effect on soft tissue.

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Needle arthroscopy was first introduced in the 1990s, yet was never adopted as standard modality due to low image quality and inconvenient machinery. However, recent innovation has led to a substantial increase in image quality and has reduced the size of supportive devices to the likes of a tablet computer[6]. In a cadaveric study, this improved version of needle arthroscopy provided easy and safe access to the ankle[6].

Based on cadaveric experience, it has been suggested to use needle arthroscopy under local anesthesia as a means to inspect the ankle joint and to simultaneously deliver an injectable in a minimally invasive yet highly accurate manner[6]. Yet, feasibility of this approach has not been tested in a patient setting so far. The cadaveric setting may differ from clinical practice, as for example patient discomfort, time pressure, scar tissue and joint stiffness may hamper a successful procedure. Therefore, the aim of this study was to assess the accuracy and patient tolerability of bedside needle arthroscopy to deliver injectable agents to the ankle joint in a clinical setting, which may include participants with advanced pathology and a history of previous ankle surgery. We hypothesized that even in such a difficult patient group, we would be able to deliver injections with high accuracy, and that procedures would be well tolerated by patients.

MATERIALS AND METHODS

A prospective pilot study of consecutive patients was conducted in our academic hospital between December 2019 and December 2020. The study was approved by our institutional ethical review board with reference 2019_203 and conducted in agreement with the 1964 Helsinki Declaration and its later amendments. All patients provided written consent for their participation. The study was monitored by our institution's monitoring board. Prior to the first inclusion, the study was registered at ToetsingOnline.nl with reference NL71185.018.19.

Patients

All patients between 18 years and 80 years of age that were planned for an injection with hyaluronic acid in the tibiotalar joint were potentially eligible for inclusion. In our center, these injections are used as a last resort of conservative management. Patients were excluded from the study who had concern for active local or systemic infection, known history of bleeding disorders, were unable to communicate informed consent, or were logistically unavailable at the time of planned needle arthroscopy.

Arthroscopic procedure

We used a 1.9-millimeter arthroscope (NanoScope, Arthrex, Naples, FL, United States) for procedures. Procedures were performed by two fellowship trained foot and ankle surgeons with extensive experience in ankle arthroscopy (SAS and GK) in an outpatient treatment room, suitable for small interventions. The patient was positioned in supine semi-sitting position on a standard operating chair. The ankle was disinfected with a chlorohexidine solution and standard surgical draping was applied. A standard anteromedial portal was utilized and located by palpation. The portal was locally anesthetized with lidocaine 2%, injected along the entire tract including the joint capsule. Once the anesthetic had taken effect, a 2-mm stab incision of the skin was made at the desired portal location. A 2.3-mm diameter cannula was positioned intra-articular, with help of a blunt obturator and slight non-invasive distraction. The obturator was removed and the arthroscope was inserted. Syringes with sterile saline could be connected to the cannula for improving visibility. If needed, the cannula was repositioned (with a maximum of three attempts) until a clear view of the intra-capsular joint space was obtained. No power tools were used and the joint capsule was not resected or debrided. Once the intra-articular view was confirmed, any injected saline was aspirated, after which the pre-packed syringe with hyaluronic acid was connected to the cannula, and the hyaluronic acid was delivered to the joint space through the cannula. The cannula was then flushed with 1cc of saline in order to deliver all the remaining hyaluronic acid. The arthroscope and cannula were removed and the 2-mm portal was closed with sterile wound closure strips. Standard post-treatment care–including 48 h of partial weightbearing–was advised. In the cases where a clear view of the joint space could not be obtained after three attempts, we converted to an intra-articular injection through a standard 21G (green) needle.

Outcome measures

The primary outcome measure was injection accuracy. An accurate injection was defined as injecting through the arthroscopic cannula with intra-articular positioning confirmed by a clear arthroscopic view of the intra-capsular joint space. As secondary outcome measures we collected intra-operative complications, need for conversion to a conventional injection, reason for conversion and procedure time (from patient entrance to patient departure from the procedure room). In addition, patient-reported outcome measures (PROMS) were collected at discharge and during a control visit 2 wk after the procedure. PROMS included numeric rating scales (NRS, 0–10) of pain at rest and during walking as experienced in the 2 wk prior to answering the questionnaire (*i.e.* in the 2 wk prior to either the intervention or the follow-up visit). At discharge, PROMS additionally included NRS of pain during the procedure, and a dichotomous promotor score, asking patients whether they would undergo the procedure again if needed. Complications (infection, neurovascular damage, pain or other complaints prompting contact with a physician) were monitored from inclusion up to study end upon completing the control visit. Follow-up and collection of PROMS was not performed by the orthopedic surgeon but by an independent PhD-fellow (TS) instead.

Analysis

We determined to include 24 patients which, applying the sample size calculation for pilot studies by Viechtbauer *et al*[7] (2015), gives 95% certainty to detect problems that arise with a probability of at least 12%. Descriptive statistics of primary and secondary outcome parameters were provided. Each variable was tested for normality with the Shapiro-Wilk test. Medians and interquartile ranges (IQR) were calculated in case of non-normally distributed data. Otherwise, means and standard deviations (SD) were provided. The Wilcoxon signed-rank test was used to compare preoperative and postoperative outcome scores. In case of a statistically significant difference in PROMS between discharge and follow-up, the number of patients that met the threshold for a minimal clinically important difference (MCID) was calculated[8]. For the NRS of pain, this MCID was set a minimal difference of three points on the 0–10 scale[9]. Data was collected using CASTOR EDC[10]. Analyses were conducted using Stata 12 (StataCorp, College Station, TX, United States).

RESULTS

Twenty-four patients were screened for eligibility and included in the study and received a needle arthroscopic injection. Eleven (46%) patients were male (Table 1). Mean age was 46.8 ± 14.5 years (range: 20–71 years). Twenty (83%) injections were performed as a temporizing biotribologic therapeutic for advanced osteoarthritis with near obliteration of the joint space. Kellgren-Lawrence grading was grade IV in 8 (33%) patients and grade III in 10 (42%) patients. Four (17%) injections were performed as a treatment modality for a talar osteochondral defect. Fourteen (58%) patients had a history of prior surgery–either open or arthroscopic–to the applicable ankle, and 11 (46%) had a history of multiple prior surgeries.

Procedure

It was possible to perform an injection with arthroscopic confirmation of accuracy in 21 (88%) patients (Table 2 and Figure 1). Conversion to a conventional injection needle was needed in 3 (12%) patients, all on account of technical inability to achieve intra-articular positioning of the needle arthroscope within three attempts. All failures occurred in patients suffering from end-stage osteoarthritis with Kellgren-Lawrence grade IV. Two of the failed cases occurred in a patient with a history of prior ankle surgery, of which 1 patient had had multiple prior surgeries. There were no intra-operative complications. Mean intra-OR time was 17 ± 5 min. Sterile wound closure strips were sufficient for wound closure in all cases and sutures were never required.

Follow-up

All (100%) patients completed the follow-up visit and questionnaire (Table 2). The follow-up visit was performed at a median of 14 d (IQR: 14–16) after the intervention. Due to restrictions in the first wave of the COVID-19 pandemic, 2 follow-up visits were conducted by phone. All other visits were conducted in person. No infectious or neurovascular complications were found. No patient contacted a physician in the

Table 1 Patient demographics at the time of the intervention (mean ± SD)

Parameter	Value
Age in yr (range)	46.8 ± 14.5 (20–71)
Sex	
Male, *n* (%)	11 (46%)
Female, *n* (%)	13 (54%)
Indication for injection	
Osteoarthritis, *n* (%)	20 (83%)
Kellgren-Lawrence Grade I (*n*)	0
Kellgren-Lawrence Grade II (*n*)	2
Kellgren-Lawrence Grade III (*n*)	10
Kellgren-Lawrence Grade IV (*n*)	8
(Osteo)chondral defect, *n* (%)	4 (17%)
Prior ankle surgery	
None, *n* (%)	10 (42%)
Any, *n* (%)	14 (58%)
Multiple, *n* (%)	11 (46%)

Table 2 Procedure and follow-up (mean ± SD)

Parameter	Value
Accurate injections, *n* (%)	21 (88%)
Accuracy by indication	
Kellgren-Lawrence Grade I [*n* accurate (% of subset)]	NA
Kellgren-Lawrence Grade II [*n* accurate (% of subset)]	2 (100%)
Kellgren-Lawrence Grade III [*n* accurate (% of subset)]	10 (100%)
Kellgren-Lawrence Grade IV [*n* accurate (% of subset)]	5 (62.5%)
(Osteo)chondral defect [*n* accurate (% of subset)]	4 (100%)
Accuracy by prior ankle surgery	
None [*n* accurate (% of subset)]	9 (90.0%)
Any [*n* accurate (% of subset)]	12 (85.7%)
Multiple [*n* accurate (% of subset)]	10 (90.1%)
Procedure time (min)	17 ± 5
Completed follow-up, *n* (%)	24 (100%)
Follow-up time (median days, IQR)	14 (IQR, 14–16)
Complications, *n* (%)	0 (0%)

NA: Not applicable; IQR: Interquartile ranges.

period between intervention and follow-up.

PROMS

The median NRS of pain during the arthroscopic procedure was 1 (IQR: 0–2) (Table 3). All (100%) patients were willing to return for another bedside needle arthroscopic injection if needed. Median NRS of pain in rest decreased from 4 (IQR: 2–7) in the 2 wk prior to the intervention, to 3 (IQR: 1–5) in the 2 wk prior to the follow-up visit (P < 0.01). In 6 patients, pain in rest decreased with at least 3 points (MCID) on the NRS

Table 3 Patient reported outcome

Activity	Intervention	Follow-up	Difference (*P* value)
Willing to return, *n* (%)	24 (100%)	NA	NA
NRS of pain (0–10)			
During procedure (median, IQR)	1 (0–2)	NA	NA
In rest (past 2 wk) (median, IQR)	4 (2–7)	3 (1–5)	< 0.01
Walking (past 2 wk) (median, IQR)	8 (6–9)	7 (4–8)	< 0.01

NA: Not applicable; NRS: Numeric rating scale; IQR: Interquartile ranges.

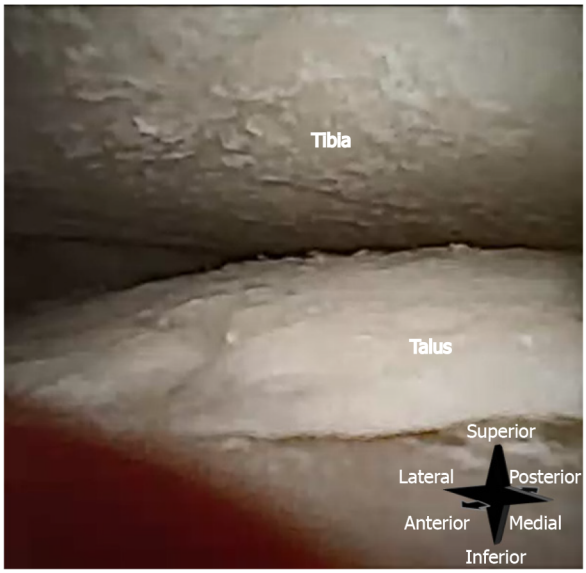

Figure 1 Intra-articular image of a right tibiotalar joint, taken with the 0° arthroscope inserted through the anteromedial portal. Substantial chondral wear can be seen on talus and tibia, with uncovered bone clearly visible.

scale. Pain during walking decreased from a median NRS of 8 (IQR: 6–9) to a median NRS of 7 (IQR: 4–8) ($P < 0.01$). In 7 patients, pain during walking decreased with at least 3 points (MCID) on the NRS scale.

DISCUSSION

Can bedside needle arthroscopy of the ankle be an accurate option for intra-articular delivery of injectable agents? Yes, but be aware that a difficult patient population with extensive scar tissue due to prior surgeries and severe joint space narrowing due to advanced osteoarthritic joint obliteration will not provide a 100% success rate. The main finding of this study was that 2-mm diameter needle arthroscopy of the ankle was able to achieve clear intra-articular positioning in 88% (21 out of 24) of cases. It was then possible to deliver hyaluronic acid in the joint space with absolute certainty in these 21 cases. The success rate was 100% in patients with less advanced osteoarthritis (Kellgren-Lawrence grade III) or lower and the success rate was 90% in patients without a history prior ankle surgery. Therefore, patient selection and counseling is important before considering inspection-injection through needle arthroscopy of the ankle. Procedures were well tolerated and there were no complications in this cohort, including a follow-up visit at 14 d.

A recent literature review by Hall[4] (2013) found that in a clinical setting, ankle injections are delivered with an accuracy ranging between 67% and 77%, if guided by palpation[4]. Although not statistically tested, the 88% accuracy this study found for needle arthroscopic injections is higher. This could be explained by the visual confirmation of the position of the arthroscope. In case of extra-articular positioning,

the arthroscope was repositioned until correctly located in the joint. Repositioning of the needle in conventional procedures still could result in an extra-articular injection.

Intra-articular positioning of the arthroscope and cannula was not achieved in 3 patients (12%). All 3 patients suffered from Kellgren-Lawrence grade IV osteoarthritis, with complete obliteration of the ventral joint space. The joint space between their talus and tibia was less than 2 mm–too narrow for a safe introduction of the arthroscope, despite the use of non-invasive distraction. In addition, osteophytes narrowed the angle in which it was possible to navigate the arthroscope. As the needle arthroscope that was used has a 0° direction of view, changing the direction of view cannot be achieved by rotating the camera, as it can with for example conventional 30° arthroscopes. Instead, the direction of view can only be changed by tilting the entire arthroscope. Osteophytes limit the possibility for this tilting of the arthroscope, which may hamper visualization of the joint. Furthermore, the flexibility of the small diameter needle scope prevents using the barrel of the scope as a lever to gain access to the joint. We therefore recommend to carefully examine the patient's radiological studies, which may constitute simple X-ray's–in case of severe osteoarthritis, before considering needle arthroscopic injections. The amount of joint distraction that can be achieved with non-invasive distraction in patients with end-stage joint destruction under local anesthesia is a subject for further study.

Fourteen patients (58%) had a history of prior surgery. We noted difficulty with arthroscope introduction in 5 of them. In conventional arthroscopy, partial synovectomy is performed to obtain a clear view in these patients[11]. Needle arthroscopic synovectomy has been performed in the knee[12], and cadaveric studies have shown the feasibility of operative needle arthroscopy in the ankle[6]. In the knee, synovectomy under local anesthesia is well tolerated by most patients[13]. For the ankle, clinical feasibility of needle arthroscopic (partial) synovectomy under local anesthesia has yet to be established. Nevertheless, whether it is acceptable to perform a synovectomy may depend on the indication for needle arthroscopy, and may be excessively invasive for a simple injection. Extensive prior surgery may hence be a contraindication for bedside needle arthroscopy in these cases.

Procedures were well tolerated by patients and there were no complications up to a 2-wk follow-up. Although this is the first study to evaluate bedside needle arthroscopy of the ankle, needle arthroscopic procedures have been performed under local anesthesia in the knee and shoulder, and were well tolerated by patients in these joints as well[14]. That the procedure is well tolerated is further substantiated by 100% of participants being willing to return for another needle arthroscopic injection if needed. A recent cadaveric study showed that needle arthroscopy of the ankle does not pose a risk of damaging major neurovascular structures when using the anteromedial portal [6], which substantiates that our current study did not find any signs of neurovascular complications at 2-wk follow-up. Although this study cannot exclude that complications with a low prevalence (such as infection) may arise, a review of 1419 patients that underwent diagnostic needle arthroscopy of the knee or shoulder found no major complications[15], providing further assurance of the safety of the procedure.

This study is limited by its design as a pilot study. It does not offer a comparison with conventional injections, nor with conventional arthroscopy or more invasive forms of anesthesia. It should rather be interpreted as a proof of feasibility of bedside needle arthroscopy of the ankle and delivery of injectable agents under local anesthesia. Arthroscopy is difficult to perform in the ankle, especially with a 0° direction of view. In that sense, it is important to note that the study may have been underpowered to detect problems or events such as rare complications that occur with a frequency of less than 12%.

The basic procedure as reviewed in this study may be further augmented in order to increase benefit to patient and physician. A recent systematic review showed that compared to MRI, needle arthroscopy has higher accuracy in diagnosing knee osteoarthritis, anterior cruciate ligament insufficiency, meniscal tears, and osteochondral defects[14]. Needle arthroscopic diagnosis and delivery of an injectable treatment would be a beneficial combination. In general, the results of this study may form the groundwork for further expansion of indications that merit needle arthroscopy of the ankle under local anesthesia, including operative procedures.

CONCLUSION

In conclusion, in this clinical pilot study, needle arthroscopy of the ankle showed to be a procedure that is well tolerated by patients under local anesthesia. It is able to

confirm intra-articular delivery of injectable agents with high accuracy. Accuracy may approach 100% by excluding patients with total ventral joint obliteration and patients with a history of extensive prior ankle surgery.

ARTICLE HIGHLIGHTS

Research background

Needle arthroscopy is rapidly attracting the interest of the orthopedic field, as recent technical innovation has increased image quality and improved surgical handling. Bedside needle arthroscopy of the ankle under local anesthesia has been proposed for intra-articular delivery of injectable agents.

Research motivation

Clinical accuracy and tolerability of this approach is not known.

Research objectives

To assess clinical accuracy and tolerability of bedside needle arthroscopy as a delivery system for injectable agents into the tibiotalar joint.

Research methods

A prospective clinical study was conducted. Adult patients who were scheduled for an injection to the ankle joint were included. The primary outcome was accuracy of bedside needle arthroscopic injections under local anesthesia. Additionally, a patient reported numeric rating scale (NRS, 0-10) of pain during the procedure and willingness of patients to return for a similar procedure if needed were recorded. Occurrence of complications was monitored from inclusion up to a 2-wk control visit.

Research results

Of 24 inspection-injections were performed. Osteoarthritis was the indication for injection in 20 (83%) cases–of which 8 cases (33%) were Kellgren-Lawrence grade IV, and 10 cases (42%) were Kellgren-Lawrence grade III. The indication was an osteochondral defect in 4 (17%) participants. Fourteen (58%) participants had a history of ankle surgery and 11 (46%) patients a history of multiple ankle surgeries. It was possible to confirm accuracy in 21 (88%) procedures. The 3 (12%) participants where this confirmation failed all suffered from Kellgren-Lawrence grade IV osteoarthritis. Participants reported a NRS of pain during the procedure with a median of 1 (interquartile ranges: 0–2), and a willingness to return of 100%. We did not encounter infections or other complications.

Research conclusions

Clinical accuracy and tolerability of bedside needle arthroscopy of the ankle as a delivery system for injectable agents are excellent. Accuracy was 100% in patients without total ventral joint obliteration.

Research perspectives

The results of this study may form the groundwork for further expansion of indications that merit needle arthroscopy of the ankle under local anesthesia, including operative procedures.

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ORIGINAL ARTICLE

Observational Study

High-resolution, three-dimensional magnetic resonance imaging axial load dynamic study improves diagnostics of the lumbar spine in clinical practice

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Institutional review board statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Bioethical Review Board at Medical University of Warsaw (AKBE/100/13—obtained on December 10, 2013).

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

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Abstract

BACKGROUND

The response to axial physiological pressure due to load transfer to the lumbar spine structures is among the various back pain mechanisms. Understanding the spine adaptation to cumulative compressive forces can influence the choice of personalized treatment strategies.

AIM

To analyze the impact of axial load on the spinal canal's size, intervertebral foramina, ligamenta flava and lumbosacral alignment.

METHODS

We assessed 90 patients using three-dimensional isotropic magnetic resonance imaging acquisition in a supine position with or without applying an axial compression load. Anatomical structures were measured in the lumbosacral region from L1 to S1 in lying and axially-loaded magnetic resonance images. A paired *t* test at $\alpha = 0.05$ was used to calculate the observed differences.

RESULTS

After axial loading, the dural sac area decreased significantly, by 5.2% on average (4.1%, 6.2%, $P < 0.001$). The intervertebral foramina decreased by 3.4% (2.7%, 4.1%, $P < 0.001$), except for L5-S1. Ligamenta flava increased by 3.8% (2.5%, 5.2%,

Data sharing statement: The dataset analyzed are not publicly available but are available from the corresponding author upon reasonable request.

STROBE statement: The guidelines of the STROBE Statement-checklist of items have been adopted.

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$P < 0.001$), and the lumbosacral angle increased.

CONCLUSION
Axial load exacerbates the narrowing of the spinal canal and intervertebral foramina from L1-L2 to L4-L5. Cumulative compressive forces thicken ligamenta flava and exaggerate lumbar lordosis.

Key Words: Lumbar spine; Low back pain; Musculoskeletal disorder; Diagnosis; Axial loading; Magnetic resonance imaging; Spine biomechanics

Core Tip: In this study, a statistically proven correlation was made between the axial loading and lumbar spinal stenosis, thickening of the ligamenta flava, narrowing of the intervertebral foramina from L1-L2 to L4-L5 and lumbar lordosis exaggeration. A novel aspect of this study was a simultaneous comparison of the dural sac size, ligamenta flava thickness, foraminal dimensions and lumbar sagittal alignment between axial loaded and recumbent three-dimensional high-resolution magnetic resonance imaging in an extensive group of lower back pain patients. This was done to conduct a detailed evaluation for better spinal surgery decision-making and spinal injections.

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INTRODUCTION

Lower back pain (LBP) remains a major worldwide public health problem that has increased substantially over several decades[1]. The problem of LBP affects epidemiology[2-5], health economics[6,7] and social aspects (disability, inability to work, limited daily activity)[8]. LBP is a common problem affecting most adults at some point during their lifetime[3,4,9]. More than half of the population may experience a pain relapse within a year, and 8% of people will have chronic pain[10]. In their systematic review, Meucci *et al*[11] revealed that chronic LBP prevalence was 4.2% in individuals aged between 24 and 39 years. The LBP prevalence equals 19.6% between 20 and 59 years of age and increases linearly from the third decade of life until 60. Chronic LBP is a significant contributor to the global disability burden[12]. Disability besides pain due to LBP is reported frequently and continues to be the leading cause of years lived with disability[13].

The vertically-oriented human spine acts as a dynamic and static column connecting the skeletal system. Substantial forces act on the longitudinal axis of the spine in the human's upright position. Spinal compression is traditionally considered the primary biomechanical mechanism associated with work-related LBP[14,15]. Human erect position can lead to increased axial compression in the lumbar spine and several side effects, including back pain. The lifting of objects raises the axial compression in the lumbar spine and increases LBP risk[16-19].

The classic works of Nachemson *et al*[20,21] from the early 1960s showed that the highest degree of intradiscal pressure in the lumbar spine occurs in standing and sitting positions, mainly when a person leans forward. The intradiscal pressure is lower when an individual is in the lying position than in the sitting and standing positions[22]. These observations were confirmed by Rohlmann *et al*[23,24] using wireless measurement. Schonstrom *et al*[25] showed that the intradiscal force difference measured at rest and axial loading acting on the spine reaches 500 N on human spine segments. The difference in intradiscal pressure observed in the spine segments is comparable to the values found in volunteers subjected to different loads and different body positions[21].

Correct, quick and precise determination of the underlying causes of back pain symptoms is crucial for many patients. Imaging for LBP is considered appropriate when clinical suspicion of severe pathology or surgery addresses a specific pathology [26,27]. Imaging may also be used to diagnose chronic LBP; however, particular indicators for appropriate imaging use are less well defined, with pain lasting longer than 6 weeks being an indicator for imaging in some guidelines but not in others[26]. Axial compression imaging may improve the diagnostics in clinical management of LBP and improve appropriate treatment decisions[28-30].

Even though the highest spinal loading occurs in the upright and sitting positions, a typical magnetic resonance imaging (MRI) examination is performed with the patient lying supine when no loads are exerted on the spine. As a result, the lying position of the examined patient poses a limitation on magnetic resonance tomography. An attempt at overcoming MRI limitations caused by the patient being in a lying position led to the introduction in clinical practice of an examination performed in the supine position with axial loading, simulating physiological loading. The load distribution among lumbar spinal structures, in general, is still an unanswered question and should be the focus of biomechanical testing. Previous studies showed that axial-loaded MRI could simulate the standing position and reveal additional valuable pathological findings not detected by conventional recumbent MRI[31,32]. Compressive loads on the vertebral discs are not the only ones occurring in the spine; load indicators other than disc compression are at least equally relevant, so attention should be paid to them. Few studies simultaneously investigated several anatomical structures in the lumbar spine using upright, open and low-field MRI[33] or axial loaded MRI[16]. However, these studies did not use dynamic three-dimensional (3D) high-resolution images and failed to measure the ligamentum flavum area, foraminal area and lumbar lordosis.

Moreover, previous studies were performed in a young, small group of asymptomatic volunteers[33], or simultaneous measurements were not correlated between the sets of variables[16]. No study has simultaneously compared dural sac size, ligamenta flava thickness, foraminal dimensions and lumbar sagittal alignment between axial-loaded and recumbent MRI in a large group of LBP patients to identify dynamic changes and associations between morphology and demography. Therefore, this study's objective was to evaluate and measure the changes presented by MRI of selected lumbar spine structures upon axial-loading compared with recumbent MRI and correlate them to morphologic changes and demographic data. Additionally, the study aimed to assess the value and potential use of axial loading in lumbar spine examinations. The detailed evaluation seems crucial for spinal surgery decision-making. The spinal injections or transforaminal[34,35] or interlaminar spinal endoscopy[36,37] can be used to relieve symptoms due to the intervertebral foramen narrowing or spinal canal stenosis caused by the thickening of the ligamentum flavum.

MATERIALS AND METHODS

We enrolled 90 patients diagnosed at the Magnetic Resonance Laboratory with LBP inclusion criteria as an indication. Exclusion criteria included significant spinal injury, osteoporosis, previous spine surgery, lack of good patient cooperation, a body mass below 40 kg and a lack of written consent from the patient. General contraindications for MRI examinations (*e.g.*, pacemakers, ferromagnetic implants, foreign bodies and claustrophobia) were also considered. A total of 46 (51%) men and 44 (49%) women were included in the study with an age and body mass index (mean ± standard deviation) of 49 ± 16 years and 26.0 ± 4.2 kg/m^2, respectively. The study was conducted according to the Declaration of Helsinki guidelines and approved by the Institutional Bioethical Review Board at Medical University of Warsaw (AK-BE/100/13 — obtained on December 10, 2013). Informed consent was obtained from all subjects involved in the study.

Lumbar spine MRI examination protocol without and after axial loading

The examination was performed using a 1.5 T MRI (Ingenia; Philips Healthcare, Eindhoven, The Netherlands). After performing recumbent MRI examinations, axial loading was applied using an external commercially available nonmagnetic DynaWell (DynaWell L-Spine; DynaWell Diagnostics, Las Vegas, NV, United States) compression device. The phase without axial loading was identical to a standard lumbar spine examination. Both the axial-loaded and unloaded MRI examinations were performed with a 3D T2-weighted Volume ISotropic Turbo spin-echo

Acquisition sequence (Table 1). According to previous disc pressure measurements[21] the chosen load was equal to 40%-50% of the patient's body weight, with equal load distribution on both legs (20%-25% of patient body mass per leg). The patient was subjected to this load in the lying position for at least 5 min before the examination.

Image analysis

Images were assessed on a dedicated workstation (IntelliSpace Portal; Philips Healthcare, Eindhoven, The Netherlands) at a single center. Based on recumbent and axial-loaded MRIs, the lumbosacral angles between the superior vertebral endplate of L1 and superior vertebral endplate of S1 were measured, enabling the observation of spine adaptations at a whole lumbar level (Figure 1). The dural sac cross-sectional area was calculated for each level from L1-L2 to L5-S1 for examination with and without axial loading. Measurements were performed by encircling the dural sac transverse area, capturing T2-weighted MRI at the same levels for phases without and with axial loading with the plane precisely positioned parallel to the midplane of the intervertebral disc (Figure 1). The vertebral foramina sagittal cross-section area was determined for each level, from L1-L2 to L5-S1, on both sides. Measurements were performed by encircling the vertebral foramina area in sagittal cross-sections on the same levels for the phase with and without axial loading (Figure 1). The cross-sectional area of the ligamentum flavum was determined for levels from L1-L2 to L5-S1 on both sides. The measurements were captured by encircling the area of the ligamentum flavum in cross-sections at facet joint levels with and without axial loading (Figure 1). The degree of disc and facet joint degeneration, the degree of spinal canal stenosis, the degree of foraminal stenosis and the degree of disc herniation were assessed on recumbent images on all disc levels according to the classifications of Pfirrmann *et al* [38], Weishaupt *et al*[39], Schizas *et al*[40], Lee *et al*[41] and the Michigan State University classification of lumbar disc herniation[42].

Statistical analysis

The assessment criterion used was the percentage difference of measured parameters with a 95% confidence interval (CI). A paired *t* test was applied at an $\alpha = 0.05$ level to verify the hypothesis regarding the statistical significance of changes observed. The Pearson correlation test was used to explore the mutual relations of the spine structural parameters. A paired *t* test was applied to determine the relationship between age and sex for each measured parameter. The statistical methods of this study were reviewed by Wojciech Michalski from the Department of Mathematical Oncology, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland. The IBM SPSS Statistics (IBM Corp., Armonk, NY, United States) version 20 for Linux OS was used for statistical analysis.

RESULTS

Ligamentum flavum

Upon axial loading, the area of the ligamenta flava was statistically significantly increased on average by 3.8% (95%CI: 2.5%, 5.2%, $P < 0.001$; Table 2).

Dural sac

Upon axial loading, the dural sac area significantly decreased on average by 5.2% (95%CI: 4.1%, 6.2%, $P < 0.001$; Table 3).

Intervertebral foramen

The area of the intervertebral foramina decreased on average by 3.4% (95%CI: 2.7%, 4.1%, $P < 0.001$) except for the L5-S1 section of the spine, which increased by 2.0% on average (95%CI: 0.5%, 3.9%, $P = 0.045$; Table 4).

Lumbosacral angle

The lumbosacral angles increased, on average, by 7.7% (95%CI: 5.7%, 9.6%, $P < 0.001$; Table 5).

Correlation analysis

A statistically significant correlation between exaggerated lumbosacral angle and age was found (Pearson correlation coefficient (r) = -0.253, $P < 0.05$). The negative correlation indicated that axial force on increasing lumbar lordosis in older patients is

Table 1 Three-dimensional Volume ISotropic Turbo spin-echo Acquisition magnetic resonance pulse parameters

Parameters	3D VISTA T2
Repetition time/Echo time (ms)	2000/90
Number of signal averaging	1
Field of View (mm)	300 × 200 × 75
Acquisition matrix	300 × 196
Acquisition voxel (mm)	1 × 1 × 0.5
Reconstruction matrix	640
Reconstruction voxel (mm)	0.47 × 0.47 × 0.5
Turbo factor	61
Sensitivity encoding factor	1.3
Scan time	06:46

3D: Three-dimensional; VISTA: Volume ISotropic Turbo spin-echo Acquisition.

Table 2 Cross-sectional area of the ligamentum flavum on the same levels with and without axial loading on both sides

Ligamenta flava(right + left) / section of the spine	Mean difference of area between unloaded and axial loading (%)	95%CI		*P* value
		Lower	Upper	
L1-L2	4.1	1.8	6.4	0.001
L2-L3	4.8	2.0	7.6	0.001
L3-L4	4.0	0.5	4.7	0.024
L4-L5	2.1	-0.5	6.3	0.116
L5-S1	4.1	2.5	5.2	< 0.001
All from L1-L2 to L5-S1	3.8	2.5	5.2	< 0.001

Negative value corresponds to a decrease. CI: Confidence interval.

less than in younger patients. Neither the area of the intervertebral foramina nor the area of the dural sac was correlated with age. Additionally, a percentage difference of the sagittal cross-section area of vertebral foramina, the cross-section area of the dural sac and ligamenta flava and the percentage difference of the lumbosacral angles did not significantly correlate with sex. The relationship testing between spine structure parameters did not deliver any significant association between any variables.

Degenerative changes

Degenerative changes of the lumbar spine are listed in Table 6.

DISCUSSION

Compression devices can be applied to high-field units. Therefore, high-resolution, 3D MRI might be obtained. This advantage of recumbent axially loaded MRI creates possibilities in determining the precise measurements and making an accurate diagnosis. The upright MRI would be a theoretically ideal diagnostic tool to simulate the spinal column under physiological conditions, but those systems are low-field MRI, which provides low image quality. Other studies have simultaneously analyzed several anatomical structures in the lumbar spine using upright, open and low-field (0.5T *vs* 1.5T in our study) MRI[33].

Table 3 Percentage difference of the cross-sectional area of the dural sac on transverse, T2-dependent magnetic resonance imaging at the same levels for phases both with and without axial loading

Dural sac/section of the spine	Mean difference of area between unloaded and axial loading (%)	95%CI		*P* value
		Lower	Upper	
L1-L2	-2.6	-3.6	-1.6	< 0.001
L2-L3	-5.5	-6.8	-4.2	< 0.001
L3-L4	-6.7	-8.9	-4.4	< 0.001
L4-L5	-8.1	-10.5	-5.7	< 0.001
L5-S1	-3.0	-4.9	-1.0	0.004
All from L1-L2 to L5-S1	-5.2	-6.2	-4.1	< 0.001

Negative values correspond to a decrease. CI: Confidence interval.

Table 4 Percentage difference of the sagittal cross-sectional area of vertebral foramina on the same levels both with and without axial loading on both sides

Intervertebral foramina (right + left)/section of the spine	Mean difference of area between unloaded and axial loading (%)	95%CI		*P* value
		Lower	Upper	
L1-L2	-4.0	-5.1	-2.9	< 0.001
L2-L3	-6.7	-8.0	-5.5	< 0.001
L3-L4	-5.1	-6.2	-4.0	< 0.001
L4-L5	-3.3	-4.8	-1.7	< 0.001
L5-S1	2.0	0.5	3.9	0.045
All from L1-L2 to L5-S1	-3.4	-4.1	-2.7	< 0.001

Negative values correspond to a decrease. CI: Confidence interval.

Table 5 Percentage difference of the lumbosacral angles between L1 and S1 measured based on recumbent and axial-loaded magnetic resonance images

Lumbosacral angle	Mean difference of angle between unloaded and axial loading (%)	95%CI		*P* value
		Lower	Upper	
From L1 to S1	7.7	5.7	9.6	< 0.001

CI: Confidence interval.

Contrary to our study, the previous study group was limited to young (*vs* any age in our study), less populated (12 *vs* 90 in our study) asymptomatic volunteers. No 3D high-resolution images and failure to measure several anatomical structures were reported. The proposed idea of applying axial-loaded MRI aimed to mimic as close as possible the load conditions occurring in the upright position. That position is currently impossible to apply in conventional recumbent high-field MRI. Devices intended for axial loading are commercially available and approved by the United States Food and Drug Administration. They also meet the New Approach Directive requirements of the European Union; yet, according to many authors, they are still in their experimental stage[43]. As a result, biomechanical testing has focused on many spinal structures simultaneously. The load distribution among the dural sac, ligamenta flava, intervertebral foramina and lumbar sagittal alignment was considered in this

Table 6 Degenerative pathologies of the lumbar spine

Analyzed factors	Grade	*n*	%
Intervertebral disc degeneration according to Pfirrmann *et al*[38] classification	1	0	0
	2	72	16
	3	196	44
	4	159	35
	5	23	5
Facet joint degeneration, according to Weishaupt *et al*[39] classification	0	300	33
	1	405	45
	2	149	17
	3	46	5
Grade of lumbar spinal canal stenosis according to Schizas *et al*[40] classification	A1	349	78
	A2	22	5
	A3	47	10
	A4	3	1
	B	20	4
	C	7	2
	D	2	0
Disc herniation according to the Michigan State University[42] classification of lumbar disc herniation	0	342	76
	1a, 1b, 1ab, 1c	88	20
	2a, 2b, 2ab, 2c	18	4
	3a, 3b, 3ab, 3c	2	0
Foraminal stenosis, according to Lee *et al*[41] classification	0	664	74
	1	168	19
	2	56	6
	3	12	1

spinal biomechanical assessment.

Dural sac

The dural sac occupies the most significant part of the spinal canal. Therefore, spinal stenosis mainly affects the dural sac, narrowed in the highest grade from all structures filling the spinal canal (Figure 2). The cross-sectional dural sac area measurement provides the most precise assessment of the spinal canal, but its time consumption is the main disadvantage of this method[44]. The results in this study showed that the mean dural sac cross-sectional area was significantly lower when loaded than relaxed at all lumbar spine levels from L1-L2 to L5-S1 (Figure 2). The rates of dynamic change were the highest at L4-L5 (mean of 8.1%; range of 5.7%-10.5%) and the lowest at L1-L2 (mean of 2.6%; range of 1.6%-3.6%).

The high sensitivity and specificity of axial-loaded MRI for detecting severe constriction were demonstrated by Kanno *et al*[32]. MRI examinations under axial loading are highly relevant in detecting central stenosis of the spinal canal, as to be confirmed by results reported by other authors[45]. Axial-loaded MRI demonstrated a significant reduction in the dural sac size and significant correlations of dural sac diameters with the upright myelogram. Therefore, axial-loaded MRI can be used to represent positional changes in dural sac size detected by upright myelography in patients with lumbar spinal canal stenosis[32]. Numerous *in vitro* experiments showed that axial loading results in spinal canal stenosis.

Schonstrom *et al*[25] specified that axial loading results in a spinal canal volume reduction in a spine segment, measured at an intervertebral disc level by about 40-50 mm^2. In their previous studies, the authors discovered that a pressure increase in the

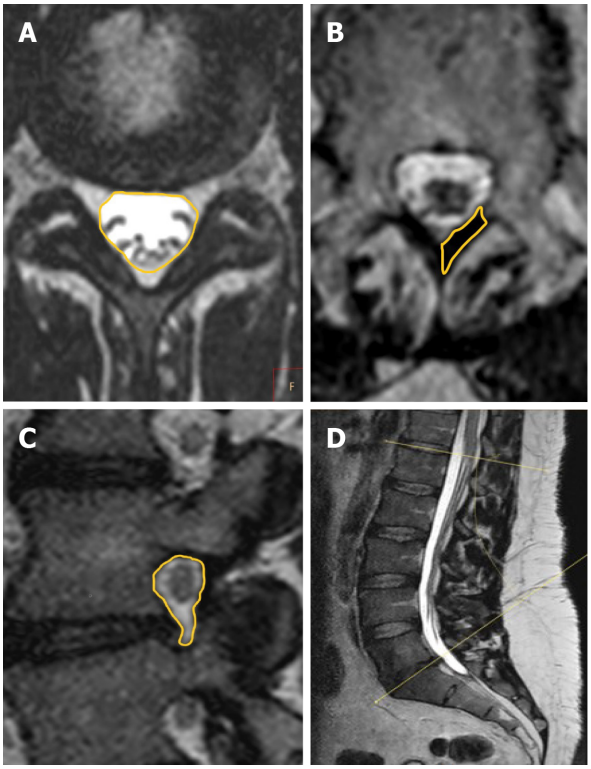

Figure 1 Specific measurements of (A) the cross-section area of the dural sac on transverse magnetic resonance imaging, (B) the cross-section area of the ligamentum flavum, (C) the sagittal cross-section area of vertebral foramina and (D) the lumbosacral angles between L1 and S1.

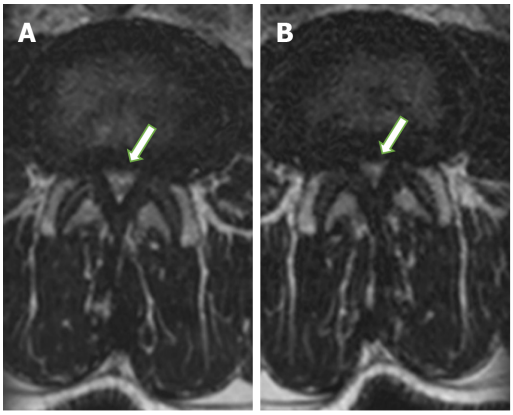

Figure 2 Transverse magnetic resonance imaging. A: Recumbent T2-weighted images. The rootlets occupy the whole of the dural sac (arrow), but they can still be individualized; B: Spinal stenosis with a reduction in the dural sac size after axial loading. No rootlets can be recognized, but some cerebrospinal fluid is still present, giving a grainy appearance to the sac (arrow).

dural sac of spinal segments reduces the spinal canal area down to approximately 79 mm^2[46]. Based on this discovery, contemporary authors assumed that 75 mm^2 is the borderline value of the dural sac cross-sectional area. Below this value, the authors suggested a diagnosis of absolute stenosis, and the range of 75-100 mm^2 indicates a diagnosis of relative spinal canal stenosis. Kim *et al*[47] arbitrarily defined a 10% reduction in the dural sac cross-sectional area as a significant reduction. They found a significant reduction in the cross-sectional area of the dural sac in 42% of patients, of which severe stenosis with a cross-sectional area lower than 75 mm^2 was found in 25% of patients.

Danielson and Willen[31] described an additional significant decrease in the cross-sectional area of the dural sac with axial-loading MRI as an area change more than 15 mm^2. They concluded that axial-loading MRI provided "additional, significant information" in 50 of 172 patients (29%). They also observed additional significant

findings in 69% of patients with neurogenic claudication, 14% of patients with sciatica and 0% of patients with LBP[31]. Of patients studied by Manenti *et al*[48], who were subjected to axial-loading MRI, 18 (45%) displayed cases of spinal canal stenosis emergence, 8 (20%) displayed cases of hernia enlargement, and 6 (15%) showed profound spondylolisthesis.

Ligamentum flavum

The ligamenta flava fills the space between the vertebral arches. They run just behind the facet joint and act as an extra reinforcement of the joint capsule. The ligamenta flava thickens with age. The ligamenta flava thickening is connected to fibrous tissue hypertrophy, which is a result of cyclooxygenase-2 and transforming growth factor-beta expression[49,50]. The changes are prominent in the dorsal part of the ligamenta flava, where the most potent axial load forces are observed[49]. This study showed that the mean cross-sectional area of the ligamenta flava was significantly higher when loaded than relaxed at all lumbar spine levels from L1-L2 to L5-S1. The rates of dynamic changes were the highest at L2-L3 (mean of 4.8%; range of 2.0%-7.6%) and the lowest at L4-L5.

According to the study of Hansson *et al*[45], it is not intervertebral discs but the ligamenta flava that have the most significant impact on spinal stenosis, being responsible for 50%-80% of spinal stenosis induced by axial loading. The case report of dynamic lumbar spinal stenosis with neurogenic claudication caused by the thickening of the ligamentum flavum, with MRI in decumbency, revealed no definite pathologic condition associated with symptoms[51]. According to some authors, the pathogenesis of thickening of the ligamentum flavum is unclear, and whether ligamentum flavum thickening is due to tissue hypertrophy or buckling remains controversial. Some studies claimed that canal narrowing, in part, results from the hypertrophy of the ligamentum flavum. In contrast, others argued that the ligamentum flavum bulges inside the spinal canal and compresses nerve tissues[49,50,52]. This information is relevant clinically because spinal stenosis may be underdiagnosed with regular MRI, and surgical intervention without adequate decompression may lead to poor outcomes.

Intervertebral foramen

Intervertebral foramina are triangular or oval at the lumbar level and broader in the coronal than the sagittal plane. Measurements recorded by encircling the intervertebral foramina sagittal cross-sections were proposed as the most accurate[53]. Our analysis of lumbar neural foramina showed that variation in the cross-sectional area of the neural foramen in the lumbar spine was significantly axially-loaded-dependent. We identified a statistically significant decrease in average percent foraminal area from recumbent to axially loaded at all levels except at L5-S1. Surprisingly, intervertebral foramina at L5-S1 widened after axial loading by 2%, on average (Figure 3).

Iwata *et al*[54] reported similar findings in computed tomography examinations using DynaWell equipment. They observed an enlargement of the intervertebral foramina area at the L5-S1 level and a simultaneous reduction in the intervertebral foramina area at L1-L2 levels to L4-L5 after axial loading. Conversely, MRI studies demonstrated a decrease in the foraminal area at all levels during weight-bearing in neutral, flexion and extension positions compared to unloaded supine imaging. The magnitude of change in the foraminal area increased as an angular motion at the segment increased. The most significant average percent decrease in the foraminal area occurs at L2-L3 and the smallest change at L5-S1, but a reduction at this level was still observed[53]. Therefore, changes caused by a compression device in foraminal dimensions at L5-S1 do not simulate physiological standing conditions.

Suppose the different types of loading simulated by DynaWell equipment and those occurring in the standing position responsible for differences in foraminal stenosis observed in those methods have not yet been determined. The axial load may be transmitted to the feet and the buttocks in the supine position. A reaction force acts on the buttocks causing the posterior rotation of the pelvis. That results in a significant decrease in the pelvic angle during axial loading[55]. According to Hioki *et al*[56], the disc wedge angles at the L5-S1 level with axial loading using DynaWell equipment differed from those in the standing posture. The magnitudes of changes were significantly smaller than in the standing position. They suggested that axial loading of the lumbar spine in the supine position decreases the angle between the L5 and S1 [56]. However, the L5-S1 angle did not significantly change in the standing posture than the controls in the supine position at rest. These observations of different lumbar-pelvic angular behavior could correspond with an enlargement of the area of intervertebral foramina at the L5-S1 level observed in our study. An awareness of these

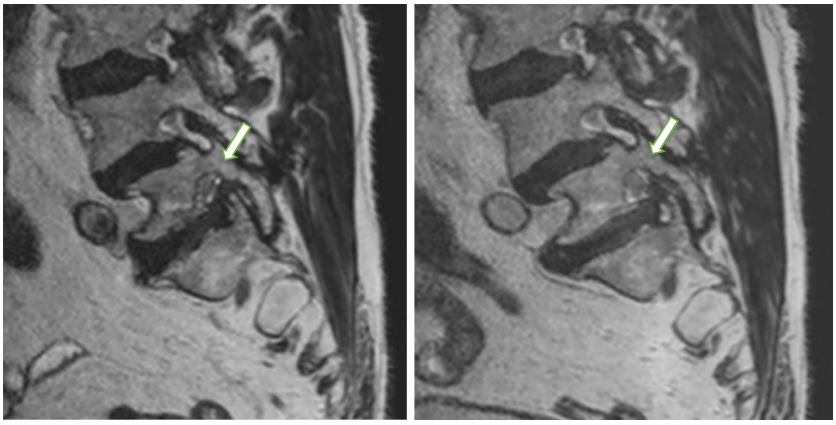

Figure 3 Sagittal magnetic resonance imaging. Morphologic changes in a foraminal zone at L5-S1 (arrow) with nerve root collapse and perineural fat obliteration were seen with and without axial loading.

phenomena is essential to allow clinicians to evaluate imaging results accurately.

The results in this study showed that the most significant foraminal constriction was by 6.7% (range of 5.5%-8.0%) under loading occurred at the L2-L3 level. Diagnostic benefits with a high grade of foraminal spinal detection could be achieved if inclusion criteria were limited to the suspicion of single spinal nerve involvement, as described by Splendiani *et al*[57]. They detected foraminal spinal stenosis at 61 of 230 levels and called it "hidden" stenosis, as it was not revealed on conventional recumbent MR examinations; it was only detected on examinations performed with the patient in the orthostatic position. The authors also discovered that stenosis of the intervertebral foramen was never found either in the presence of normal intervertebral discs or in the absence of facet disease in either the clinostatic or orthostatic position[57].

Lumbosacral angle

The spine is highly resistant to axial pressure. That resistance depends on the size and shape of the spine as well as spine curvatures. The human spine, at an early stage, consists of only one curvature: spine kyphosis. The following curvatures occur when the human develops the erected position: (1) At the cervical level: lordosis (cervical lordosis); (2) At the thoracic level: kyphosis (thoracic kyphosis); (3) At the lumbar level: lordosis (lumbar lordosis); and (4) At a sacral level: kyphosis (sacral kyphosis).

Curvatures in the sagittal plane make the spine more durable compared to the straight column. Therein one function of the lumbar lordosis is to provide a higher bearing resistance. Lumbar lordosis in the sagittal plane of the spine is unique only in the human population. It is not observed in any other animal. The changes in lordosis markedly affect the stabilizing sagittal moments.

Our results indicated that lordosis of the spine varies from the initial sagittal curvature by +7.7° after axial loading, responsible for more lordotic posture. Older patients show lower increases in lumbar lordosis when exposed to an axial force. As we observed a decreased elasticity of the spine in the older population, it is worth proposing axial-loading MRI as elasticity imaging: an innovative "elastography" method designed for the lumbar spine to explore the age of the spine, the percentile grids of degenerative changes.

Huang *et al*[58] reported that the mean lumbosacral angle was 37° in unloaded MRI examinations and increased to 39° after axial loading. Our lumbar spine biomechanics analysis also showed that axial loading increases lumbar lordosis. According to Hioki *et al*[56], lumbar axial loading with DynaWell in the supine position can simulate the lumbar spine position in the standing position. This loading device alters lumbar sagittal alignment differently from an upright standing position at the L5-S1 level.

Conversely, lumbar lordosis was more extensive after the axial load in the supine position compared to the standing position, according to Madsen *et al*[59]. This intriguing observation that the lumbosacral angle was 6° larger in the supine position than in the standing position, as explained by the author, was due to patients leaning against MRI walls to maintain a safe position and immobility when standing. Meakin *et al*[60] suggested that patients in the standing position are exposed to additional bearing forces. Patients with a lumbosacral angle smaller than the mean in an unloaded examination tend to straighten the spine after additional bearing forces. Patients with a lumbosacral angle greater than the mean in an unloaded examination

were observed to increase lumbar lordosis after additional bearing forces.

Correlation analysis

Simultaneous measurements of the percentage difference of the sagittal cross-section area of vertebral foramina, the cross-section areas of the dural sac and ligamenta flava as well as the percentage difference of the lumbosacral angles offered new information. According to our data, a statistically significant correlation exists between exaggerated lumbosacral angle and age (r = -0.253, P < 0.05). A negative correlation was found and showed that older patients have a lower increase in lumbar lordosis when exposed to axial force, similar to that found in the spine in the standing position. The percentage difference of the sagittal cross-section area of vertebral foramina, the cross-section areas of the dural sac and ligamenta flava, as well as the percentage difference of the lumbosacral angles, did not significantly correlate with each other and sex.

Limitations

This study has significant limitations. The research's main limitation is that all patients in the study were referred for MRI examinations for LBP, and there was no asymptomatic healthy control group. These results may not apply to asymptomatic, dynamic foraminal or spinal stenosis in the healthy population. Another potential limitation is that the inter-rater assessment has not been calculated. The force equal to half the body weight may not necessarily represent the lumbar spine load while standing. There may be a bias of data in the comparison between axial loading and standing conditions. Further comparative analyses between standing and axially-loaded MRI findings in the supine position would provide more clinically relevant information.

Another source of weakness in this study was the lack of computational approach in automatic image recognition based on machine learning and deep learning to ease radiological measurements of the lumbar spine. However, it is within the scope of our scientific interests, and we hope to expand artificial intelligence in image recognition and segmentation to automate lumbar spine assessment and to obtain a good level of clinical prediction. In our opinion, high resolution 3D imaging will make automatic image recognition more accurate. We showed in this study, that high resolution 3D MRI is feasible under axial compression. Volume ISotropic Turbo spin-echo Acquisition techniques have been used to acquire high-resolution, contiguous, thin-section isotropic images for complex spine anatomy and replace several two-dimensional acquisitions. The voxels generated by the 3D acquisition are submillimeter and measure the same in each direction, allowing the images to be reformatted with equal resolution in any direction.

CONCLUSION

The lumbar spine MRI is one of the most frequently performed examinations of all MRIs, but the MRI does not correlate significantly with back pain causes. The current study may help clinical practice understand spine physiology exposed to external forces, better-clarifying indications for axial load, and help identify the relationship between imaging examination results and perceived symptoms. A comparative evaluation of images obtained before and after axial loading of the spine showed changes in lumbosacral angles between L1 and S1, the dural sac cross-sectional area, the sagittal cross-sectional area of the intervertebral foramina and the cross-sectional area of the ligamentum flavum. Consistency in detecting central stenosis and ligamenta flava thickening between studies supports using an axial load of 50% body weight to simulate relaxed standing in the supine position. Changes in foraminal dimensions at L5-S1 do not affect physiological standing conditions. Axial loading intensifies the narrowing of the intervertebral foramina. Applying an axial compressive load increases lumbar lordosis, whereas the smallest changes were observed in older patients.

ARTICLE HIGHLIGHTS

Research background

Biomechanics of the individual lumbar spine structures are important since the overall spinal adaptation to compressive forces is comprised of the cumulative changes of respective elements.

Research motivation

There is a lack of works simultaneously comparing dural sac size, ligamenta flava thickness, foraminal dimensions and lumbar sagittal alignment between axial loaded and recumbent magnetic resonance imaging (MRI) in an extensive group of lower back pain patients.

Research objectives

To help the surgeons in the choice of the spinal endoscopy and spinal injections. The objective of the study was to evaluate the changes depicted by MRI of chosen lumbar spine structures upon axial-loading in comparison with recumbent MRI.

Research methods

The study covered 90 individuals assessed with three-dimensional volume isotropic acquisition MRI, first imaged in the supine position with no axial load and then again following application of an axial compressive load. Based on recumbent MRI as well as axial-loaded ones, the following were measured: the dural sac area, the ligamenta flava, the intervertebral foramina from L1-L2 to L5-S1 and the lumbosacral angle.

Research results

We found out that axial loading intensifies the narrowing of the spinal canal, thickens the ligamenta flava, narrows the intervertebral foramina from L1-L2 to L4-L5 and exaggerates lumbar lordosis.

Research conclusions

Our study reveals that there is a correlation between force compression and intensification of the lumbar spinal stenosis, intervertebral foramina narrowing, ligamenta flava thickening as well as increasing lumbar lordosis due to axial loading.

Research perspectives

There is a need to introduce computational approaches in automatic image recognition based on machine learning and deep learning to ease radiological measurements of the lumbar spine and obtain a good level of clinical prediction. Moreover, it is worth proposing axial-loading MRI as an elasticity imaging: an innovative "elastography" method designed for the lumbar spine to explore the age of the spine and the percentile grids of degenerative changes.

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ORIGINAL ARTICLE

Prospective Study

Comparing shoulder maneuvers to magnetic resonance imaging and arthroscopic findings in patients with supraspinatus tears

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Abstract

BACKGROUND

Shoulder maneuvers and magnetic resonance imaging (MRI) are performed to diagnose supraspinatus tendon tears regardless of arthroscopy exam. Although there are many studies on this subject, there is a lack of studies comparing the sensitivity (Se) and specificity (Sp) of shoulder maneuvers and MRI to arthroscopic findings (intact, partial, or full thickness supraspinatus tendon tear).

AIM

To compare the diagnostic values of shoulder maneuvers with MRI for supraspinatus tendon tears in patients undergoing shoulder arthroscopy.

METHODS

A total of 199 consecutive patients from four orthopedic centers met the eligibility criteria of shoulder pain persisting for at least four weeks. They were prospectively enrolled in this study from April 2017 to April 2019. Seven clinical tests (full can, empty can, drop arm, Hawkins', painful arc, Neer's sign and resisted external rotation) and MRI were performed, and all were compared with surgical findings. Full can, empty can and resisted external rotation tests were interpreted as positive in the case of pain and/or weakness. We assessed the Se, Sp, accuracy, positive predictive value (PPV) and negative predictive value (NPV), positive and negative likelihood ratio and diagnostic odds ratio for overall, partial and full-thickness supraspinatus tears.

guardian, provided written consent prior to study enrollment.

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RESULTS

MRI had the highest Se for overall (0.97), partial (0.91) and full-thickness (0.99) tears; moreover, MRI had the highest NPV: 0.90, 0.88 and 0.98 for overall, partial and full-thickness tears, respectively. For overall supraspinatus tears, the Se and PPV were: Painful arc (Se = 0.85/PPV = 0.91), empty can (pain) (Se = 0.80/PPV = 0.89), full can (pain) (Se = 0.78/PPV = 0.90), resisted external rotation (pain) (Se = 0.48/PPV = 0.87), drop arm (Se = 0.19/PPV = 0.97), Neer's sign (Se = 0.78/PPV = 0.93) and Hawkins' (Se = 0.80/PPV = 0.88). MRI had the highest PPV (0.99). The Hawkin's test had the highest false positive rate in patients with intact tendons (0.36). The Sp of the empty can and full can (both tests positive for pain and weakness), drop arm and MRI were: 0.93, 0.91, 0.98 and 0.96, respectively. For partial and full-thickness tears, the empty can test (positive for pain and weakness) had a Sp of 0.93, and the drop arm and MRI had the same Sp (0.98).

CONCLUSION

Physical examination demonstrated good diagnostic value, the drop arm test had a Sp as good as MRI for supraspinatus tears; however, MRI was more accurate in ruling out tears. The Hawkins' test had high false-positive findings in patients with intact tendons.

Key Words: Rotator cuff injuries; Physical examination; Magnetic resonance imaging; Arthroscopy

Core Tip: Shoulder maneuvers and magnetic resonance imaging (MRI) are performed to diagnose supraspinatus tendon tears regardless of arthroscopy exam. The shoulder maneuvers are useful for diagnosing supraspinatus tears in patients for whom surgery is being considered; however, they showed limited values in ruling out tears compared with MRI. Moreover, some shoulder maneuvers had high false-positive findings in patients with intact tendons.

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INTRODUCTION

Several shoulder maneuvers have been described and performed on patients undergoing shoulder arthroscopy; however, previous studies have shown that only the empty can and full can tests accurately diagnose supraspinatus tears[1]. Moreover, other studies demonstrated that the drop arm test has the highest specificity (Sp) for supraspinatus tears[2].

For diagnostic confirmation of clinical findings, magnetic resonance imaging (MRI) has been used to evaluate rotator cuff tears (RCTs). MRI showed high sensitivity (Se) and Sp for full thickness tears; however, poor Se for detecting partial tears[3]. Moreover, MRI is valuable in surgical planning of RCTs, allowing a detailed assessment of the tear size and muscle atrophy[4-7].

Systematic reviews point out limitations in the accuracy studies of clinical tests and imaging exams for diagnosing RCTs, and these reviews suggested new research with improved methodological standards[3,8-10]. The main weakness identified was the lack of standardization of the clinical tests, small sample size, absence of blinded evaluators, long time interval between the index tests and arthroscopy, retrospective method evaluation and the use of MRI as a reference standard instead of arthroscopy [3,9].

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Although the literature is extensive on this subject, there is a lack of studies that compared the Se and Sp of shoulder maneuvers and MRI for supraspinatus tears. Therefore, the aim of this study was to evaluate the diagnostic values of seven clinical tests and MRI for supraspinatus tears in patients undergoing shoulder arthroscopy. We hypothesized that clinical tests will be as specific as MRI in diagnosing supraspinatus tendon tears.

MATERIALS AND METHODS

Study design

We carried out a prospective multicenter accuracy study at four orthopedic centers (Sao Paulo Hospital, Christóvão da Gama Hospital and Maternity, Wladimir Arruda Hospital and the Japanese-Brazilian Beneficent Hospital of São Paulo) from April 2017 to April 2019. The study was approved by an institutional review board under registration number 1662/2016 and registered on the ISRCTN registry platform (ID: ISRCTN13083925 – https://doi.org/10.1186/ISRCTN13083925)[11,12].

The inclusion criteria were patients who had an indication of arthroscopy for RCTs with symptoms of shoulder pain for at least 4 wk. The patients included in this study underwent shoulder maneuvers, MRI and arthroscopy; some of these patients were treated with physiotherapy for RCTs between the physical examination and arthroscopy. Patients excluded were those with adhesive capsulitis, glenohumeral osteoarthritis, or shoulder instability, three months after the physical examination, MRI and arthroscopy.

The following demographic information was obtained: Gender, age, symptoms duration (months), side involved, dominance of the affected limb, and history of previous shoulder trauma. Moreover, the time between the index tests (shoulder maneuvers and MRI) and the reference standard (arthroscopy) was evaluated.

Physical examination

Seven clinical tests (full can, empty can, drop arm, resisted external rotation, Hawkins', painful arc, and Neer's sign) were independently performed by four experienced orthopedic shoulder surgeons, in all patients sequentially, following a random order according to the choice of each evaluator and were not always performed in the same order. These tests were chosen based on previously published studies that evaluated the diagnostic values of the shoulder maneuvers for RCTs. The empty can, full can, Hawkin's painful arc and Neer's sign were standardized according to their original description; the drop arm and resisted external rotation tests, according to the description in the study by Hanchard *et al*[9]. Before the start of the study, all four evaluators underwent training to standardize the technique and the positivity criteria of the shoulder maneuvers, in a sample of patients who were not included in this study. Clinical tests were conducted following an average interval of two minutes between each maneuver and a goniometer was used to measure the angles in the limb assessed. The evaluators were blinded to any previous clinical examination and imaging exams but had access to the history and demographic data of the patients. Only one shoulder surgeon assessed each patient.

The seven clinical tests were performed as described below:

Empty can test: With the arm at a position of 90° of abduction in the scapula plane and internal rotation (thumb pointing down), the patient was asked to isometrically resist a downward pressure applied by the examiner[13].

Full can test: With the arm at 90° of abduction in the plane of the scapula and external rotation (thumb pointing up), the patient was asked to resist a downward pressure applied by the examiner isometrically[14].

Drop arm test: The patient elevated the arm above 90° of abduction, using a goniometer, passively by the examiner; the support was removed, and the patient attempted to lower the arm actively in the plane of abduction. This maneuver was considered positive if the patient did not hold the position or if the arm dropped abruptly when lowering the arm in the coronal plane[9,15].

Resisted external rotation test: The patient stands, elbow at side and flexed at 90°, shoulder in neutral rotation, and then asked to externally rotate the shoulder maximally against the tester's isometric resistance, applied at the wrist[9].

Hawkins' test: The upright patient's arm was passively positioned at 90° of shoulder and 90° of elbow flexion. The examiner then forced an internal rotation of the patient's shoulder. The test was considered positive if pain was reported[16].

Neer's sign: The tester passively elevated the patient's arm in the plane of the scapula, preventing scapular movement by holding with the other hand. The test was considered positive if pain occurred during the elevation[17].

Painful arc: The patient actively elevates the shoulder to full elevation, and then lowers it in the scapula plane. The test was interpreted positively if pain was reported during elevation, lowering, or both, between 60˚ and 120˚[18].

The muscle strength of empty can, full can and resisted external rotation was manually measured and interpreted positively if the patient was unable to overcome the resistance imposed by the examiner or if the strength decreased in relation to the contralateral side[1]. If weakness was observed, the test was interpreted as positive. The pain was not graduated, and any level of pain when performing the maneuver was considered positive. The empty can, full can and resisted external rotation tests were interpreted as positive in the case of pain and/or weakness.

MRI

MRI results were evaluated by two blinded musculoskeletal radiologists, who had no prior information on the patient's physical examination. The radiologists evaluated each MRI together and there was a consensus on diagnosis of the lesions. MRI was performed using 3.0 Tesla devices, and the shoulder was placed in a dedicated receive-only shoulder coil. The supraspinatus was evaluated in the axial, oblique coronal, and oblique sagittal planes, at 4 to 5-mm section thickness. The sequences performed were two T1-weighted planes centered on the rotator cuff muscles: The axial plane, covering from the greater tubercle of the humerus to the spinal edge of the scapula, and the oblique sagittal plane, covering the tuberosity to the medial third of the scapula. In T2-weighted imaging, three acquisition planes were chosen: The axial plane, from the top of the acromioclavicular joint to the lower recess of the glenohumeral joint; oblique coronal plane, parallel to the supraspinatus and covering the entire scapular-humeral joint; and the oblique sagittal plane, perpendicular to the supraspinatus, from the distal end of the tendon to the middle part of the rotator cuff muscle belly. The supraspinatus was classified as intact tendon, partial or full-thickness tears according to the fluid signal intensity in T2-weighted coronal and sagittal scans.

Arthroscopy

Arthroscopy was the reference standard and was performed by two experienced orthopedic shoulder surgeons. The principal surgeon was involved in the clinical history and the preoperative physical examination; the assistant was blinded to all the clinical tests and MRI. All patients were placed in the lateral decubitus position with an anterior pad and another in the back, under general anesthesia, and a brachial plexus block. Eleven pounds of balanced suspension was used with the arm in 30˚ to 45˚ of abduction and 30˚ to 45˚ of forward flexion, and posterior inclination of the back to leave the glenoid parallel with the horizontal. The standard posterior portal was used to evaluate the supraspinatus tendon from the articular side. Through the lateral portal, the tendon was assessed from the subacromial space with a 30˚ arthroscope. A probe was used to identify tears, and the supraspinatus tendon was classified as intact, partial or full-thickness tears.

Sample size

The sample size was calculated assuming that the Se was 0.90, the prevalence of RCTs in the general population was 22%, a confidence interval (CI) of 95% with a marginal error of 0.10, resulting in a sample size of at least 157 patients[19-21].

Statistical analysis

The clinical tests and MRI results were compared with the surgical findings of arthroscopy to analyze the diagnostic values. Statistical analysis included the Se, Sp, positive predictive value (PPV), negative predictive value (NPV), accuracy, diagnostic odds ratio (DOR), and likelihood ratio[22]. These ratios were used to predict overall, partial and full-thickness tears. The Se and Sp are presented with the 95%CI. Tests were performed using SPSS software (ver. 25 for Mac; IBM Corp., New York, United States).

RESULTS

A total of 720 patients were consecutively seen at four orthopedic centers, 213 had an indication for shoulder arthroscopy and were included. Fourteen patients were

excluded because the period between the performance of the index tests (shoulder maneuvers and MRI) and arthroscopy was greater than three months, and 199 patients met enrollment criteria for the final analysis. Demographic data were collected and are shown in Table 1.

A total of 47 intact tendons, 62 partial tears (32 bursal-side and 30 articular-side tears) and 90 full-thickness tears (70 supraspinatus, 20 supraspinatus and infraspinatus tears) were found during arthroscopy. The arthroscopy was performed within a mean of 37 d (range, 1 to 83 d) after the physical examination and within 55 d (range, 4 to 89 d) after MRI.

MRI had the highest Se for overall tears (Table 2) (Se = 0.97). Among the clinical tests, the painful arc had the highest Se (Se = 0.85) and the empty can (positive for pain and weakness) had the best performance (DOR = 40). The drop arm test had the highest Sp (0.98), whereas the Sp for MRI for diagnosis of supraspinatus tears was 0.96. The shoulder maneuvers presented low values to rule out tears and the empty can test had the highest NPV between the physical examinations (0.70). The drop arm test and MRI had the highest PPV (0.97 and 0.99, respectively).

The false positive results for overall tears were: Painful arc (0.28), empty can (pain = 0.19/pain and weakness = 0.08), full can (pain = 0.19/pain and weakness = 0.11), resisted external rotation (pain = 0.20/pain and weakness = 0.06), drop arm (0.04), Neer's sign (0.19), Hawkin's (0.36), and MRI (0.02).

For partial tears (Table 3), MRI had the highest Se (0.91); however, MRI had the same Sp (0.98) as the drop arm test. For full thickness tears (Table 4), the empty can test (positive for pain and weakness) had a Se = 0.84; Sp of the drop arm was 0.98, and the MRI had a Se = 0.99 and Sp = 0.98.

DISCUSSION

This study demonstrated the significance of clinical tests for the diagnosis of supraspinatus tears in patients with an indication for shoulder arthroscopy. The Sp of the drop arm test for supraspinatus tears was similar to that of MRI. On the other hand, the physical examination demonstrated limited diagnostic value in ruling out tears when compared to MRI.

The strengths of this study were the inclusion of a consecutive and representative sample of patients; experienced shoulder surgeons performed the physical examination; the technique was standardized, and the positivity criterion for each clinical test was fulfilled. Therefore, we demonstrated that trained orthopedists could perform clinical tests with high Sp for the diagnosis of supraspinatus tears[3,23-27]. Moreover, arthroscopy was utilized as a reference standard, a minimally invasive surgical procedure that is the gold standard for diagnosis and is widely used to treat RCTs[1]. Through arthroscopy, the evaluator can inspect and probe the partial articular and bursal-side tears, assess the rotator cuff footprint accurately and perform a general examination of the shoulder joint in order to identify and treat associated rotator cuff lesions[3].

To standardize shoulder maneuvers is challenging due to the high variability in performance and interpretation. The empty can test, for example, adopts the interpretative criteria of pain, muscle weakness, or both, affecting Se and Sp, as demonstrated in this study[8,9]. Muscle weakness was previously demonstrated in other studies as a reliable criterion, and in our study, the pain associated with weakness obtained the highest Sp[1,28]. We observed that many patients with supraspinatus tears had pain associated with weakness, demonstrating that pain can be a cause for functional disability when performing the test[1,28], as described by Jobe *et al*[13,29].

The empty can, full can and resisted external rotation tests showed improved results when positive for pain and weakness. Positivity only for pain in these tests had better Se, but less Sp; the positivity only for muscle weakness occurred in just a few cases and it was not possible to perform statistical analysis for this specific positivity criterion. The diagnostic values of these three clinical tests were calculated according to positivity only for pain and pain associated with weakness.

Another methodological criterion adopted here was establishing a time limit between physical examination, MRI and arthroscopy, a criterion little used in other accuracy studies and cited as one of the weaknesses in systematic reviews[3,9]. In this study, we choose a three-month interval between the index tests and arthroscopy, to reduce the interpretation bias, different to that in other studies[5,30-33]. The ideal would be to carry out the index tests and arthroscopy in the same day or week;

Table 1 Demographic data of the patients studied, median and standard deviation are shown

Patient variables (*n* = 213)	Statistic *n* (%)
Median age (yr)	47.4; SD = 13.2; range 19 to 76
Symptoms duration (mo)	21.2; range 1 to 144
Gender	
Male	123 (57.7)
Female	90 (42.3)
Laterality	
Right	131 (61.5)
Left	82 (38.5)
Dominant arm	
Dominant	129 (60.5)
Non-dominant	84 (39.4)
History of previous trauma	
Yes	73 (34.3)
No	140 (65.7)

Table 2 Diagnostic values for overall tears

Test	Se	95%CI	Sp	95%CI	Ac	PPV	NPV	LR +	LR -	DOR
Painful arc	0.85	0.79-0.90	0.73	0.60-0.84	0.83	0.91	0.60	3.22	0.20	16.27
Empty can										
P	0.80	0.71-0.87	0.82	0.69-0.90	0.81	0.89	0.68	4.35	0.24	17.78
P and W	0.75	0.63-0.84	0.93	0.81-0.98	0.82	0.94	0.70	10.75	0.27	40.00
Full can										
P	0.78	0.69-0.85	0.81	0.68-0.90	0.79	0.90	0.63	4.15	0.27	15.26
P and W	0.63	0.50-0.74	0.91	0.78-0.96	0.74	0.91	0.63	6.76	0.41	16.53
Resisted external rotation										
P	0.48	0.39-0.57	0.84	0.71-0.92	0.59	0.87	0.43	3.01	0.62	4.87
P and W	0.40	0.31-0.50	0.95	0.85-0.99	0.58	0.95	0.43	8.89	0.62	14.25
Drop arm	0.19	0.13-0.25	0.98	0.89-1.00	0.37	0.97	0.26	9.21	0.83	11.10
Neer's sign	0.78	0.71-0.84	0.82	0.69-0.90	0.79	0.93	0.53	4.26	0.27	15.92
Hawkins'	0.80	0.73-0.85	0.65	0.51-0.77	0.77	0.88	0.49	2.30	0.31	7.53
MRI	0.97	0.93-0.99	0.96	0.86-0.99	0.97	0.99	0.90	23.76	0.03	752

Se: Sensitivity; Sp: Specificity; Ac: Accuracy; PPV: Positive predictive value; NPV: Negative predictive value; LR +: Positive likelihood ratio; LR -: Negative likelihood ratio; DOR: Diagnostic odds ratio; CI: Confidence interval; P: Positive for pain; W: Positive for weakness; MRI: Magnetic resonance imaging.

however, we chose the limit of three months, mainly due to the logistics of the orthopedic centers included in the study, as there is a waiting list for these procedures [34].

We demonstrated high Sp and PPV of the drop arm test, unlike Somerville *et al*[33], who mentioned that no clinical test in isolation is sufficient to diagnose RCTs. Our results showed that the drop arm test is valuable for confirming overall supraspinatus tears (PPV = 0.97). The drop arm test had a similar Sp to MRI for supraspinatus tears; however, one factor contributing to the high Sp of these clinical tests was the possible association of supraspinatus and infraspinatus tears in patients included in this study.

Table 3 Diagnostic values for partial tears

Test	Se	95%CI	Sp	95%CI	Ac	PPV	NPV	LR +	LR -	DOR
Painful arc	0.78	0.66-0.86	0.75	0.61-0.85	0.76	0.81	0.70	3.10	0.30	10.40
Empty can										
P	0.74	0.61-0.84	0.82	0.69-0.90	0.78	0.81	0.75	4.06	0.31	12.99
P and W	0.70	0.55-0.81	0.93	0.81-0.98	0.81	0.91	0.75	10.00	0.32	30.77
Full can										
P	0.72	0.59-0.82	0.81	0.68-0.90	0.76	0.82	0.71	3.84	0.34	11.10
P and W	0.57	0.41-0.71	0.91	0.79-0.96	0.75	0.84	0.71	6.12	0.48	12.80
Resisted external rotation										
P	0.43	0.32-0.55	0.84	0.71-0.92	0.61	0.78	0.52	2.70	0.67	4.01
P and W	0.25	0.15-0.39	0.95	0.85-0.99	0.58	0.87	0.52	5.61	0.78	7.18
Drop arm	0.09	0.04-0.18	0.98	0.89-1.00	0.46	0.86	0.43	4.30	0.93	4.62
Neer's sign	0.72	0.60-0.81	0.83	0.70-0.91	0.76	0.86	0.68	4.30	0.34	12.63
Hawkins'	0.73	0.61-0.82	0.67	0.52-0.78	0.70	0.75	0.64	2.19	0.40	5.44
MRI	0.91	0.81-0.96	0.98	0.89-1.00	0.94	0.98	0.88	42.59	0.09	444.67

Se: Sensitivity; Sp: Specificity; Ac: Accuracy; PPV: Positive predictive value; NPV: Negative predictive value; LR +: Positive likelihood ratio; LR -: Negative likelihood ratio; DOR: Diagnostic odds ratio; CI: Confidence interval; P: Positive for pain; W: Positive for weakness; MRI: Magnetic resonance imaging.

Table 4 Diagnostic values for full-thickness tears

Test	Se	95%CI	Sp	95%CI	Ac	PPV	NPV	LR +	LR -	DOR
Painful arc	0.91	0.84-0.95	0.75	0.61-0.85	0.86	0.91	0.75	3.64	0.12	30.00
Empty can										
P	0.86	0.73-0.94	0.82	0.69-0.90	0.84	0.81	0.87	4.70	0.17	28.15
P and W	0.84	0.65-0.94	0.93	0.81-0.98	0.90	0.87	0.91	12.04	0.17	70
Full can										
P	0.85	0.72-0.92	0.81	0.68-0.90	0.83	0.82	0.85	4.54	0.18	24.76
P and W	0.72	0.52-0.86	0.91	0.78-0.96	0.84	0.82	0.85	7.74	0.31	25.07
Resisted external rotation										
P	0.56	0.41-0.70	0.84	0.71-0.92	0.71	0.74	0.70	3.51	0.52	6.71
P and W	0.58	0.43-0.72	0.95	0.85-0.99	0.77	0.92	0.70	12.79	0.44	29.17
Drop arm	0.25	0.18-0.35	0.98	0.89-1.00	0.49	0.96	0.39	12.12	0.76	15.88
Neer's sign	0.83	0.74-0.89	0.83	0.70-0.91	0.83	0.91	0.70	4.97	0.21	24.12
Hawkins'	0.85	0.76-0.91	0.67	0.52-0.78	0.79	0.84	0.68	2.54	0.23	11.20
MRI	0.99	0.95-1.00	0.98	0.89-1.00	0.98	0.99	0.98	46.35	0.01	3266

Se: Sensitivity; Sp: Specificity; Ac: Accuracy; PPV: Positive predictive value; NPV: Negative predictive value; LR +: Positive likelihood ratio; LR -: Negative likelihood ratio; DOR: Diagnostic odds ratio; CI: Confidence interval; P: Positive for pain; W: Positive for weakness; MRI: Magnetic resonance imaging.

Physical examination has already been demonstrated in previous studies as limited in ruling out RCTs[1,33]. The limitations of the shoulder maneuvers for excluding supraspinatus tears were also shown in our study; moreover, the painful arc and Hawkins' tests had the highest false-positive rates in patients with intact tendons.

Physical examination alone cannot quantify the size and extension of the supraspinatus tear, muscle atrophy, and associated rotator cuff lesions (biceps tendon pathologies and acromioclavicular joint osteoarthritis). Therefore, imaging exams,

such as radiography, ultrasonography, or MRI, are essential to determine surgical indication[33].

Limitations

First, the reliability of the clinical tests, MRI and arthroscopy was not evaluated. Previous studies demonstrated a moderate to substantial agreement of the empty can, painful arc and external rotation resistance tests, but a fair agreement for the Hawkins' and the Neer's sign[35]. We suggest that future studies should evaluate mainly the reliability and analysis of Se and Sp of the physical examination.

Second, muscle weakness was evaluated manually using subjective criteria according to each tester. We did not use a dynamometer for objective data collection, as some studies considered a 20% decrease in strength in relation to the contralateral side, a positivity criterion for weakness[36]. Moreover, we did not quantify pain when performing each maneuver, with a visual analogue scale, for example, and any shoulder pain during the test was considered positive.

Third, the principal surgeon performing the arthroscopy was not blinded to the shoulder maneuvers and MRI; however, to reduce this bias, we included a second surgeon's evaluation, blinded to physical examination and MRI.

CONCLUSION

Physical examination demonstrated good diagnostic value, showing that the drop arm test had a similar Sp to MRI for supraspinatus tears. However, MRI had higher Se compared with the shoulder maneuvers and was more accurate in ruling out supraspinatus tears.

ARTICLE HIGHLIGHTS

Research background

Shoulder maneuvers and magnetic resonance imaging (MRI) are performed in current practice in patients with rotator cuff tears (RCTs); however, there is insufficient evidence as to which clinical test is efficient for diagnosing supraspinatus tears.

Research motivation

The motivation for this study was the exponential increase in MRI requests and little appreciation of physical examination in patients with RCTs.

Research objectives

The objective of this study was to compare the accuracy of clinical tests with MRI for diagnosing supraspinatus tears.

Research methods

A prospective multicenter accuracy study of seven shoulder maneuvers and MRI for supraspinatus tears in patients undergoing arthroscopy was performed.

Research results

MRI and the drop arm test had the highest specificity (0.99 and 0.97, respectively) for overall supraspinatus tears; the Hawkin's test had the highest rate of false-positive findings (0.36) in patients with intact tendons.

Research conclusions

Shoulder maneuvers had good diagnostic value for supraspinatus tears; however, MRI had the highest diagnostic value for ruling out tears.

Research perspectives

Futures studies are necessary to analyze the accuracy of clinical tests and MRI for infraspinatus and subscapularis tears.

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SYSTEMATIC REVIEWS

Long-term outcomes of the four-corner fusion of the wrist: A systematic review

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Abstract

BACKGROUND

Four-corner fusion (4CF) is a motion sparing salvage procedure that is used to treat osteoarthritis secondary to advanced scapholunate collapse or longstanding scaphoid nonunion advanced collapse. Little is known about the long-term survivorship and outcomes of 4CF.

AIM

To report on clinical and functional long-term outcomes as well as conversion rates to total wrist fusion or arthroplasty.

METHODS

The systematic review protocol was registered in the international prospective register of systematic reviews (PROSPERO) and followed the PRISMA guidelines. Original articles were screened using four different databases. Studies with a minimum Level IV of evidence that reported on long-term outcome after 4CF with a minimum follow-up of 5 years were included. Quality assessment was performed using the Methodological Index for Non-Randomized Studies criteria.

RESULTS

A total of 11 studies including 436 wrists with a mean follow-up of 11 ± 4 years (range: 6-18 years) was included. Quality assessment according to Methodological Index for Non-Randomized Studies criteria tool averaged 69% ± 11% (range: 50%-87%). Fusion rate could be extracted from 9/11 studies and averaged 91%. Patient-reported outcomes were extracted at last follow-up from 8 studies with an average visual analog scale of 1 ± 1 (range: 0-2) and across 9 studies with an average Disabilities of the Arm, Shoulder and Hand score of 21 ± 8 (range: 8-37).

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At last follow-up, the cumulative conversion rate to total wrist fusion averaged 6%. There were no conversions to total wrist arthroplasty.

CONCLUSION
The 4CF of the wrist is a reliable surgical technique, capable of achieving a good long-term patient satisfaction and survivorship with low rates of conversion to total wrist fusion.

Key Words: Four-corner fusion; Partial wrist arthrodesis; Midcarpal arthrodesis; Scapholunate collapse wrist; Scaphoid nonunion advanced collapse; Scaphoid nonunion

Core Tip: Four-corner fusion is a motion sparing salvage procedure that is used to treat osteoarthritis secondary to scaphoid advanced collapse or longstanding scaphoid nonunion advanced collapse. Our systematic review evaluated long-term clinical and radiographic outcomes of the four-corner fusion and critically appraised the methodology of studies. The results showed that four-corner fusion is capable of achieving a good long-term patient satisfaction and survivorship with low rates of conversion to total wrist fusion. Recommendations for future research are provided.

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INTRODUCTION

Four-corner fusion (4CF) is a motion sparing salvage procedure that is used to treat osteoarthritis secondary to advanced scapholunate collapse or longstanding scaphoid nonunion advanced collapse. Proximal row carpectomy (PRC) and 4CF are the two mainly used surgical techniques in such cases[1]. The decision to choose one technique over the other is primarily based on the surgeon's preference and experience, as long-term results are not clearly elucidated in the current literature so far[2]. 4CF seems to show longer survivorship, where PRC seems to provide better wrist motion[1,3-5]. Since the introduction of the 4CF by Watson and Ballet in 1984[6], various fixation techniques have been described, including Kirschner wires, headless compression screws, staples and plates[6-9]. However, using these techniques, different potential complications have been observed, in particular: nonunion, progressive osteoarthritis (OA) or hardware impingement/irritation[1,10-12].

The long-term survivorship and ultimate conversion rate of 4CF to wrist arthrodesis remains an unelucidated aspect. Although different studies are emerging that report on long-term outcomes of 4CF, it remains difficult to draw conclusions based on individual studies due to heterogeneity of outcome measures and surgical techniques. Hence, it was the aim of the current study to provide a systematic approach on evaluating evidence reporting on the long-term outcomes of 4CF with appropriate tools for critical appraisal.

MATERIALS AND METHODS

Search strategy

A systematic computer-based database search was conducted using CENTRAL (Cochrane Central Register of Controlled Trials), MEDLINE (Pubmed), EMBASE and Web of Science Core Collection. A total of fifteen combinations for each database using the following key-words were used: "four corner," "4 corner," "midcarpal," "scapholunate advanced collapse" and "scaphoid nonunion advanced collapse" with

the terms "surgery," "fusion" and "arthrodesis." All published studies from January 1, 1978 until January 1, 2020 were included in the systematic search. First, a blinded and independent process of selection was carried out by two authors (D.K., P.K.) based on title and abstract. Next, a thorough analysis of eligible studies was performed by evaluating full texts. Any excluded study together with the reason of exclusion was noted and compared between readers. Studies reporting clinical or radiographic outcomes of 4CF for the treatment of degenerative wrist conditions were selected based on predefined eligibility criteria. The protocol of a parallel ongoing systematic review used by the same group regarding the 4CF has been published and registered in the international prospective register of systematic reviews (PROSPERO) under the registration number: CRD42020164301. Inclusion and exclusion criteria are emphasized in Table 1.

Data extraction and quality assessment

Data collection included fusion rates, revision rates and conversion rates to total wrist arthrodesis. Wrist range of motion (ROM), including wrist flexion and extension, total flexion-extension arc as well as radial-ulnar deviation, was extracted. Grip strength was noted as percentage of the opposite hand. Patient-reported outcome measures were included as the Disabilities of the Arm, Shoulder and Hand questionnaire (DASH) and the visual analog scale (VAS) scores. Where available, data regarding incidence of radiolunate arthritis was included. The quality of all the studies was then assessed using the Methodological Index for Non-Randomized Studies criteria[13]. Methodological Index for Non-Randomized Studies criteria assess eight critical aspects of the study design for non-comparative clinical studies and an additional four aspects of study design for comparative clinical studies. Each item is given a score of zero if information is not reported, one if information is reported but inadequate, and two if information is reported and adequate. Therefore, the maximum possible score is 16 for non-comparative studies and 24 for comparative studies. Each score was then converted into a percentage to harmonize the scoring system.

Statistical analysis

The statistical analysis was performed using Review Manager (RevMan Cochrane) and Comprehensive Meta-Analysis Software. For quantification of methodological inconsistency and heterogeneity across studies, an I^2 test was performed, with a P value of $P = 0.10$. A level of more than 75% was considered as considerable. This has assessed whether observed differences in results are compatible with chance alone.

RESULTS

Systematic database search

The initial database search yielded 4726 studies. After removal of duplicates, 2323 studies remained. Next, screening based on title and abstract was performed, and 126 studies remained for further assessment. These were then screened for eligibility against the inclusion and exclusion criteria based on abstract and full-text review. Finally, 11 studies could be included in the final analysis (Figure 1) with the reasons for exclusion separately emphasized in the flow-chart.

Quality assessment

A quality assessment was performed in all included studies (Table 2). There were seven retrospective case series[3,5,14-18], three retrospective cohort studies[19-21] and one prospective cohort study[22]. The calculated average from scores according to the Methodological Index for Non-Randomized Studies criteria tool was 69.0% ± 11.1% (range: 50%-87%).

Demographics, indications and surgical fixation techniques

A total of 463 wrists was included for further analysis (Table 2). The mean age at time of surgery over all included studies was 49 ± 7 years (range: 34-63 years). The most frequent indications were degenerative wrist conditions such as scapholunate collapse (10/11 studies)[3,5,14-19,21,22] or scaphoid nonunion advanced collapse (8/11 studies)[3,5,15-19,21]. Other less frequent indications were scaphoid chondrocalcinosis advanced collapse[16], an unclassified OA[5,20] and perilunate OA[21]. The following fixation techniques were used: Kirschner wires[3,5,14,15,18,19,21], locking or non-locking plates[3,16,17,21], staples[3,22] and screws[3,21].

Table 1 Criteria for study selection

Inclusion criteria	Exclusion criteria
Human studies in English or German language	Oral presentations, cadaveric or review articles, animal studies
Minimum Level IV case series studies using Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence	Language not in English or German
Four corner fusion surgery using any technique	Minimum follow-up less than 5 yr
A minimum follow-up of 5 yr	Inflammatory arthropathy as etiology
Clinical and radiographic data including patient-reported outcomes, grip/pinch strength, range of motion, fusion rates, revisions or complications have been reported	Insufficient outcome data reported

Table 2 Demographics, surgical techniques and patient-reported outcomes

Author	Year	Study design	Number of wrists	Indication	Mean age (yr)	Fixation Technique	VAS		DASH		MINORS (%)
							Preop	Postop	Preop	Postop	
Cha SM	2013	Retrospective case series	40	SLAC	47	K-wires	6.3	2.0	44	17	75
Luegmair M	2012	Retrospective case series	24	SLAC, SNAC, SCAC	53	Plates	-	-	-	19	75
Bain GI	2010	Prospective cohort study	31	SLAC	47	Staples	6.0	1.0	-	-	87
Berkhout MJL	2015	Retrospective cohort study	8	SLAC, SNAC	45	K-wires	-	0.3	-	-	62
Kitzinger HB	2003	Retrospective case series	37	SLAC, SNAC	46	K-wires	2.7	1.7	-	24	62
Trail I	2015	Retrospective case series	116	SLAC, SNAC	47	K-wires, Plates, Staples, Screws	-	1.9	-	37	62
Neubrech F	2012	Retrospective case series	60	SLAC, SNAC, unclassified OA	63	K-Wires	-	1.4	-	20	87
Odella S	2018	Retrospective case series	20	SLAC, SNAC	53	Plates	-	2.0	-	17	62
Traverso P	2017	Retrospective case series	15	SLAC, SNAC	49	K-wires	-	-	-	8	62
Wagner ER	2017	Retrospective cohort study	51	Unclassified OA	34	Plates	-	-	-	19	75
Williams J	2018	Retrospective cohort study	61	SLAC, SNAC, perilunate OA	52	K-wires, Plates, Screws	-	1.0	-	27	50
Total/Averages			463		49			1.4		21	69
SD					± 7			± 0.6		± 8	± 11

SD: Standard deviation; VAS: Visual analog scale; DASH: Disabilities of the Arm, Shoulder and Hand questionnaire; SLAC: Scapholunate advanced collapse; SNAC: Scaphoid nonunion advanced collapse; SCAC: Scaphoid chondrocalcinosis advanced collapse; MINORS: Methodological items for non-randomized studies; OA: Osteoarthritis; K-wires: Kirschner wires.

Patient-reported outcomes

Preoperative VAS and DASH scores were only reported in a minority of studies (3 for VAS[14,15,22] and 1 for DASH[14]), which did not allow direct pre- to postoperative comparison (Table 2). Eight studies reported on postoperative VAS score and averaged 1 ± 1 (range: 0-2) at the latest follow-up. Postoperative data on DASH scores were pooled from 9 studies[3,5,14-18,20,21], which averaged 21 ± 8 (range: 8-37).

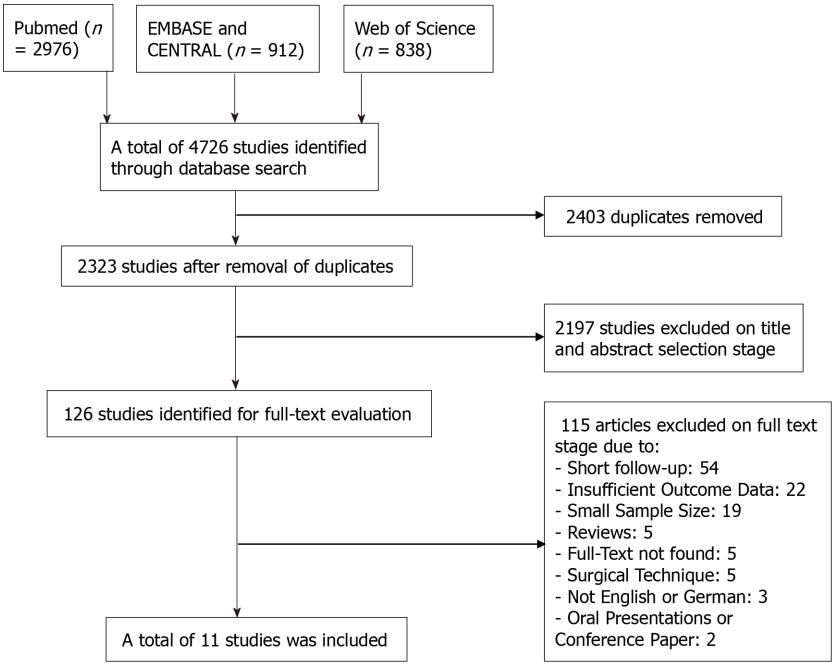

Figure 1 Flowchart of the systematic search.

Fusion rates, revisions and survivorship

The mean follow-up was 11 ± 4 years (range: 6-18 years) (Table 3). Revision rates were reported in 8 studies[3,14,16-18,20-22] and had an overall average of 13% (range: 5%-34%). Nine studies (82%)[3,14,16-22] included data on the total number of nonunions, averaging 9% (range: 0%-24%) at last follow-up, resulting in a fusion rate of 91% (range: 76%-100%). Eight studies[3,14,16-18,20-22] reported on conversion rates to a total wrist fusion (TWF). A conversion to a TWF was needed on average in 6% of cases (range: 0%-20%). There were no cases reported of conversion to total wrist arthroplasty.

Development of radiocarpal osteoarthritis

None of the included studies reported on preoperative signs of radiocarpal OA (Table 3). Five studies[5,14,15,18,20] reported on postoperative signs of radiocarpal OA of grade 2 or higher with an average incidence of 42% ± 26% (range: 5%-73%) at an average follow-up of 13 ± 3 years (range: 8-18 years). This was determined radiographically on conventional radiographs.

Grip strength and range of motion

Preoperative grip strength was only available in 5 studies and preoperative data on ROM in only 4 studies (Table 4), which did not allow meaningful comparison to the postoperative results. The postoperative grip strength was noted in 8 studies[3,5,14-17,20,22] and averaged 68% ± 18% of the contralateral side (range: 30%-85%). Total postoperative flexion-extension arc, noted in 10 studies[3,5,14-20,22], was on average 66 ± 9 (range: 54-87). Postoperative ROM for radial-ulnar deviation, available in 9 studies[3,5,14-16,18-20,22], averaged 34 ± 6 (range: 26-49).

Statistical analysis

The level of evidence of studies that were included lacked randomized controlled trials and did not allow performance of meta-analysis.

DISCUSSION

This is the first systematic review to investigate outcomes of the 4CF procedure at the long-term follow-up. The most important finding of the study is that 4CF can achieve good long-term patient satisfaction as well as good functional results. This can be observed out of the pooled data with low VAS values and positive DASH scores on

Table 3 Fusion rates, survivorship including rates of conversion to total wrist fusion and complications

Author	Number of wrists	Fixation technique	Nonunion (*n*)	Fusion (%)	Revisions (%)	Conversion to TWF (%)	Complications
Cha SM	40	K-wires	0	100	2 (5)	1 (3)	1 x impingement
Luegmair M	24	Plates	2	92	2 (8)	0	-
Bain GI	31	Staples	3	90	5 (16)	2 (7)	1 x delayed union
Berkhout MJL	8	K-wires	1	88	-	-	1 x CRPS, 1 x delayed union
Kitzinger HB	37	K-wires	-	-	-	-	-
Trail I	116	K-wires, plates, staples, screws	28	76	14 (12)	6 (5)	3 x impingement
Neubrech F	60	K-wires	-	-	-	-	-
Odella S	20	Plates	0	100	1 (5)	0	1 x implant loosening
Traverso P	15	K-wires	0	100	2 (13)	1 (7)	-
Wagner ER	51	Plates	6	88	15 (29)	6 (12)	1 x infection, 8 x impingement
Williams J	61	K-wires, plates, screws	3	95	21 (34)	12 (20)	4 x impingement, 1 x ulnar impaction, 1 x infection
Totals/Averages	463		43 (9%)	91 ± 7	62 (13%)	28 (6%)	

TWF: Total wrist fusion; CRPS: Complex regional pain syndrome; K-wires: Kirschner wires.

Table 4 Range of motion and grip strength

Author	Grip strength (%)		ROM Flexion-extension		ROM radial-ulnar (%)	
	Preop	Postop	Preop	Postop	Preop	Postop
Cha SM	71	85	84	66	45	39
Luegmair M	38	70	57	64	24	30
Bain GI	27	30	78	57	35	30
Berkhout MJL	-	-	-	87	-	49
Kitzinger HB	69	80	68	62	35	34
Trail I	-	53	-	60	-	26
Neubrech F	-	85	-	63	-	30
Odella S	-	75	-	79	-	-
Traverso P	-	-	-	69	-	33
Wagner ER	60	65	-	54	-	32
Williams J	-	-	-	-	-	-
Averages	53	68	72	66	35	34
SD	± 17	± 18	± 10	± 10	± 8	± 6

ROM: Range of motion; SD: Standard deviation; Preop: Preoperative; Postop: Postoperative.

last follow-up. An average fusion rate over 90% could be achieved, however with large variations across studies. Trail *et al*[3] reported a high nonunion percentage with only 76% fusion, further indicating the future need of 4CF for technique improvements and advancements in implant choice. Surprisingly, in the case of a successful 4CF, only an average of 6% of ultimate conversion to TWF was observed. This was in the context of lacking data on the preoperative state of the radiolunate joint, where a substantial amount could have been present at the time of surgery.

Nevertheless, the quality assessment provided important data on the evidence level of the studies, where relevant issues were elucidated. First, there were no double-blinded randomized controlled trials. Second, the single prospective cohort study, as declared by authors, had a questionable design whereas only the data collection might have been prospective[22]. The lack of preoperative data for almost all functional outcomes (ROM, grip strength) in the majority of studies precludes the quantification of the clinical gain from surgery[5,17-21]. Another important limitation was the fact that the outcomes were mostly reported in a cumulative fashion and not longitudinally over time. As such, a subgroup analysis of outcomes based on etiology (degenerative or post-traumatic) or the creation of a Kaplan-Meier survivorship curve to observe the time points of conversions could not be performed.

Although many treatments are available for scapholunate collapse and scaphoid nonunion advanced collapse wrist[23], the main debatable alternative to 4CF is the PRC[24,25]. A systematic review of long-term outcomes of PRC studies reported a reoperation rate of 14.3%[26].Of particular value is to mention that these failures were not only represented by conversions to TWF but also contained cases where revision arthroplasty was undertaken[4]. As such, the reoperation rates and conversion rates to TWF were not equal in this systematic review[26]. Generally, it was thought that PRC might yield better ROM[27]. However, this cannot be stated consistently, as recent systematic reviews and meta-analysis question the clinical relevance of differences that were observed between these techniques[2]. These relevant differences were limited to ROM, grip strength and patient-reported outcomes. In contrast, another systematic review reported a benefit in 4CF in terms of grip strength[28].

A further subject that was recently explored is the cost-effectiveness of PRC, where findings yielded either superior[29,30] or similar results[31] when compared to 4CF. Revision rates, especially during early follow-up, are higher in 4CF among some reports[21], highlighting impingement of hardware and nonunion as main reasons of revision[32]. This is attributed by authors to technical challenges and aspects, such as incomplete removal of the cartilage and subchondral bone, which is a key step of the procedure[11], quality and location of bone graft[33] as well as compression and carpal height achieved[34]. Optimal placement has yet to be defined to avoid revisions in 4CF due to impingement[32].

As such, in the context of continuous debate, an analysis of the long-term results, especially of the ultimate conversion rate to TWF or wrist arthroplasty, is crucial in determining the long-term benefit when choosing the surgical treatment option. The current systematic review is a substantial contribution to the understanding and knowledge of 4CF long-term outcomes as well as an analytical exploration of the limitations of studies (sources of heterogeneity and bias) that provide recommendations for future work.

CONCLUSION

The 4CF of the wrist is a reliable surgical technique, capable of achieving a good long-term patient satisfaction and survivorship with low rates of conversion to total wrist fusion.

ARTICLE HIGHLIGHTS

Research background

Four-corner fusion (4CF) is a motion sparing salvage procedure that is used to treat osteoarthritis secondary to advanced collapse or longstanding scaphoid nonunion advanced collapse. Proximal row carpectomy and 4CF are the two mainly used surgical techniques in such cases. The decision to choose one technique over the other is primarily based on the surgeon's preference and experience, as long-term results are not clearly elucidated in the current literature so far.

Research motivation

The long-term survivorship and ultimate conversion rate of 4CF to wrist arthrodesis remains poorly described. As various fixation techniques have been employed (Kirschner wires, headless compression screws, staples, plates), different potential complications have been observed, in particular, nonunion, progressive osteoarthritis or hardware impingement/irritation. There is no consensus on the best surgical

implant and no synthesis on the long-term outcomes.

Research objectives

To provide a systematic approach on evaluating evidence reporting on the long-term outcomes of 4CF with appropriate tools for critical appraisal. We aimed to compare patient-reported outcomes, fusion rates, grip strength, range of motion and rates of development of radiocarpal osteoarthritis and revision to total wrist fusion.

Research methods

A study protocol for the systematic search was registered prospectively in the international prospective register (PROSPERO) and performed according to the PRISMA guidelines. Data collection included fusion rates, revision rates and conversion rates to total wrist arthrodesis. Wrist range of motion, including wrist flexion and extension, total flexion-extension arc, as well as radial-ulnar deviation, was extracted. Grip strength was noted as percentage of the opposite hand. Patient-reported outcome measures were included as the Disabilities of the Arm, Shoulder, and Hand questionnaire and the visual analog scale scores (Table 4). Where available, data regarding incidence of radiolunate arthritis was included. The quality of all the studies were then assessed using the Methodological Index for Non-Randomized Studies criteria.

Research results

A total of 11 studies including 436 wrists with a mean follow-up of 11 ± 4 years (range: 6-18 years) was included. Quality assessment according to Methodological Index for Non-Randomized Studies criteria tool averaged 69% ± 11% (range: 50%-87%). Fusion rate could be extracted from 9/11 studies and averaged 91%. Patient-reported outcomes were extracted at last follow-up from 8 studies with an average visual analog score of 1 ± 1 (range: 0-2) and across 9 studies with an average Disabilities of the Arm, Shoulder, and Hand score of 21 ± 8 (range: 8-37). The postoperative grip strength was noted in 8 studies and averaged 68% ± 18% of the contralateral side. Total postoperative flexion-extension arc was on average 66 ± 9. At last follow-up, the cumulative conversion rate to total wrist fusion averaged 6%.

Research conclusions

The 4CF of the wrist is a reliable surgical technique, capable of achieving a good long-term patient satisfaction and survivorship with low rates of conversion to total wrist fusion.

Research perspectives

Future studies should define their study populations and protocols a priori before analysis. More in-depth details regarding patient selection (mostly preoperative data on range of motion, grip strength and radiolunate osteoarthritis) should be provided that would allow objective comparison.

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