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EDITORIAL

Genetics of congenital anomalies of the hand

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Abstract

Congenital anomalies of the hand are malformations occurring during the development of the human limb, and present as isolated disorders or as a part of a syndrome. During the last years, molecular analysis techniques have offered increasing knowledge about the molecular basis of hand malformations. Disturbances in the signaling pathways during the development of the upper limb result in malformations of the upper extremity. At present, several genes have been identified as responsible for hand anomalies and other have been recognized as suspect genes related to them. Different and new high throughput methods have been introduced for the identification of the gene mutations. In the current editorial, we summarize concisely the current molecular status of isolated hand genetic disorders and the recent progress in molecular genetics, including the genes related to the disorder. This progress improves the knowledge of these disorders and has implications on genetic counselling and prenatal diagnosis.

Key Words: Hand; Gene; Mutation; Molecular; Diagnosis; Disorders

Core Tip: The genetic basis of hand disorders is elucidated by the expansion of knowledge and introduction of molecular analysis techniques which contribute to the identification of new genes responsible for them. New genes and mutations are being isolated and correlated with the disorder based on the advances in sequencing technology, such as next generation sequencing and genetic consultation, and future therapeutic developments are enhanced. There appears to be a gap in the literature concerning the knowledge about the genetic basis of all hand disorders. The current molecular status of them is discussed and a summary of different genes, already identified or suspected to be related with them, is presented.

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INTRODUCTION

Congenital anomalies of the hand very often have an autosomal dominant pattern of inheritance and most of them have a monogenic genetic basis with variable penetrance[1]. They are related with a disturbance of the normal procedure of the development of the limb, with diverse aetiology and variable clinical features, and their proposed classification system has changed throughout the years, incorporating a rather molecular than anatomic scope of the phenotypes[2]. Initially, the Swanson Classification of congenital anomalies of the hand, including nine categories of malformations, was used by the International Federation of Societies for Surgery of the Hand Committee on Congenital Conditions, as it was considered effective according to the knowledge at the time. Later on, as the awareness of pathogenetic routes and molecular basis of limb formation expanded, the object modeling technique classification was presented, dividing hand anomalies into four groups: Malformations (which include the majority of the disorders), deformations, dysplasias, and syndromes[3].

To date, several loci and disease-causing genes, including all four categories of hand disorders, have been identified in humans, and correlated to specific phenotypes.

Since these phenotype manifestations are indicators that the fetus or the newborn may suffer from a syndrome, the ability to identify the potential syndromes associated with these anomalies, is important for the clinician. Additionally, it is important to distinguish between syndromic and non-syndromic cases for reasons of genetic counselling. Therefore, we present a concise summary of the main genes that are responsible for the disorders, whose etiology is mainly based on known genetic and not external factors, and lead to hand disorder phenotypes when mutated.

POLYDACTYLY

Preaxial/Radial polydactyly

Preaxial polydactyly is a malformation described by an extra digit on the radial side of the hand with an incidence as high as 1 in 3000 births. It follows an autosomal dominant inheritance model with reduced penetrance[4]. Thumb polydactyly has been further subdivided into six subtypes by Wassel according to the level of (metacarpal, proximal, or distal phalange) and the extent of duplication (partial and complete)[5,6]. Next generation sequencing (NGS) analysis in a patient with Wassel III polydactyly identified three gene mutations as follows: (1) Substitution c.1639 G>T in *RPGRIP1* gene; (2) Insertion of adenine in *TMEM216* gene; and (3) A>G nucleotide substitution (c.490) in *FBN1* gene. In a patient with Wassel IV duplication, the following mutations were identified: (1) Adenine duplicated in exon 45 of *CEP290* gene; (2) Two substitutions in *RPGRIP1* gene, c.1639 G>T and c.685 G>A; (3) Adenine insertion in *TMEM216* gene, c.432-11 432-10 insA; (4) Substitution G>C c.8249 in *MEGF8* gene; and (5) Substitution T>A c.548 in *CEP164* gene. These mutations are suspected to be involved in the formation of thumb duplication phenotype[7]. Another suspected way of development of preaxial polydactyly is the overexpression of *HES1* gene. The produced protein is considered to intervene in SHH/GLI signaling axis and results in the manifestation of preaxial polydactyly[8]. The disease gene locus with triphalangeal thumb was identified in chromosome 7q36[9]. Point mutations (105C>G, 305A>T, 323T>C, 404G>A, 295T>C, 4909C>T, 297G>A, 334T>G, 402C>T, and 545G>A) have been identified, and a 739A>G transition near the 5-end of the zone of polarizing activity regulatory sequence (*ZRS*) and a 621C>G mutation in the *ZRS* of the *LMBR1* gene have also been mapped[10,11]. Two more novel mutations (ZRS131A>T and ZRS474C>G) correlated with preaxial polydactyly were identified in a recent study of a Chinese family[12]. No mutations have been identified for index finger polydactyly, which is inherited with an autosomal dominant trait[13].

Postaxial polydactyly

Postaxial polydactyly presents with extra digits on the ulnar side of the hands. Mutations in genes *ZNF141, GLI3, IQCE, GLI1, FAM92A1, KIAA0825*, and *DACH1* have been isolated and their involvement in this manifestation is identified[14].

Responsible gene loci have been mapped to 7pl5-q11.23, 13q21-q32, 19p13.2-p13.1, 7q21-q34, and 13q13.3- 13q21.2 regions using genome-wide scan[15]. Subsequently, two heterozygous mutations, p.A765PfsX14 and p.R539TfsX12 in *GLI3* gene, and P.T474I mutation in the *ZNF141* gene have been identified using exome sequencing[16-18]. Recently, a new suspected mutation in *GLI1* gene (c.1133 C>T) was isolated in an Indian family with the disorder and a mutation in *KIAA0825* gene has been isolated and suspected, although the role of the protein encoded by this gene in limb formation is still unclear[19,20].

Central polydactyly and complex types of polydactyly

Central polydactyly phenotype is characterized by duplication of the 2nd, 3rd, or 4th digit[21]. No disease causing locus or gene responsible for central polydactyly has been identified. Mirror image polydactyly is characterized by mirror-image duplication of fingers and toes[22]. A mutation of the *MIPOL1* gene at 14q13 and two heterozygous deletions including the *PITX1* gene were identified[23].

SPLIT-HAND MALFORMATION

Split-hand malformation may occur as an isolated trait or accompanied with other defects. It manifests as a clinically heterogeneous disorder characterized by absent central digital rays, which result in median clefts of the hand. Responsible mutations map to chromosome 7q21.3-q22.1, chromosome Xq26, and chromosome 10q25[24]. *LBX1, BTRC, POLL, FBXW4*, and *BTRC* gene mutations are reported as responsible for the disease[25]. Recent molecular studies have expanded the list of suspected gene mutations. A *TP63* gene translocation and *FGFR1, BHLHA9, LRP6, UBA2*, and *WNT10B* gene mutations have been recently identified[26-30].

RADIAL RAY DEFECTS

Radial ray defects occur as an isolated malformation or syndromic. They are characterized by partial or complete absence of radial ray structures. Radial defects comprise a large group of diseases. They are associated with *TBX3* gene, coding for a T-box transcriptional factor. *TBX3* is widely expressed in a variety of tissues including forelimbs and hindlimbs, epithelium of the mammary gland, the genital tubercle, and the uterus[31].

DEFECTS IN DORSO-VENTRAL PATTERNING

This disorder category involves nail-patella syndrome, which is autosomal dominant and is expressed with defects affecting the nails, skeleton, kidneys, and eyes. Loss of function mutations in the *LMXlB* gene lead to the syndrome[32,33]. *LMXlB* is involved in determination of dorso-ventral patterning of the limb. A mutation of *WIF1* gene has been isolated as a potential novel cause of the phenotype[34].

BRACHYDACTYLY

Brachydactyly phenotype may present as an isolated defect or in association with other malformations and refers to disproportionately short fingers and toes. Isolated brachydactylies usually occur as autosomal dominant traits and show a high degree of phenotypic variability. A locus on chromosome 5p13.3-p13.2 and the Indian hedgehog gene on chromosome 2q35-36 are involved in Type A1 brachydacty[35]. A mutation in the human bone morphogenetic protein receptor 1B gene (*BMPR1B*) on chromosome 4q can cause Type A2 brachydactyly. Mutations in growth/differentiation factor-5 gene (*GDF5*) alter the receptor binding affinities and can also cause symphalangism. No gene or locus for Type A3 brachydactyly has been identified. Type B Brachydactyly phenotype involves isolated mutations in the receptor kinase-like orphan receptor 2 gene (*ROR2*) on 9q22[36]. Type C Brachydactyly phenotype is considered to be caused by mutations in *GDF5*[37].

SYNDACTYLY

Syndactyly is characterized by the fusion of soft and/or bony tissue of the fingers of the hand and is the most common congenital malformation of the hand in North America and Europe. Syndactyly can occur as an isolated malformation or as part of a syndrome. *HOXD13, FBLN1, GJA1, LMBR1, LRP4, GREM, FGF16,* and *BHLHA9* genes are incriminated for the disorder, when mutated[38]. Syndactyly type I presents as fusion between the middle and ring fingers. It is an autosomal dominant malformation and the most common type of syndactyly. Mutations in human chromosome 2q34-q36 have been isolated. Syndactyly type II is a dominantly inherited malformation. Its phenotype contains soft tissue syndactyly between the middle and ring fingers and sometimes clinodactyly or camptodactyly of the little finger. *HOXDl3* gene mutations are involved in this disorder[39]. Syndactyly type III affects the ring and little fingers with the middle phalanx of the little finger being absent or rudimentary. Mutations in Connexin 43 are involved in this type of syndactyly. Syndactyly type IV manifests as syndactyly of all fingers, and syndactyly type V as metacarpal synostosis. The genetic background of the last two types is not yet investigated[40].

CONCLUSION

Genetic hand disorders and their genetic heterogeneity and allelic heterogeneity between families indicate more complex mechanisms besides simple Mendelian inheritance. These mechanisms include underlying genetic, epigenetic, and environmental factors[41]. With the advent of NGS technology, including exome sequencing and whole-genome sequencing, new mutations causing hand malformations are isolated and the molecular pathogenesis is exposed. Systematic bioinformatics analysis of the responsible genes, using high-throughput sequencing, is a valuable tool in establishing the precise genotype–phenotype correlations of hand genetic disorders. Diagnosis is still largely postbirth, although prenatal diagnosis *via* molecular and genetic methodologies exists. The expansion of our knowledge related to the mutations leading to different phenotypes, with the use of next generation sequencing analysis, will contribute to prenatal diagnosis, prediction of operative treatment strategy, and potential future applications in gene therapy.

FOOTNOTES

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REVIEW

Changes in trends of orthopedic services due to the COVID-19 pandemic: A review

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Abstract

As of June 10, 2022, the World Health Organization has recorded over 532 million documented coronavirus disease 2019 (COVID-19) [(Coronavirus) SARS-CoV-2] cases and almost 6.3 million deaths worldwide, which has caused strain on medical specialties globally. The aim of this review is to explore the impact that COVID-19 has had on orthopedic practices. Providers observed a rapid decline in the number of orthopedic patients' admissions due to cancellation of elective procedures; however, emergent cases still required treatment. Various observational studies, case reports, and clinical trials were collected through a PubMed database search. Additional sources were found through Google. The search was refined to publications in English and between the years of 2019 and 2021. The keywords used were "COVID-19" and/or "Orthopedic Injuries". Thirty-seven studies were retained. The pandemic brought on significant changes to the mechanism of injury, number of admissions, type of injuries, and patient outcomes. Mortality rates significantly increased particularly amongst patients with hip fractures and COVID-19. Road traffic injuries remained a common cause of injury and domestic injuries became more prevalent with lockdown. Social isolation negatively affected mental health resulting in several orthopedic injuries. Telehealth services and separation for COVID-positive and COVID-negative patients benefited both patients and providers. While hospitals and medical facilities are still facing COVID-19 case surges, it is important to understand how this pandemic has impacted preparation, care, and opportunities for prevention education and ongoing care.

Key Words: Orthopedics; Surgery; Lockdown; Mental health; Telehealth; COVID-19

Core Tip: Previous and impending surges of coronavirus disease 2019 have caused a disruption in orthopedic specialties in elective procedures and changed the causation and outcomes of emergent cases. The pandemic has also impacted patient care and short-term and long-term outcomes.

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INTRODUCTION

Now entering the third year of the coronavirus disease 2019 (COVID-19) [caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] pandemic, the number of globally reported cases continues to increase at a rapid rate despite the introduction of authorized vaccines. As of June 10, 2022, there have been almost 532 million cases and over 6.3 million deaths worldwide[1]. Hospitals continue to be overwhelmed with positive cases as new variants emerge. Hospital protocols in patient care have been changing to keep health care workers and patients safe and to keep resources on hand[2]. Non-emergent procedures were delayed in stages to reduce the burden on healthcare services. The long-term effects of these delays have not yet been fully understood as the pandemic continues. These delays occurred across all specialties. In particular, many orthopedic surgeries were postponed, being one of the most common specialties to oversee elective procedures.

The lockdown brought on by the pandemic presented many challenges; routine procedures became more complex, patients were forced to seek medical care later than anticipated due to fear of contracting the disease or an overload in medical care facilities, and unavailability of rehabilitation centers postoperatively due to COVID-19 restrictions. Furthermore, limited mobility in certain age groups may have impacted bone and joint health. The focus of this review is to assess the overall impact that COVID-19 has had on patient care in the orthopedic service and evaluate new management methods for future implementation.

CLINICAL PRESENTATIONS

The PubMed database was searched for relevant studies. The search was refined to publications in English and between the years 2019 and 2021. The keywords used were "COVID-19" and/or "Orthopedic Injuries". Observational studies, clinical trials, and case reports were included in the selection process. Reviews, meta-analyses, and systematic reviews were excluded. Articles that were related to spinal injuries or oncology were also excluded due to the complex nature of these cases. This review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Additional resources were found using a Google web search (Figure 1). The Baishideng Publishing Group Reference Citation Analysis (RCA) tool was used to create and verify citations according to the journal's guidelines. The RCA tool also provided the Impact Index for articles. A total of 37 articles were identified and selected for the review (Table 1).

Lower extremity fractures

Campbell *et al*[3] utilized a prospective and retrospective study to compare the management of open lower limb fractures (oLLFs) in the pre- and peri-COVID pandemic periods. oLLFs comprised of open fractures of long bones, and hind or mid foot. A 64% reduction in ED attendances pre-COVID (25264) compared to that peri-COVID (9042) and 18% reduction in oLLFs have been observed. Despite a decrease of almost 50% in traffic, road traffic accidents (RTA) were still the most common cause of injury in this COVID period. There was a rise in incidents of oLLFs following a fall from a height, mostly seen in relatively young patients due to an increased incidence of suicide. Despite reassignments of junior surgical staff, some senior level surgical staff remained committed to provide emergency orthopedic surgery care that resulted in timely intervention of open long bone fractures.

Hip fractures & outcomes

Egol *et al*[4] researched the mortality and major complications in hip fracture care during the pandemic across seven musculoskeletal care centers across New York. The study focused on the health care

Table 1 Description of studies collected for the review

Title	Author	Country	Study during lockdown?	Extremity injured	Patient outcomes	Article impact index
Lower extremity fractures						
The COVID-19 Pandemic: The effect on open lower limb fractures in a London major trauma centre - a plastic surgery perspective	Campbell *et al*[3]	England	Yes	Lower extremity fractures	Despite a 64% reduction in ER attendance and 50% decrease in traffic, RTA were the most common mechanism of injury and oLLFs were reduced from 22 to 18; there was a rise in oLLFs in those with mental health diagnoses	1
Increased Mortality and Major Complications in Hip Fracture Care During the COVID-19 Pandemic: A New York City Perspective	Egol *et al*[4]	United States	Yes	Hip fractures	Rates of mortality in hip fracture patients in COVID-positive, suspected COVID, and COVID-negative groups were 35.3%, 7.1%, and 0.9%, respectively	28
Hip fracture care and mortality among patients treated in dedicated COVID-19 and non-COVID-19 circuits	Ojeda-Thies *et al*[5]	Spain	Yes	Hip fractures	COVID-negative patients were able to receive timely and adequate care; COVID-positive patients also received adequate care but there were delays in surgeries; separating COVID-positive and negative patients helped efficiently treat patients	1
Effect of Covid-19 on best practice care of hip fracture patients: An analysis from the National Hip Fracture Database (NHFD)	Tyas *et al*[6]	UK	Yes	Hip fractures	COVID-19 led to a significant reduction in best practice tariff with decreases in timely surgery, postoperative delirium, 20-d mortality, length of stay, and timely orthogeriatric review	0
Rehabilitation guidance for hip fracture patients during the COVID-19 pandemic using chat software: A new model	Gao *et al*[7]	China	Yes	Hip fractures	Complications and mortality were higher in the group that did not use WeChat; complications included UTIs, deep vein thrombosis, dislocation, and infections	1
Hip Fracture Outcomes During the COVID-19 Pandemic: Early Results From New York	Lebrun *et al*[8]	United States	Yes	Hip fractures	Mortality was 56% amongst COVID-19 patients and were at higher risk for pneumonia and hyperinflammation	19
IMPACT-Scot report on COVID-19 and hip fractures	Hall *et al*[9]	Scotland	Yes	Hip fractures	Low platelet count was an indicator for an increased risk of COVID-19 infection and COVID-19 was related with an increased risk of 30-d mortality	27.5
Hip fracture care during Covid-19: a regional trauma centre's experience	Crozier-Shaw *et al*[10]	Ireland	Yes	Hip fractures	Though there was a 20% reduction in hip fractures, the 30-d mortality rate increased from 2.2% to 8.3% and having COVID-19 also increased mortality rates	2
Clinical Characteristics and Perioperative Complication Profiles of COVID-19-Positive Patients Undergoing Hip Fracture Surgery	Galivanche *et al*[11]	United States	Yes	Hip fractures	COVID-positive patients presented with more comorbidities which resulted in a higher incidence of adverse events perioperatively	0
Treatment of Proximal Femoral Fragility Fractures in Patients with COVID-19 During the SARS-CoV-2 Outbreak in Northern Italy	Catellani *et al*[12]	Italy	Yes	Femur fractures	Surgery is required for positive outcomes, but respiratory stabilization is crucial to ensure survival, comfort, and stability	30
Influence of coronavirus disease 2019 pandemic state of emergency in orthopaedic fracture surgical treatment	Mitkovic *et al*[13]	Serbia	Yes	All	Overall number of fractures decreased, female patients were observed more for femoral neck fractures	2.5
The effect of COVID-19 pandemic on the care of fragility hip fracture patients in the United Kingdom	Orfanos *et al*[14]	United Kingdom	Yes	Hip fractures	Early intervention resulted in better outcomes, higher mortality rates amongst COVID-positive patients	0
How SARS-CoV-2 Pandemic Changed Traumatology and Hospital Setting: An Analysis of 498 Fractured Patients	Brayda-Bruno *et al*[15]	Italy	Yes	All	More femoral fractures during COVID era, average injury age increased to 69, separating COVID-negative and positive patients allowed patients to remain negative, faster diagnoses to discharge times	0
Do standards of care and early outcomes of periprosthetic fractures change during the	Zagra *et al*[16]	Italy	Yes	All	Delays in surgery, hip fractures were associated with higher mortality rates, 60% of orthopedic patients were at risk of developing	0

COVID-19 pandemic? A multicentre study					perioperative complications	
Perioperative management of patients with hip fractures and COVID-19: A single institution's early experiences	Muse *et al* [17]	United States	Yes	Femur fractures	Early intervention improved patient outcomes in COVID-positive patients; spinal anesthesia was used to prevent viral aerosolization; treatment plans should be altered based on severity of infection	1.5
Foot and ankle trauma management during the COVID-19 pandemic: Experiences from a major trauma unit	Shah *et al* [18]	England	Yes	Foot and ankle fractures	Telemedicine aided in reducing patient-provider contact and eased the burden of follow-up	1
Effect of the COVID-19 pandemic on foot surgeries	Kuliński *et al*[19]	Poland	Yes	Foot fractures	Total orthopedic surgeries declined by 55% and elective surgeries were not eliminated. The length of stay was decreased by 2.5 d for adults and 1.7 d for children	0
Outcomes of orthopaedic trauma surgery in COVID-19 positive patients	Al-Humadi *et al*[20]	United States	Yes	Lower Extremity	Operations in COVID-positive patients were accomplished with anticoagulation and hematologic and pulmonary management; complications and mortality still occurred	0
Upper extremity fractures						
Patient care modifications and hospital regulations during the COVID-19 crisis created inequality and functional hazard for patients with orthopaedic trauma	Dunkerley *et al*[21]	United Kingdom	Yes	Upper extremity fractures	The increase in use of telemedicine services resulted in 12% of patients discharged with potentially unstable fractures with a danger of mal-union	1.5
A Call to Arms: Emergency Hand and Upper-Extremity Operations During the COVID-19 Pandemic	Diamond *et al*[22]	United States	Yes	Hand and upper extremity	A 40% increase in volume injuries attributed to high risk behaviors such as lawlessness, assault, and high-speed auto accidents; lack of social and physical impacted and aggravated injuries	2
Upper extremity emergencies during SARS-COV-2 pandemic: Turnout trends	Fyllos *et al* [23]	Greece	Yes	Upper extremity fractures	The mechanisms for which emergency upper extremity and hand and wrist injuries occurred were mostly from domestic accidents such as new hobbies	0
The impact of COVID-19 on shoulder and elbow trauma in a skeletally immature population: an Italian survey	Gumina *et al* [24]	Italy	Yes	Shoulder and elbow	Pediatric cases decreased by 84.6%, shoulder and elbow traumas were caused by domestic accidents	1.5
Other fractures						
Outcomes of Orthopaedic Trauma Services at a UK Major Trauma Centre During a National Lockdown and Pandemic: The Need for Continuing the Provision of Services	Donovan *et al*[25]	United Kingdom	Yes	All	Theater time increased by 14 min due to new PPE requirements. Complication and mortality rates remained unchanged and there was not a higher risk of transmitting COVID-19 in the hospital	0.5
Proximal femur fractures in COVID-19 emergency: the experience of two Orthopedics and Traumatology Departments in the first eight weeks of the Italian epidemic	Maniscalco *et al*[26]	Italy	Yes	Femur fractures	There was a decrease of emergency ortho cases by 26.8%; femur fractures decreased, and other fracture types increased; school traumas were 0%, sports injuries decreased by 75.3%, work injuries decreased by 42.2%	0
Evaluation of containment measures' effect on orthopaedic trauma surgery during the COVID-19 pandemic: a retrospective comparison between 2019 and 2020	Druel *et al* [27]	France	Yes	Upper extremity, lower extremity, hand fractures	Work-related accidents, RTAs, and altercations decreased, but domestic accidents increased. Rates of infection decreased; overall there was a 28.7% decrease in trauma surgery patients	3
Impact of the COVID-19 pandemic on the trauma and orthopaedic department at level one Major Trauma Centre in the republic of Ireland	Elbardesy *et al*[28]	Ireland	Yes	All	Adult distal radius fractures increased by 88% and pediatric elbow fractures decreased by 13%. Fractures were mostly caused by independent outdoor activities	0
The impact of COVID-19 on orthopaedic trauma: A retrospective comparative study from a single university hospital in Italy	Andreozzi *et al*[29]	Italy	Yes	All	Average age of patients increased, 67% of injuries occurred in the home, and the most commonly injured body part was the hand	0

Effects of COVID-19 pandemic curfew on orthopedic trauma in a tertiary care hospital in Turkey	Kalem *et al* [30]	Turkey	Yes	All	Center saw a 65% decrease in upper extremity injuries. Overall human movement has decreased by about 40% which is correlated to the decrease in admissions	0
Elective surgeries						
COVID-19 consent and return to elective orthopaedic surgery: allowing a true patient choice?	Clough *et al* [31]	England	Yes	All	Rates of COVID-19 were lower at elective surgery compared to trauma sites	1
Practice patterns						
The Effect of COVID-19 on Orthopedic Practices and Surgeons in Louisiana	Kale *et al* [32]	United States	No	All	COVID-19 restructuring led to delays in care, injuries not properly healed, and increase in pain.	2
A clinical pathway for pre-operative screening of COVID-19 and its influence on clinical outcome in patients with traumatic fractures	Meng *et al* [33]	China	Yes	All	Average wait time to surgery increased by 4.1 d, resulting in complications such as pneumonia, fever, venous thromboembolism, and cardiovascular complications	7.5
Lessons Learnt from Managing Orthopaedic Trauma During the First Wave of the COVID-19 Pandemic at a UK District General Hospital	Patel *et al* [34]	United Kingdom	Yes	All	Delays to surgery were doubled and postoperative complications were more present but were not directly associated with COVID-19 status	1
Effect of COVID-19 on surgical management of open fractures and infection rates: A tertiary care experience in Indian set-up	Gupta *et al* [35]	India	Yes	All- open fractures	Even though this center saw a decrease of cases, there was a delay of patient presentation to the ER, delay in administering antibiotics, and an increase of emergency temporary fixations, infection rates, and readmissions	0.5
Pooling of neglected and delayed trauma patients - Consequences of 'lockdown' and 'Unlock' phases of COVID-19 pandemic- A retrospective cohort analysis from a tertiary centre	Saini *et al* [36]	India	Yes	Upper and lower extremity fractures	Complications (blood loss, requirement for bone grafts) rates increased, delays to surgery significantly increased from an average of 8.23 d to 21.38 d	0
Miscellaneous						
Mortality risk of surgically managing orthopaedic trauma during the COVID-19 pandemic	Balakumar *et al*[37]	United Kingdom	Yes	Femur fractures	The risk of contracting COVID-19 perioperatively was 11%, separating COVID-negative and -positive patients did not improve patient outcomes	0
Effect of COVID-19 on Ulnar Collateral Ligament Reconstruction in Major League Baseball Pitchers	Paul *et al* [38]	United States	No	Ulnar Collateral Ligament	Decreased movement had an impact on ulnar collateral ligament reconstruction rates when sporting practices resumed	0
The patterns and management of fracture patients under COVID-19 outbreak in China	Yu *et al*[39]	China	Yes	Upper and lower extremity fractures	Delays in surgery, decrease in total number of patients but increase in forearm, thigh, hand, and foot fractures. Hip fractures most prevalent	2

system's response to the essential care of its hip fracture patients and its effects on patient outcomes. This prospective study was employed from February 1, 2020 through April 15, 2020, to compare 138 recent and 115 pre-COVID hip fracture patients. Patients with recent hip fractures were grouped into three classes: COVID-positive, suspected COVID, and COVID-negative groups. The COVID-negative patients underwent surgery immediately whereas COVID-positive patients' surgery was delayed. The approach to surgery for hip fractures was the same regardless of COVID status. The majority of patients received general anesthesia and a proportion of patients underwent spinal anesthesia. As expected, higher mortality was found in COVID-positive patients compared to suspected or COVID-negative patients: 35.3%, 7.1%, and 0.9% respectively.

Ojeda-Thies *et al*[5] retrospectively studied patients treated for hip fractures during the COVID-19 pandemic from March 1, 2020 through May 1, 2020. This center divided 64 patients into three cohorts: pre-cohort of 17 patients, 14 COVID-positive patients, and 33 COVID-negative patients. More than 90% of patients received spinal anesthesia. There was a higher incidence of COVID positivity (23.5%) rate after the patients were discharged from the hospital following hip surgery and 50% of those patients died. That resulted in separating the anesthesia circuit for COVID-positive and COVID-negative patients. The study revealed that separate circuits for COVID-19 and non-COVID-19 patients allows adequate hip fracture care, despite delayed surgery in patients with severe respiratory illness from COVID. Separating patients that were not infected from those that were, helped with the efficiency of

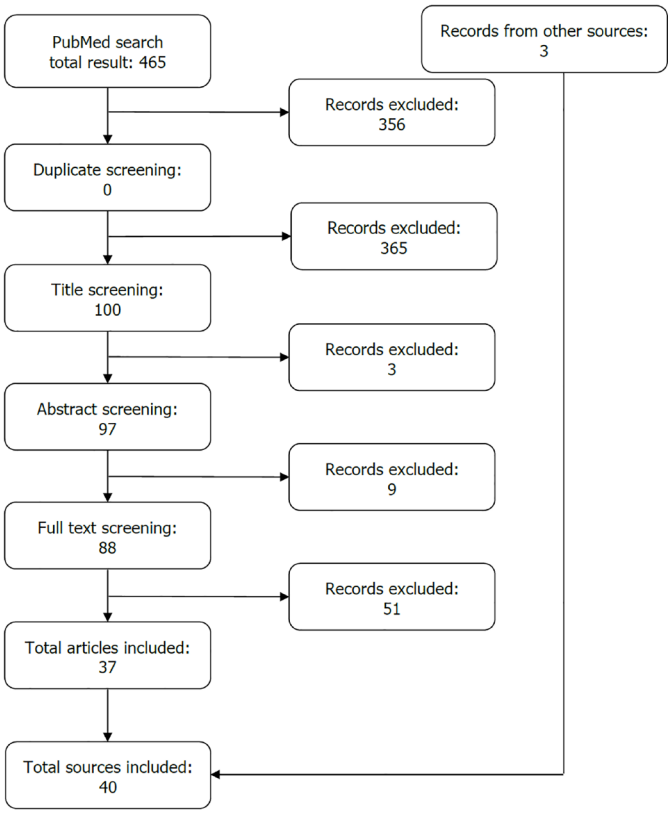

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Figure 1 PRISMA Diagram for Literature Screening using the keywords "COVID-19" and/or "Orthopedic Injuries". Observational studies, clinical trials, and case reports were included in the selection process. Reviews, meta-analyses, and systematic reviews were excluded. Articles that were related to spinal injuries or oncology were also excluded. This review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Additional resources were found using a Google web search.

treating fractures amongst COVID-negative patients and significantly reduced the 30-day mortality and the conversion rates.

Tyas *et al*[6] studied the effect of COVID-19 on Best Practice Tariff for hip fractures in 40000 patients collected from the National Hip Fracture Database (NHFD) from England, Wales, and Northern Ireland. Best Practice Tariff was used to optimize care for patients, incentivize providers, and yield better outcome. Quality metrics such as timely surgery, postoperative delirium, 30-d mortality, hospital length of stay, and timely orthogeriatric review were assessed. Researchers concluded that COVID-19 led to a significant reduction in best practice tariff. Prompt geriatric review dropped over the review period. Significant changes in bone health assessments, reduction in falls assessments, and postoperative delirium were also observed. Mortality rates peaked at 13.7%. Therefore, it is important to maintain the quality care and assessment of geriatric hip fractures and management in next pandemic.

Gao *et al*[7] piloted a study at a hospital in China for tracking hip fracture patients postoperatively and providing rehabilitation guidance using a chat software called WeChat. The study selected 80 patients and divided them into two equal groups of observation and control. The control group was given traditional discharge instructions and the observation group received additional instructions that provided continuous instruction of physical therapy exercises through WeChat apps. This study was done at the peak season of COVID-19 between February 1, 2020 and April 30, 2020. Complications and mortality were significantly higher in the control group. Complications observed include urinary tract infections, deep vein thrombosis, dislocation or fracture around prosthesis, surgical site infection, and pneumonia. It was recommended that during the COVID-19 pandemic, it was helpful to use WeChat or another similar chat software to guide the rehabilitation of hip fractures to minimize postoperative complications.

LeBrun *et al*[8] studied 59 hip fracture patients in New York City over a 5-wk period, from March 20, 2020 to April 25, 2020 during the COVID-19 pandemic. Centralized care was established for emergency hip fracture management. Patients were separated into COVID-positive and COVID-negative groups based on infection status. The study showed that hospital mortality was significantly increased in the COVID-positive patients (56%) compared to COVID-negative patients (4%). All deaths in COVID-positive patients were related to COVID-19. COVID-positive patients were also at higher risk for complications such as pneumonia or hyperinflammation.

Hall *et al*[9] assessed the effects of COVID-19 on 30-d mortality for 317 patients with hip fractures in a multicenter retrospective study. The effects of social lockdown on the epidemiology of hip fractures were also assessed. Results showed that COVID-19 was independently related with an increased risk of 30-d mortality in hip fracture patients.

Crozier-Shaw *et al*[10] studied hip fracture care pre-COVID (45 hip fractures) and peri-COVID (36 hip fractures). A 20% reduction in hip fracture presentation was noted; however, the 30-day mortality was increased from 2.2% to 8.3%. Despite improved quality indicators that were observed in hip fracture management during the COVID-19 period, there was a 3-fold increase in mortality. Although four patients tested positive on swab test for COVID-19, two of them died. Therefore, COVID-19 was associated with increased mortality in hip fracture patients that were positive and undergoing surgery. Researchers found that these findings will be important to apply to orthogeriatric care during future COVID-19 waves.

Galivanche *et al*[11] collected 42002 patients through claims data that had undergone hip fracture surgical repair between April and December 2020. Of these, 678 were COVID-positive and while there were no significant differences in age, sex, or procedure type between the patients who were tested positive or negative for COVID-19, COVID-positive patients did present with a higher incidence of comorbidities. Propensity score matching was used to balance the two groups (COVID-positive *vs* COVID-negative). After matching, the COVID-19-positive group had a higher incidence of adverse events perioperatively such as venous thromboembolism (6.64% compared to 3.43%) and pneumonia (11.21% compared to 4.56%).

Catellani *et al*[12] studied 16 patients with femoral neck fractures that were COVID-positive with active infection and were receiving protocolized treatment for COVID-19 during the pandemic in northern Italy. Three patients died before surgery because of complications from COVID-19. After surgery, four patients died of respiratory failure. The overall mortality of hip fracture with active COVID-19 infection was 43.7%. Surgical mortality of hip fracture in patients with active COVID-19 infection was 30.77%. Patients who underwent surgery in the face of active infection had to pass strict criteria. Most patients received spinal anesthesia. A stabilization of respiratory parameters was observed in COVID-positive patients after the surgery. It was suggested that surgery may have contributed to the overall respiratory stability of patients, mobilization, comfort, and improvement in physiological ventilation in COVID-19-positive patients with proximal femoral fragility fractures.

Mitkovic *et al*[13] investigated the frequency and distribution of orthopedic fractures during the stay-at-home lockdown in Serbia. Researchers examined how the lockdown influenced the frequency of different fracture types. Staying at home for 54 d decreased the total number of fractures by 18.9% and females were more likely to suffer from femoral neck fractures during this time. However, femoral neck fractures occurred more frequently in the state of lockdown than during the same period in a non-emergency state in 2019. Mitkovic type method of external fixation was assumed to be an alternative method of tibial fracture fixation during the lockdown. That methodology presumed to be a reducing factor of intraoperative COVID-19 transmission among medical staff and hospitalization time.

Orfanos *et al*[14] performed a retrospective study on geriatric patients aged 60 years and above who sustained hip fracture after a fall in the United Kingdom. Of the 199 patients, 102 were included from the COVID-19 pandemic period and was compared to 97 patients from the same period in 2019. Approximately 11% of patients tested positive for COVID during the observation period. A higher proportion of female patients suffered hip fracture from a fall. However, mortality was found to be higher amongst males between the two groups (P = 0.005). There was no significant difference between the groups regarding 30-d all-cause mortality and morbidity. Early surgical intervention along with sufficient optimization prior to surgery in a COVID-positive patient was critical for his/her survival. Patients were also moved rapidly to rehabilitation facilities which aided in recovery.

Brayda-Bruno *et al*[15] studied 498 fracture patients in Italy during the COVID-19 pandemic to assess how the pandemic has changed traumatology and the hospital setting. It was assessed that unspecified femoral fractures were much more common in this time period than the previous time period (181/352 compared to 57/146). The average age of orthopedic patients prior to the pandemic was 61 years of age compared to during the pandemic which was 69 years of age. This institution required COVID-19 testing which expedited orthopedic services by separating COVID-negative and -positive patients. Patients that were admitted as COVID-negative remained COVID-negative during admission. Ten patients died in the pandemic group compared to zero deaths in the control group. Out of these ten patients, three died due to comorbidities and seven due to thromboembolic events related to COVID-19. Time between diagnoses and discharge was significantly lower (P = 0.03) despite an increase in orthopedic cases. The difference was attributed to early operative intervention in the pandemic group.

Zagra *et al*[16] conducted a retrospective multicenter study in patients with periprosthetic fractures (PPF) during COVID-19 pandemic in northern Italy. Out of 1390 patients, 38 were found to suffer from PPF. Most of the patients had femoral PPF. There was no difference in the incidence of PPF during the pandemic when compared with the earlier year prior to the pandemic. Routine screening for COVID-19 was performed and found around 10% or more with COVID-19 positivity because of positive test or the positive symptoms and imaging findings. Standard operative care was performed in PPF patients during the pandemic. Hip fracture was associated with increased 30-d mortality in COVID-positive patients compared to COVID-negative patients. Approximately 60% of PPF patients developed complic-

ations.

In a letter to the editor, Muse *et al*[17] used a retrospective case series of five COVID-19 orthopedic patients who sustained hip fractures, one femoral neck fracture and four intertrochanteric fracture, that underwent surgery at Montefiore Medical Center, New York. As per recommendation, hip fracture should be repaired within 48 h of admission to reduce mortality and morbidity, but only three out of the five patients underwent surgery within the 48 h timeframe and two had surgeries after 72 h of admission. While regional anesthesia is safe for COVID-positive patients, spinal anesthesia was used to prevent viral aerosolization in four patients. Only one patient received general anesthesia. None of the patients died. The most common complication was the need for packed red blood cell transfusion. Providers suggested that surgical treatment plans can be delayed if necessary.

Foot and ankle fractures

Shah *et al*[18] evaluated the impact of the pandemic on foot and ankle services in a single trauma center in the UK using a retrospective cohort study. A total of 206 patients were evaluated from admission to discharge to compare pre-lockdown and lockdown phases and stable and unstable fractures. Of 100 patients with stable ankle fractures, 35 (35%) were discharged from the emergency department without a planned follow-up. The majority of patients who presented unstable fractures required some form of interventions. Some of the patients were sent home with cast, advised elevation, non-weight bearing, and to follow up for definite treatment. In another group, partial fixations were employed to reduce intraoperative time and avert the need for invasive surgeries. Most of the operated patients were followed up within 2 wk for a wound check. Patients were advised on pain and plaster management to avoid face-to-face interactions with providers. Telemedicine reduced the patient-physician contact and reduced the burden of follow-up.

Kuliński *et al*[19] researched the effect of the COVID-19 pandemic on both elective and emergency foot surgeries on 145 orthopedic patients in Poland. The data showed a reduction in the total number of orthopedic admissions by 55% during the pandemic. Elective orthopedic interventions declined by 72% and emergency orthopedic interventions increased by 27% during the pandemic as compared to pre-pandemic era. Length of hospital stay decreased by 2.5 d in adults and 1.7 d in children. There was a decline of 32% in the number of patients coming to ED for injuries. The pandemic did not affect the average age of patients and the male to female ratio. It is suggested that the COVID-19 pandemic has affected the epidemiology and prevalence of foot surgeries in children and adults.

Al-Humadi *et al*[20] conducted a retrospective case series of 11 patients to investigate outcomes of lower extremity trauma surgery in COVID-19-positive patients. Most of the patients had hip fractures and the rest sustained femur and tibia and fibular fractures. Orthopedic operations in COVID-19-positive patients were successfully done with patient anticoagulation and hematologic and pulmonary management. These three were optimized prior to surgery to reduce venous thromboembolic events and avoid blood transfusion. Complications such as deep vein thrombosis, acute renal failure, and pneumonia still occurred and two patients died postoperatively. The patients who died were more than 50 years old and had a prior history of more than one comorbid condition.

Upper extremity fractures

Dunkerley *et al*[21] noted that the pandemic has decreased operative intervention of unspecified upper extremity fractures and increased the use of telemedicine clinics. In this prospective study which was performed at the peak of the COVID-19 outbreak from April 14 through April 28, 2020, of the 154 patients that were analyzed, 51% were managed as in a normal circumstance, whereas 49% of managements were impacted by the pandemic. Of those affected, 12% were discharged at diagnosis with potentially unstable upper extremities fractures, and this had the danger of mal-union. Additionally, 29% were discharged from the orthopedic virtual clinic as opposed to having in person clinical or radiological follow-up. Nurses in the trauma team would virtually request patient care instructions from physicians working remotely. Discharged patients were fixated with removable immobilization. Follow-up surveys given to patients who were treated by the virtual clinic showed a very high satisfaction rate of 4.8/5. While telemedicine played a vital role in orthopedic management and is economical and efficient to both patients and providers, there is a potential risk of poor outcomes such as mal-union, requiring corrective treatments in the future.

Diamond *et al*[22] conducted a multi-center study from two Level I trauma centers in Pennsylvania and California. Researchers studied the occurrence of emergency upper extremity operations during the COVID-19 pandemic specifically during shelter-on-place orders. Injuries included trauma to the forearm, hand, wrist, and finger. It was found that there was a 40% increase in volume attributed to high-risk behavior which was defined as lawlessness, assault, and high-speed auto accidents. Additionally, it was found that home improvement projects, lack of social and physical resources, and delay of treatment due to avoidance of treatment facilities are also impacting the high volume of upper extremity injuries.

Fyllos *et al*[23] compared the turnout of patients with orthopedic, upper extremity, and hand and wrist emergencies during pre-pandemic and peri-pandemic periods. During the pandemic, it was found that the numbers of patients with orthopedic, upper extremity, and hand and wrist problems (*e.g.*, arthritis and tendinopathy) were significantly reduced by 57.09%, 49.77%, and 49.95%, respectively,

compared to a patient population in 2019. However, upper extremity injury emergencies (*e.g.*, fractures and dislocations) increased from 37.17% to 43.32% and hand and wrist injury emergencies increased from 25.07% to 29.15%. Although other causes of injury have decreased, it is suggested that the increase of domestic accidents from new hobbies during the lockdown have been the probable cause of the surge.

Gumina *et al*[24] evaluated 404 patients under the age of 18 that were treated at the trauma center for shoulder and elbow injuries before and during the pandemic (from March 8, 2020 through April 8, 2020). Young people typically incur high-energy injuries from social activities, school activities, sports, parks, and clubs. Due to the prohibition of these events, injuries caused by these activities were almost eliminated. There were no cases of contusions, physeal fractures, other fractures, or dislocations of the elbow. The shoulder and elbow injuries seen at this center were mainly caused by falls in the home, offering an opportunity for education.

Other injuries

Donovan *et al*[25] performed a retrospective case-controlled study at a Level 1 trauma center in the UK. Factors such as anatomical area of injury, cause of injury, operative procedure, type of anesthesia, total operating time, complications, and 30-d mortality were analyzed against a dataset of 248 patients. The 248-patient dataset was comprised of 142 patients that required 165 operations pre-pandemic and 106 peri-pandemic patients that underwent 124 operations. During the COVID period, the results showed a 30% decrease in overall orthopedic injuries due to a reduced number of road traffic accidents and sporting injuries. Also, the number of hip fractures and low impact injuries remained the same. Operative time increased by 14 min due to the new personal protective equipment (PPE) requirements. During the COVID-19 pandemic, a higher number of patients received spinal anesthesia and fewer patients received general anesthesia. Complications and mortality rates did not change. The incidence of COVID-19 in the patients tested in the hospital and in the general population at the time of the study was the same at 8.5%.

Maniscalco *et al*[26] conducted a study on the impact of COVID-19 on orthopedic traumas presenting to the emergency orthopedic departments in Parma and Piacenza Hospital, Italy, evaluating patients admitted with proximal femur fractures. The study collected data for patients between February 22, 2020 and April 18, 2020 and was compared with 2019 data. The results showed a decrease in orthopedic cases at the ER by 26.8%. Regular mechanisms of injury vastly changed, where there was a 19.1% increase of the traumas occurring in the home, sports injuries decreased by 75.3%, work injuries decreased by 42.2%, and school traumas were reduced to 0%. A decrease in femur fractures from 38.9% to 33.5% was also observed during the pandemic. A higher mortality was reported during the pandemic in elderly patients with femur fracture due to COVID-19.

Druel *et al*[27] studied the effects of COVID-19 containment measures on 888 orthopedic trauma surgeries during the pandemic at a trauma center in France. Participants were divided into three cohorts: Reference, pre-containment, and containment groups. The occurrence of domestic accidents increased from 51.6% to 64.8% whereas work-related accidents, altercations, and RTA decreased. The decrease in the number of cases (from 6.7% to 4.0%) could be due to fear of going to medical facilities, fear of containment rules, or minimizing the seriousness of symptoms. Overall, the results showed a decrease of 28.7% in the number of patients undergoing trauma surgery services during the containment period.

Elbardesy *et al*[28] investigated the impact of COVID-19 pandemic on trauma and orthopedic center in Ireland among 505 patients. The study was conducted between March 1, 2020 and April 14, 2020 and compared patients from 2019 in the same time period. The total number of trauma and orthopedic surgeries performed decreased by 10.5%. Likewise, the number of pediatric orthopedic procedures decreased by 40.32%. Adult distal radius and pediatric elbow fractures increased by 88% and 13%, respectively, while hip fractures remained the most common trauma. Overall, the COVID-19 pandemic led to a decrease in the total number of trauma surgeries. Notably, injuries directly related to solo outdoor activities such as ankle, radius, elbow, and hand fractures increased.

Andreozzi *et al*[29] performed a retrospective comparative study of the impact of COVID-19 on orthopedic trauma in Italy. They analyzed the impact of the lockdown on acute orthopedic trauma. The overall number of admissions in the pre-COVID era was 995 as compared to 204 during COVID-19 outbreak. Average age of patients (51.9 years old) was significantly higher during the pandemic as compared to pre-pandemic (41.4 years old). Most injuries (65.7%) occurred at home during the pandemic as compared to 32.3% pre-pandemic. The most injured extremity during the pandemic was the hand (14.2%) compared to before the pandemic which was polytrauma (22.8%). While overall rates of acute traumas have decreased, the incidence of hip fractures remained high, indicating a need for focus on orthogeriatric care.

Kalem *et al*[30] studied the effect of COVID-19 pandemic on the prevalence and epidemiology in 361 orthopedic trauma patients in Turkey. The study examined the fractures distribution in three age categories (≤ 20 years, 21-64 years, and ≥ 65 years). The overall number of admissions decreased by 50.9% and upper extremity injuries decreased by 65%. The type of trauma and the mechanism of injury changed with a significant increase in low energy trauma and the upper extremities more affected during the pandemic (49.9% *vs* 30.5% peri-pandemic and pre-pandemic, respectively). However, there

was no difference in occurrence of fractures in geriatric patients. It is suggested that the decrease in admissions was parallel with a 40% decrease in overall human movement.

Elective surgeries

Clough *et al*[31] examined the risk of contracting COVID-19 in patients undergoing orthopedic surgery. The data was collected for March 2020 to June 2020. The 225 orthopedic trauma surgery patients were separated into three surgery sites to minimize the perioperative spread of COVID infection. At the acute site that had both COVID-positive and COVID-negative patients undergoing surgery for upper and lower limb fractures, the incidence of post-surgical COVID infection was 6.5% with a 50% mortality rate. Seven (8.3%) of the 84 patients who underwent surgeries for femoral neck fractures became positive, of whom five (71%) died. On the other hand, of the patients who had surgeries in the hospital that only performed elective cases, only 0.9% patients developed COVID-19 without any mortality.

Practice pattern

Kale *et al*[32] analyzed the effects of COVID-19 on orthopedic practices. A survey study was conducted with orthopedic surgeons by Louisiana Orthopaedic Association (LOA) at the peak of the pandemic. The response rate of the survey was 33%. The survey found that most surgeons delayed their elective surgeries. The decrease of patients in offices resulted in substantial loss of revenue. Furthermore, there was an increase in pain and deformities in patients due to the delay in elective procedures. Researchers found that many surgeons increased their revenue with the use of telehealth. This adaptation opens a new era of medicine.

Meng *et al*[33] performed a case series study at Beijing Chaoyang Hospital. Researchers aimed to analyze clinical outcomes of patients that were required to undergo orthopedic surgery. Fracture types included clavicle, scapular, vertebral compression, and upper and lower extremity fractures. Results showed an increase in average wait time from injury to surgery of 8.7 ± 3.4 d in March and April 2020 from 4.6 ± 2.6 d in the same period in 2019, almost doubling waiting time for surgeries in the pandemic. A higher percentage of patients in the pandemic developed complications such as pneumonia, fever, venous thromboembolism, and cardiovascular complications. This led to introduction of a novel clinical pathway for preoperative screening of COVID-19 in traumatic orthopedic patients, thereby reducing waiting time from injury to surgery.

Patel *et al*[34] conducted a retrospective study on orthopedic patients in the UK during in the pre-COVID-19 (328 patients) and peri-COVID-19 (178 patients) eras. The sample included patients with periprosthetic, pelvis, spine, upper and lower extremity, or multiple fractures. There was a reduction in orthopedic patients during the peri-COVID period and restructuring of orthopedic services in response to the COVID-19 pandemic was associated with a delay in surgery (4.91 d compared to 2.94 d) and increase in severity of postoperative complications such as nausea, vomiting, and superficial phlebitis. Complications, however, were not associated with COVID-19 status. Fast-track emergency operative orthopedic services during the pandemic were recommended.

Gupta *et al*[35] performed a retrospective study to compare the surgical management of upper and lower extremity open fractures during the pre-COVID (89 patients) and peri-COVID (52 patients) eras. The results showed that despite the decrease in total trauma cases, there were delays in presentation to the ED. Due to this interruption, there was a delay in administration of first dose of antibiotics; however, there was no significant delay in presentation to surgery. There was a trend of higher infection rate perhaps due to delay in antibiotics administration.

Saini *et al*[36] performed a retrospective study on 488 upper and lower limb fracture patients in India to explore the consequences of neglected and delayed care during and after the lockdown. It was discovered that the average delay in surgical time and hospital stay was significantly increased during each period. During lockdown, the average delay was 8.23 ± 6.1 d and after lockdown the average delay was 21.38 ± 26.14 d. Complications such as blood loss, stay in the ICU, surgical time, and requirement for bone grafts were greatly increased after the lockdown period was over though not statistically significant. Out of 45 patients who developed non-union or malunion, 42 required corrective procedures.

Miscellaneous

Balakumar *et al*[37] researched the risk of operating on a variety of urgent orthopedic cases during the COVID-19 pandemic first lockdown, between March 26, 2020 and May 20, 2020, for clinical decision making and efficiency of medical resource utilization. Researchers included 433 patients in the study. The average age of the patients was 65 years and the majority were involved in low energy mechanism, with femoral neck fracture being the dominant orthopedic injury. Of all patients, 72% were treated at an elective surgery site (ESS) and 23% were treated at major trauma centers (MTC). The overall mortality in femoral neck fracture was identified at 15.9%. Higher mortality was observed at the ESS (13.7%) compared to the MTC (7.7%). The higher mortality at the ESS was observed in patients who were tested positive for COVID (40.1% *vs* 20%). The main outcome was mortality risk considering that orthopedic patients were being treated at the MTC which admitted both COVID-positive and COVID-negative patients. It was suggested that there was an 11% rate of contracting COVID-19 peri-operatively due to

being admitted to the hospital. However, using a site not designated for treating COVID-19 patients for orthopedic surgery and performing surgery at an ESS did not improve the outcome of mortality, risk of infection, or length of stay.

Paul *et al*[38] studied the effect of COVID-19 on ulnar collateral ligament repair (UCLR) in 106 major league baseball (MLB) players. The study observed at all pitchers of the MLB who underwent UCLR repair and found no difference in overall UCLR repair from baseball seasons 2017 through 2020 (n = 16, 20, 16, and 18). However, when the repair was examined with the number of games played pre-pandemic compared to pandemic season, it was found that pitchers were about three times more likely to undergo UCLR repair after the COVID-19 lockdown. The higher rate of UCLR was most likely due to the lack of preseason activity during lockdown periods.

Yu *et al*[39] compared patterns and management of fracture patients in the pre-COVID and peri-COVID eras (January 24, 2020 through March 9, 2020) in China. Fracture types included upper and lower extremities and vertebra. Researchers found a 42% decrease in the number of orthopedic patients during the COVID-19 pandemic. Time of injury to hospitalization of the patients did not change; however, time of injury to operation significantly increased during the pandemic (4.5 ± 4.1 d *vs* 2.0 ± 1.5 d, P < 0.001) when compared with 2019 data. Similarly, length of stay of patients after surgery was longer in the pandemic when compared to 2019 data. Mandatory screenings delayed surgery by more than 48 h. It was recommended that screening of emergency patients should be a priority to minimize risk of infection among other patients and hospital staff.

CONCLUSION

The presentation of coronavirus, while not entirely mysterious, was bound to have unprecedented effects on healthcare workers, regulations in medical specialties, and patients. Orthopedic specialties globally observed numerous changes over the evolution of the pandemic. Orthopedic cases varied in severity. Medical facilities were forced to create alternative treatment plans for emergent and elective orthopedic procedures, and the data presented showed the impact of COVID-19 on orthopedic injury. Some of the changes implemented during this time showed to be beneficial and could be potential long-term solutions for optimizing medical orthopedic management.

Hip replacements are generally the most common elective procedure, but elective procedures were halted and therefore most institutions did not perform them. Hip fractures have still been very common during this time[4,25,28]; however, the pandemic has increased the mortality and complication rate particularly amongst COVID-positive patients[5,8,11,16,38]. The importance of early treatment and proper rehabilitation was strongly emphasized in order to ensure prompt recovery[14].

Mechanism of injury also changed during the pandemic. COVID-19 impacted the number of RTAs significantly as well as sporting injuries due to lockdowns and cancellation of group gatherings[3,25,27]. Work injuries also decreased significantly due to lockdowns and remote work[26,28]. School traumas were reduced as students were engaged in online learning[24,26]. With the vast population sheltering at home, there was a dramatic increase in domestic injuries that included home improvement projects, running, and cycling[22,28,29]. There was also a rise from 18% to 35% in oLLFs in patients with mental health conditions, implying that social isolation even if necessary, negatively impacts mental health[3,22]. A 40% increase in upper extremity injuries due to high-risk behaviors was observed during this time which could also be a consequence of social isolation[22].

The use of telehealth services was introduced in several facilities to alleviate the burden on healthcare facilities as well as limit exposure of both patients and providers to COVID-19. Virtual patient care proved to have a positive impact on the rehabilitation of patients postoperatively, lowering the rate of complications[7]. The use of telehealth services, while beneficial, did have adverse effects in patients that required more hands-on treatment[21]. These patients will be required to seek care or corrective treatment for the injury in the future[21]. To take full advantage of the benefits of telehealth, the screening for the patients that can be seen virtually should be stringent in order to ensure quality care.

From the management changes that were seen during this period, there were some takeaways that should be emphasized in current standards of practice. Early intervention was and should be a priority. This is essential for patients with hip fractures or other severe fractures to minimize the risk of mal-union. Telehealth was a service to bridge the gap in healthcare for those that were COVID-positive and needed treatment or even for facilities that were not allowing any patients to be seen in person[7]. This is a service that in the future would be valuable to patients that are immobile, are ill, or have transportation issues[40]. Since appropriate PPE allows healthcare providers to treat COVID-19 patients with minimal exposure, separating COVID-positive and COVID-negative patients allowed for timely injury management and COVID management. Knowing that COVID-19 will continue to be prevalent, separating COVID-positive and negative patients can help expedite treatment for both groups of patients. This literature review emphasized the necessity of being prepared to perform routine but emergent procedures even in unprecedented crises.

There were some limitations in this study. The previous and current literature does not allow us to explore how new approaches in orthopedic management would impact patient care in the long term.

Also, as we are still facing COVID-19 surges, the data to support an outcomes study is not yet available. Further research should be conducted to examine how orthopedic injury management has changed when COVID-19 is at its nadir.

To summarize, while hospitals and medical facilities are still facing COVID-19 case surges, it is important to understand how this pandemic has impacted the various specialties of healthcare. Significant changes were noted in orthopedic practices since the start of the COVID-19 pandemic including different mechanisms of injury, higher mortality rates, and injury to different areas of the body. Changes that positively impacted patient outcomes should be made standards of practice and practices that negatively impacted patient outcomes should be actively evaluated to not only be avoided in regular care but also in times of crises.

FOOTNOTES

Author contributions: Obamiro E conducted the initial screening of sources and wrote the manuscript; Trivedi R acquired additional sources, and wrote and edited the manuscript; Ahmed N developed the research question, acquired additional sources, and wrote and edited the manuscript.

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Basic Study

Role of the posterior deep deltoid ligament in ankle fracture stability: A biomechanical cadaver study

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Abstract

BACKGROUND

The deltoid ligament is a key component of ankle fracture stability. Clinical tests to assess deltoid ligament injury have low specificity. In supination external-rotation (SER) type-IV ankle fractures, there is either a medial malleolus fracture or deltoid ligament injury. These injuries are often considered unstable, requiring surgical stabilisation. We look to identify the anatomical basis for this instability. This study investigates the anatomical basis for such instability by re-creating SER type ankle fractures in a standardised cadaveric study model, investigating the anatomical basis for such instability.

AIM

To investigate the anatomical basis for fracture instability in SER type ankle fractures.

METHODS

Four matched pairs of cadaveric limbs were tested for stability both when axially loaded and under external rotation stress. Four matched pairs of cadaveric limbs (8 specimens) were tested for stability when axially loaded to 750 N with a custom rig. Specimens were tested through increasing stages of SER injury in a stepwise fashion before restoring the lateral side with open reduction and internal fixation (ORIF). Clinical photographs and radiographs were recorded at each step. We

defined instability in accordance with well accepted radiological parameters: > 4 mm medial clear space opening on a mortise-view radiograph or > 7 degrees of talar tilt.

RESULTS

All specimens with an intact posterior deep deltoid ligament were stable. Once the posterior deep deltoid ligament was sectioned there was instability in all specimens. Stabilisation of the lateral side prevented talar shift, but not talar tilt.

CONCLUSION

If the posterior deep deltoid ligament is intact then SER fractures can be managed without surgery. If the posterior deep deltoid is incompetent, ORIF and cautious rehabilitation is recommended because the talus can still tilt in the mortise.

Key Words: Trauma; Fracture stability; Biomechanics; Cadaveric study; Basic science

Core Tip: The deltoid ligament is a key component of ankle fracture stability. No fracture with an intact posterior deep deltoid ligament demonstrated instability on axial loading or rotational stress. This study suggests the instability can only occur in the presence of posterior deep deltoid ligament deficiency, supporting the non-operative treatment of many ankle fractures. If the posterior deep deltoid ligament is intact then supination external-rotation fractures can be managed without surgery. If the posterior deep deltoid is incompetent, open reduction and internal fixation and cautious rehabilitation is recommended because the talus can still tilt in the mortise.

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INTRODUCTION

Ankle fractures are common and yet there is wide variation in how they are managed[1]. The concept of ankle fracture stability has long been used to guide whether an ankle fracture can be managed non-operatively or whether operative stabilisation is required[2]. In practice, the criteria used to define a stable ankle fracture have been open to interpretation. Understanding of this issue has progressed over recent years. Many stable fractures are still treated operatively. This leads to increased costs both in terms of surgical admission for treatment and in dealing with complications in fractures which may have been safely managed without surgery[3,4].

To determine whether operative stabilisation is required or not, a precise understanding of the injured parts of the ankle is required. The widely used Danis-Weber Classification, which forms the basis of the AO Classification, is not adequate for distinguishing between stable Weber B fibula fractures and unstable Weber B fibula fractures[5]. The Lauge-Hansen classification offers a better understanding of which bony and ligamentous structures are injured[6].

The Lauge-Hansen Classification was introduced over 70 years ago[6]. The structures that are injured progress in an orderly fashion, depending upon the position of the foot at the time of injury and the type of force applied. The foot is either Supinated or Pronated. The applied force is either rotational (external or internal) or translational (abduction or adduction). Supination external-rotation (SER) injuries are the most common type of ankle fracture. In SER injury, supination of the foot means that the lateral structures are tight and so these are the first to fail. Next to fail, as rotation continues, is the posterior part of the ankle and finally the medial side.

Lauge-Hansen[6] described 4 stages to SER injury. SER-I is injury to the anterior inferior tibio-fibular ligament. With further force, an oblique fibula fracture will occur (SER-II). The next structure to fail is either the posterior malleolus or the posterior inferior tibiofibular ligament (SER-III). In the final stage, deltoid ligament injury or medial malleolar fracture occurs (SER-IV). Lauge-Hansen[6] based his classification upon laboratory simulation with cadaveric specimens. In clinical practice there is variation in both the foot position and force applied. Injury patterns therefore vary from patient to patient.

SER injuries account for 80% of ankle fractures[1]. Diagnostic difficulty arises in cases where there is a fibula fracture (Weber B) but no posterior malleolus fracture or medial malleolus fracture. Where there is a fracture of the medial malleolus then the diagnosis of SER-IV (and instability) is generally considered straightforward. If the medial side of the joint has no fracture, then determining whether the injury is a stable SER-II (with no deltoid ligament injury) or an unstable SER-IV (with injury to the deltoid ligament) is challenging.

Defining the presence of ligamentous medial injury is not straightforward. Traditionally, medial tenderness and ecchymosis have been used as clinical signs of deltoid ligament injury. Studies have demonstrated, however, no correlation between medial tenderness and deltoid ligament incompetence. DeAngelis *et al*[7] examined 55 patients with SER injuries and found that only 25% of patients who were tender medially had a positive external rotation stress radiograph. Twenty-five percent of patients without medial tenderness also had a positive external rotation stress radiograph. This, along with the earlier studies by McConnell *et al*[8] and Egol *et al*[9], demonstrate that clinical findings are of little value in determining ankle fracture stability. Clinical assessment alone is unreliable. Radiological studies with ultrasound and magnetic resonance imaging have also proven of little use in clinical practice[10-15].

It has been argued that a formal examination under anaesthesia (EUA) of the injured ankle will demonstrate instability in "ligamentous bi-malleolar" fractures. Whilst this strategy would reliably discriminate between SER-II and SER-IV, such an approach is impractical given the large number of patients. The Gravity Stress View was introduced to demonstrate, without formal EUA, whether the deltoid ligament complex is competent (no talar shift) or not (talar shift demonstrated)[16,17]. However, this technique has subsequently been shown to have a high rate of false positives[18]. Ankles may appear unstable because of ankle plantarflexion which gives the false impression of a wide medial clear space[19].

Weightbearing radiographs are now considered to be the best means of demonstrating whether a Weber B ankle fracture is stable (SER-II) or unstable (SER-IV)[18]. Properly conducted weightbearing radiographs show whether the ankle is stable under physiological load. The implication of this is that the deltoid ligament is sufficiently competent to maintain the position of the talus in the mortise when the ankle is held at 90 degrees. This study did not address the question of partial deltoid ligament injury and whether that affects stability.

The anatomy of the deltoid ligament has been described in various levels of detail[20]. For the purposes of understanding ankle fractures, the deltoid ligament can be usefully considered to have three components: Superficial; deep anterior tibio-talar and deep posterior tibio-talar. Michelson *et al*[21], in a cadaveric study, investigated stability when both the superficial and deep deltoid ligaments were sectioned, using a gravity stress-view. They showed increased medial clear space in all 8 specimens. This study did not investigate which components of the deltoid ligament complex gave the ankle mortice stability. In particular, the authors did not distinguish between the roles of the two components of the deep deltoid ligament. The superficial ligament is not crucial to the maintenance of the talus in the mortice. The deep deltoid ligament is. It has been shown that the posterior deep deltoid (tibio-talar) ligament is the thickest component[22], that it is tight when the ankle is plantigrade and that the anterior component is tight in plantarflexion[23]. We designed our protocol to investigate the contributors to ankle fracture stability in SER type injuries, including the posterior and anterior portions of the deep deltoid ligaments.

MATERIALS AND METHODS

Thawed fresh-frozen cadaveric specimens from the tibial plateau to the foot were used. The tissues were used in accordance with the Human Tissue Act 2004, with all investigators undergoing appropriate training prior to study commencement. Four matched pairs of specimens were tested using the protocol (8 specimens in total). A bespoke jig was used, capable of axially loading and simultaneously applying torque through a cadaveric specimen. The jig was designed to load the specimens with 750 N and to permit mortise-view and lateral view radiographs to be taken using an image intensifier. 750 N was selected to recreate the single leg standing force of a 75 kg individual. The image intensifier was operated by a radiographer. In this study we re-created a fracture of the lateral malleolus with a subsequent injury to the deltoid ligament in line with Lauge Hansen SER type IV injury. We did not specifically investigate bony medial malleolus fractures.

With the intact specimen in the jig and axially loaded to 750 N, a baseline mortise-view radiograph was taken. This radiographic view was repeated using the image intensifier at each step in a systematic reproduction of SER injury. Structures were divided in the order in which they fail during a Lauge-Hansen SER type injury. The osteotomy was performed using an oscillating saw from the level of the distal most aspect of the syndesmosis posteriorly, to its most proximal aspect anteriorly, completely dividing the fibula. The osteotomy was fixed using a standard AO technique. A single cortical lag screw across the fracture site and a 1/3 tubular stainless steel plate, with 2 uni-cortical cancellous screws and 3 bi-cortical cortical screws fixing the neutralisation plate either side of the fracture. A tri-cortical screw was placed across the syndesmosis. The anterior deep deltoid and posterior deep deltoid were divided

sequentially - firstly the anterior 50% of the ligament, and secondarily the posterior 50% to allow for subtle variations in anatomy and maintain reproducibility between specimens. At each step the specimen was axially loaded with 750 N and radiographs were obtained. Each radiograph was investigated for signs of instability, defined in our study as > 4 mm medial clear space and/or 7 degrees of talar tilt (Figure 1A, Table 1).

RESULTS

None of the 8 specimens showed any evidence of instability either with axial loading or with rotational force until division of the posterior deep deltoid ligament. Apparent stability under axial loading was still evident in all 8 specimens through every step of the experiment, even when the posterior deep deltoid ligament was divided (Figure 1B). When the specimens were subjected to external rotation force, all 8 specimens were stable at steps A to E of the experiment (up to and including division of the anterior deep deltoid ligament). However, instability was demonstrated in all 8 specimens after division of the posterior deep deltoid ligament. Talar tilt and talar shift were both demonstrated (Figure 1C). All specimens demonstrated > 4 mm medial clear space and > 7 degrees of talar tilt.

After fixation of the osteotomy, external rotation stress views and continuous screening showed < 4 mm medial clear space. All 8 specimens demonstrated talar tilt > 7 degrees (Figure 1D). All ankles were stable until we divided the posterior deep deltoid ligament. At this point instability was only reproduced on external rotation stress testing. Even with the posterior deep deltoid ligament divided, specimens showed no talar shift on axial loading with 750 N.

DISCUSSION

Ankle injuries follow patterns that are well understood and these patterns form the basis of the Lauge-Hansen classification[6]. The introduction of a more simple classification, relying solely upon description of the fibula fracture, led to indiscriminate fixation of fibula fractures. The presence of a Weber B fracture was considered an indication for surgery, since the fibula was felt to be the primary stabiliser of the ankle[24]. More recently, demonstrable instability of the talus within the mortise has become the indication for surgery. Interest is currently focused on how best to identify this instability[1-3,25].

This study reproducibly demonstrates that with an intact posterior deep deltoid ligament the talus remains stable beneath the tibial plafond when loaded axially and when subject to external rotation stress testing. Anatomical studies have highlighted different components of the deltoid ligament[22,24,26]. Imaging studies have confirmed that a partial deep deltoid ligament injury can occur and this means that the SER-IV injury is a heterogeneous group[10].

In SER-IV injuries the medial side may have a fracture or ligament injury. The medial malleolus fracture fragment may be large or small. Small fracture fragments may affect the anterior colliculus and this represents the attachment of the anterior deep deltoid ligament[27]. A large fracture fragment of the medial malleolus includes the whole deep deltoid attachment - the anterior colliculus with the anterior deep deltoid ligament and the posterior colliculus with the posterior deep deltoid[28]. After fixation of a large medial malleolus fracture the joint is stable. This highlights the primary importance of the posterior deep deltoid ligament. Medial side integrity determines ankle stability, and the key structure is the posterior deep deltoid ligament. This concept can be extended from medial side fractures to medial side ligamentous injuries. If the deep deltoid is partially injured and the posterior component is intact, then the ankle is stable. However, such stability is only conferred by the posterior deep deltoid ligament when it is tight, with the ankle in a plantigrade position.

Gougoulias *et al*[1] proposed that SER-IV injuries be subdivided into types a and b. They recommended management strategies based on assessment of stability with weightbearing X-rays (Table 2). According to their recommendations, in SER-IVa injuries the posterior deep deltoid is intact (IVa) so the ankle fracture can be immobilized and treated without surgery. The foot should be maintained at 90 degrees to the leg. This is best achieved in a formal below-knee walking cast and not with a removable boot. If the plantigrade position is lost then there is potential for a poor result, with late deltoid ligament insufficiency[29-31]. In SER-IVb injuries, where the posterior deep deltoid ligament is also injured, the ankle is unstable and operative stabilisation of the fibula fracture should be considered.

Our study highlights the importance of the posterior deep deltoid ligament in SER injuries. Only once the posterior deep deltoid ligament was divided did the specimens become unstable. When the posterior deep deltoid ligament is intact (SER-IVa) the injury can be treated non-operatively but, like Gougoulias *et al*[1], we recommend that a formal plantigrade below knee walking cast is used. All SER-IVb injuries were unstable in our study. Gougoulias *et al*[1] recommended open reduction and internal fixation (ORIF) of the fibula for these injuries. In our study, axially loaded specimens still appeared stable, with no talar shift. The bony anatomy and soft tissue envelope are likely factors conferring this

Table 1 Study protocol

Experimental step	Specimen
A	Intact
B	AITFL divided
C	Fibula osteotomy at the level of syndesmosis
D	PITFL divided
E	Superficial and anterior deep deltoid ligament divided
F	Posterior deep deltoid ligament divided
G	Fracture & syndesmosis fixation

AITFL: Anterior inferior tibiofibular ligament; PITFL: Posterior inferior tibiofibular ligament.

Table 2 Management recommendations based on weight-bearing X-rays as suggested by Gougoulias *et al*[1]

Fracture type	NWB XR	WB Xray	Deep deltoid ligament	Management
SER-II	Stable	Stable	Intact (PTTL & ATTL)	Boot & WB
SER-IVa	Unstable	Stable	Partial tear (ATTL only)	WB Cast 6/52
SER-IVb	Unstable	Unstable	Ruptured (PTTL & ATTL)	ORIF

SER: Supination external-rotation; AITFL: Anterior inferior tibiofibular ligament; PITFL: Posterior inferior tibiofibular ligament; ORIF: Open reduction and internal fixation; NWB: Non weight bearing; WB: Weight-bearing.

stability. The experimental setup only tested the axially loaded specimens in a plantigrade position. Radiological determinants of instability vary with the position of the ankle[19]. When rotational force was applied the SER-IVb specimens, all were markedly unstable (Figure 1B). This supports the recommendation that ORIF of the fibula should be used to restore stability. When we tested SER-IVb specimens after fibula ORIF, talar tilt was still demonstrable. We would go further than Gougoulias *et al* [3] and recommend that, postoperatively, SER-IVb injuries should be immobilized in a plantigrade position to allow proper healing of the deltoid ligament. Physiotherapy protocols should also be modified to avoid late deltoid insufficiency. Deltoid ligament repair has been suggested as a potential supplementary treatment for SER-IVb injuries, however at this stage, deltoid repair appears to have no effect on functional outcome scores[32].

This study has limitations. Eight specimens is a small sample size, but the uniformity of our results make it highly improbable that the conclusions would differ if further specimens were tested. A syndesmosis screw is not routinely used in the fixation of SER-IV fractures. Some authors advocate a "hook test" after fibula fixation but randomized controlled studies have found no benefit with the addition of a position screw, even when talar shift was observed after fibula ORIF in the short or medium term[33,34]. We added the syndesmosis screw so that the controversial role of mild syndesmosis instablilty after ORIF could be excluded as a reason for talar displacement.

The results of this study show that if the posterior deep deltoid ligament is intact, the ankle is stable. We did not investigate specifically whether an intact anterior deep deltoid ligament would also afford stability if the posterior deep deltoid is torn. However, Tornetta[27] have already demonstrated the prime importance of the posterior deep deltoid ligament.

The results of our study provide further evidence that the majority of SER injuries can be treated non-operatively. Injury to the posterior deep deltoid ligament is the watershed. Clinicians choosing non-operative treatment for SER-IV fractures - both types a and b - should carefully consider immobilisation and rehabilitation protocols. This is because of our finding that that talar tilt occurs even after fibula ORIF when the posterior deep deltoid ligament is divided.

Operative stabilisation of SER-IVb fractures should be followed by cautious postoperative care, holding the ankle in a plantigrade position to allow the posterior deep deltoid ligament to heal. SER-IVa fractures can be successfully managed non-operatively but, since stability depends upon the posterior deep deltoid, immobilisation of the ankle at 90 degrees is indicated. For this reason, a cast rather than a removable boot is suggested. Operative fixation of the fibula might permit more rapid rehabilitation. The merits of surgery, and the potential complications, should be discussed with patients on an individual basis.

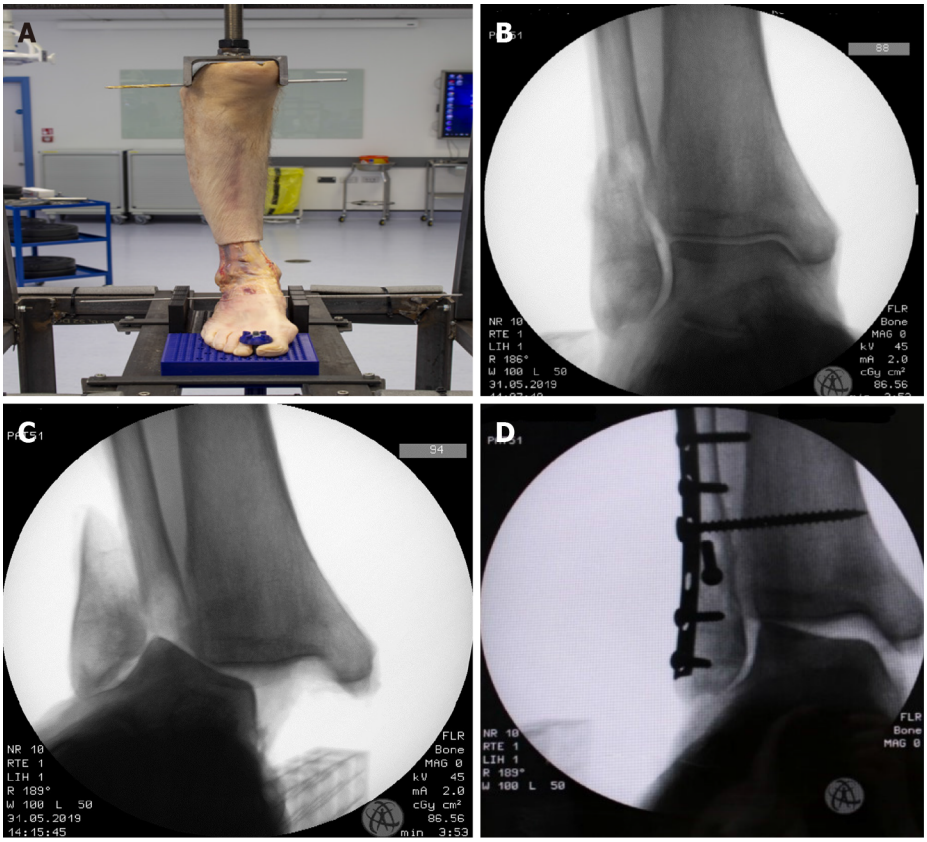

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Figure 1 Experiment set-up. A: Experiment set-up; B: Specimen under load at stage E showing no talar tilt or shift; C: Same specimen under dynamic stress testing demonstrating shift and tilt at stage F; D: Specimen after fixation under stress testing demonstrating talar tilt - step G.

This cadaver study demonstrates the critical importance of the posterior deep deltoid ligament in ankle stability after SER-IV fracture. The results increase the body of evidence supporting the non-operative management of ankle fractures, even those injuries that initially appear to be potentially unstable. Our results also suggest that even when treated with ORIF, an SER-IVb fracture may demonstrate talar tilt on external rotation. Whether this leads to detrimental outcomes in patients remains unclear. Deltoid ligament repair is an area of current interest with recent research suggesting although repairing the deltoid ligament may improve radiological parameters, it has yet to demonstrate improved patient reported outcome measures[32].

It is generally accepted that more severe ankle injuries perform worse long term, particularly giving a greater risk of ankle arthrosis or reflex sympathetic dystrophy[35]. Clinical studies are required to further evaluate these recommendations. One area of interest, lies within the fact that all axially loaded specimens with an intact posterior deep deltoid appeared stable until external rotation stress was applied. Further studies could demonstrate whether some of these injuries, apparently stable in a weight bearing cast, are in fact unstable. If held appropriately in cast it is as yet unknown whether this finding is clinically significant. We believe that these findings should stimulate debate regarding the management of SER-IV fractures. Non-operative treatment of SER-IVa injuries relies upon an intact posterior deep deltoid ligament, and this only affords stability when the ankle is plantigrade.

CONCLUSION

If the posterior deep deltoid ligament is intact then SER fractures can be managed without surgery. If the posterior deep deltoid is incompetent, ORIF and cautious rehabilitation is recommended because the talus can still tilt in the mortise.

ARTICLE HIGHLIGHTS

Research background

Ankle fractures are common injuries, with supination external-rotation (SER) type injuries being the most common sub-group. Operative intervention in the form of open reduction and internal fixation (ORIF) should be reserved for patients with unstable fractures. There is debate within the literature as to which ankle fractures should be fixed and why, with some of this controversy relating to the degree of deltoid ligament injury required to create such instability and necessitate operative intervention.

Research motivation

We feel that many SER type ankle fractures are stable injuries which can be treated non-operatively. Reducing the incidence of unnecessary operations will reduce potential morbidity for patients and reduce healthcare costs. Through the authors' previous experience in cadaveric dissection, it was felt the posterior portion of the deep deltoid ligament was usually thick and strong, which may afford an ankle fracture stability. We created our protocol to investigate the anatomical basis for ankle fracture instability.

Research objectives

To identify the anatomical basis for instability in SER type ankle fractures.

Research methods

A bespoke jig was created to load a thawed cadaveric ankle specimen both with axial load and rotational torque. The 8 sepecimens were loaded both axially and with external rotation during each stage of a SER type ankle fracture, with AP radiographs recorded at each stage. The radiographs were investigated for evidence of ankle fracture instability in terms of talar shift and talar tilt. A detailed description of the study method is included in the research paper. To our knowledge, our study design is unique answering a question which has never previously been anss in a cadaveric basic science study.

Research results

We determined no evidence of radiological instability in any specimen with an intact posterior deep deltoid ligament. Only on disruption of the posterior deep deltoid ligament instability possible under our test conditions.

Research conclusions

Only ankle fractures with a damaged posterior deep deltoid ligament should require operative intervention. With an intact posterior deep deltoid ligament, the ankle can be held in a neutral position, with the ligament reducing the talus within the ankle mortise.

Research perspectives

Clinical studies to investigate the functional outcomes between SER injuries treated operatively and non-operatively may provide further evidence to support the non-operative treatment of ankle fractures with an intact deep deltoid ligament. Further clinical studies are also needed to investigate the functional outcomes of patients following a SER-IVb type injury. It is unclear whether subtle rotational instability may continue following fibular ORIF. Our cadaveric study suggests rotational instability can occur following ORIF of the fibular in these injuries due to the disrupted posterior deep deltoid ligament. It is unknown whether this remains *in vivo* after appropriate immobilisation in a plaster cast. If instability remains, further investigation into the role of deltoid ligament repair is needed.

FOOTNOTES

Author contributions: McCormack DJ, Aziz S, Kirmani S, Faroug R, Wright G, Mangwani J are responsible for performing the experiment; McCormack DJ, Aziz S, Kirmani S, Faroug R, Wright G, Mangwani J, and Solan M contributed to the manuscript preparation.

Institutional review board statement: Institutional approval for research involving human cadaveric tissue - Keele University, United Kingdom 2019.

Informed consent statement: Cadaveric specimens were used in accordance with the Human Tissue Act, no specific informed consent was required.

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ORIGINAL ARTICLE

Basic Study

Anatomic relationship of extensor indicis propius and extensor digitorum communis: Implications for tendon transfer

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Abstract

BACKGROUND

The extensor indicis proprius (EIP) tendon is a frequently used donor for a variety of tendon transfers, most commonly for reconstruction of the extensor pollicis longus (EPL). EIP is known to have frequent anatomic variants including split tendons and variations in tendon arrangement.

AIM

To characterize the anatomy of the EIP at the level of the extensor retinaculum, where tendon harvest is often performed, and share our preferred technique for EIP to EPL transfer.

METHODS

Twenty-nine fresh-frozen cadaveric forearms without history of forearm or hand injury or surgery were dissected. Tendon circumference and relationship of the EIP and extensor digitorum communis to the index (EDCI) at the metacarpophalangeal (MCP) joint and the distal extensor retinaculum were recorded. Distance from the distal extensor retinaculum to the EIP myotendinous junction was measured.

RESULTS

EIP was ulnar to the EDCI in 96.5% of specimens (28/29) at the distal edge of the extensor retinaculum. In the remaining specimen, EIP was volar to EDCI. Tendon circumference at the distal extensor retinaculum averaged (9.3 mm ± 1.7 mm) for EDCI and 11.1 mm (± 2.7 mm) for EIP (P = 0.0010). The tendon circumference at the index MCP joint averaged 11.0 mm (± 1.7 mm) for EDCI and 10.6 mm (± 2.1 mm) for EIP (P = 0.33). EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum whereas EIP had a greater circumference in only 31% (9/29) of specimens at the MCP joint.

CONCLUSION
The EIP tendon is frequently ulnar to and greater in circumference than the EDCI at the distal extensor retinaculum, which can be taken into consideration for tendon transfers involving EIP.

Key Words: Surgical anatomy; Tendon transfer; Extensor digitorum communis; Extensor indicis proprius; Tendon harvest; Cadaveric Dissection

Core Tip: We found that extensor indicis proprius (EIP) was consistently ulnar to extensor digitorum communis to the index in 96.5% of specimens at the distal extensor retinaculum. The EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum. This research contributes to the body of knowledge on extensor tendon anatomy and facilitates the smaller incisions and dissection of EIP needed for tendon transfers.

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INTRODUCTION

The extensor indicis proprius (EIP) is a redundant extrinsic extensor of the index finger. It is present in 96.5% of the population and is commonly used for tendon transfers[1]. To correctly harvest the EIP and plan procedural incisions, a thorough understanding of the arrangement of the extensor tendons and their junctural connections is required.

Understanding the variability in anatomic relationships is important when harvesting EIP through a small incision. These variations have been documented in clinical and anatomic studies[2]. The EIP originates from the dorsal aspect of the ulna, the interosseus membrane, and the extensor pollicis longus (EPL) septum[3]. It has the most distal muscle belly of all the extensor tendons, and is the only muscle belly that enters the fourth compartment, under the extensor retinaculum and deep to the extensor digitorum communis (EDC) tendons[1]. Multiple studies have noted that anatomic variants are frequent (10%)[4-7] with regards to arrangement and number of slips. Defining each slip as the presence of independent fascial sheaths at the metacarpal level, the EIP has been cited to have double slips in 16% and triple slips in 7% of cadaveric studies[5]. Gonzalez *et al*[6] classified the arrangement of EIP and extensor digitorum communis to the index (EDCI) at the metacarpophalangeal (MCP) joint into six types: (1) Single EIP ulnar to a single EDCI; (2) Single EDCI between two slips of EIP; (3) Two slips of EIP ulnar to a single EDCI; (4) Single EIP ulnar to two slips of EDCI; (5) Single EIP radial to a single EDCI; and (6) Single EIP volar to a single EDCI. The most common arrangement is a single EIP inserting ulnar to a single EDCI on the extensor hood in 81%-98.3% of specimens[1,4,6], volar to the EDCI in 10% to 11%[4,5,7], and radial to EDCI in 3%-8%[5]. In other tendon transfers, tendon circumference may also be used as a distinguishing characteristic. Celik *et al*[8] examined the width and thickness of EDCI and EIP tendons at the level of mid-diaphyseal metacarpal bones and found similar thickness for EDCI and EIP (1.5 mm ± 0.4 mm and 1.47 mm ± 0.38 mm respectively). To our knowledge, no studies have examined the relationship and anatomy of the EIP and EDCI at the level of tendon harvest.

Clinical relevance

EPL ruptures occur in 0.7% of non-displaced distal radius fractures and 3% of dorsally displaced distal radius fractures[9,10]. Tendon attrition is attributed to friction and compression in the poorly vascularized third compartment between the extensor retinaculum and displaced bone fragments of the dorsal radial tubercle[11]. EIP to EPL transfer is one of the most common tendon transfers in the upper extremity. In addition to anatomic proximity and its redundancy for index finger extension, EIP is synergistic to EPL: The motion of extending the index finger and the thumb interphalangeal (IP) joint is commonly performed together during tasks, allowing patients to recover thumb extension after transfer without extensive relearning. Many techniques exist for harvesting and performing this tendon transfer. The incision for harvest can be made longitudinally or transversely, at the level of the distal or proximal extensor retinaculum, and transfer can occur with two incisions or three with a pulvertaft distal to the retinaculum[12]. Classically described, this tendon transfer has been performed through three incisions: A transverse incision over the MCP joint to transect the ulnar EIP, a longitudinal incision over the thumb metacarpal to dissect out the ruptured tendon and carry out the transfer, and a longitudinal

incision at the extensor retinaculum to identify EIP and perform tendon harvest. However, technique adaptations may be considered that use the anatomic relationship of these tendons. We performed a cadaveric study to evaluate the relationship between EDCI and EIP and share our preferred surgical technique for EIP to EPL tendon transfer. We sought to characterize the circumference and relationship of the EIP and EDCI tendons at the distal extensor retinaculum, which is relevant for tendon identification when performing an EPL transfer.

MATERIALS AND METHODS

Specimens

Twenty-nine skeletally mature fresh frozen cadaveric forearms ages 19 to 52 were obtained. Clinical histories confirmed no previous trauma or surgery to the donor. Tendons were defined as independent bands originating from muscle. Tendons were occasionally divided into one or more separable smaller slips at the retinaculum. Individual slips were defined distal to the muscle belly with independent fascial sheaths.

Dissection

All specimens were dissected with a single dorsal longitudinal incision made just ulnar to Lister's tubercle extending from the index MCP joint to proximal to the extensor retinaculum. Subcutaneous fat and superficial nerves and veins were elevated in a single flap and tenosynovium was dissected off the EDCI and EIP. The extensor retinaculum was identified as oblique transverse fibers with roughly parallel proximal and distal edges. A 4-0 Prolene suture was used to measure the circumference of the two tendons at the distal edge of extensor retinaculum and the MCP joint (Figure 1) with a single simple knot, and dissection scissors were used to cut the knot at the intersection. The remaining Prolene suture was then measured with a ruler to derive circumference of the tendon. Prolene was chosen for its high intrinsic memory and thus decreased risk for error in measurement of small caliber circumference tendons[13]. The distance in millimeters between the distal edge of the extensor retinaculum and the myotendinous junction of EIP was measured as well. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Statistics

To assess our sample with a statistical two-tailed significance of 0.05, power of 80%, and effect size r = 0.6, our a priori power analysis yielded a sample size of 25 was required. Paired t-tests were applied to compare the values obtained from the EIP and EDCI tendon measurements at the distal extensor retinaculum and MCP joint. $P < 0.05$ was considered to be significant.

RESULTS

Twenty-nine fresh frozen human cadaver forearms were dissected. They were from 20 men and 9 women. The right forearm was dissected in 16 cases and the left in 13 cases. None of the specimens had vascular or nerve variations that were apparent upon dissection. None had evidence of prior surgery to the hand, forearm, or wrist, and clinical histories of the specimens confirmed no history of trauma to the area.

In all but one specimen, the EIP tendon was ulnar to the EDCI tendon (96.5%, 28/29); in the remaining specimen, the EIP was volar to the EDCI. The tendon circumference at the distal edge of the extensor retinaculum averaged 9.3 mm (± 1.7 mm) for the EDCI and 11.1 mm (± 2.7 mm) for the EIP (P = 0.001). The tendon circumference at the index MCP joint was measured to be 11.0 mm (± 1.7 mm) for the EDCI and 10.6 mm (± 2.1 mm) for the EIP (P = 0.331). The EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum whereas the EIP had a greater circumference in 31% (9/29) of specimens at the MCP joint. The distance from the distal extensor retinaculum to the myotendinous junction of EIP varied widely but averaged 16.2 mm (± 11.1 mm), which is similar to findings in other studies[11] (Table 1). We did not find significant differences in tendon circumference between specimens of different sex, but overall the tendon circumferences were lower for females as compared to male specimens (Table 2). In addition, the distance between the distal extensor retinaculum to myotendinous junction was lower in female specimens compared to that of males (Table 2); this was also not statistically significant.

In one specimen, the EIP tendon was split at the extensor retinaculum, with the radial branch joining the EDCI tendon at the MCP. However, both slips of the EIP were still found to be ulnar to the EDCI tendon at the distal extensor retinaculum (Figure 2).

Table 1 Specimen demographics and measurements

Laterality	Age (yr)	Sex	Circumference at dER (mm)		Circumference at MCP (mm)		EIP distance from dER to myotendinous junction (mm)	Relationship of EIP to EDCI
			cEDCI	cEIP	cEDCI	cEIP	EIP	
Left	52	M	8	15	12	14	29	EIP ulnar
Left	54	F	9	10	13	10	15	EIP ulnar
Right	38	M	12	13	12	12	16	EIP ulnar
Left	48	M	12	15	14	13	15	EIP ulnar
Right	54	F	11	11	13	9	14	EIP ulnar
Right	30	M	7	8	11	8	20	EIP ulnar
Left	24	M	11	12	9	10	18	EIP ulnar
Right	44	M	9	14	11	14	23	EIP ulnar
Left	38	F	9	8	10	9	27	EIP ulnar
Right	57	F	9	12	11	13	18	EIP ulnar
Right	19	M	8	9	10	10	2	EIP ulnar
Right	44	M	11	13	11	11	37	EIP ulnar
Left	30	M	7	5	14	9	22	EIP ulnar
Left	49	F	9	13	10	10	4	EIP ulnar
Left	19	M	9	9	8.5	11	2	EIP ulnar
Right	48	M	9	8	9	9	48	EIP ulnar
Right	48	M	8	14	12	14	25	EIP ulnar
Left	44	M	11	13	12	8	17	EIP ulnar
Right	24	M	10	14	13	12	13	EIP ulnar
Left	35	M	14	10	14	10	10	EIP ulnar
Left	20	M	9	11	10	8	2	EIP ulnar
Right	20	M	9	13	8	11	3	EIP volar
Left	20	F	10	7	11	8	10	EIP ulnar
Right	21	F	9	10	10	9	3	EIP ulnar
Left	40	M	7	11	10	8	24	2 slips of EIP ulnar
Right	49	F	7	8	11	11	4	EIP ulnar
Right	33	M	9	12	9.5	12	18	EIP ulnar
Right	20	F	9	10	9	8	6	EIP ulnar
Left	33	M	9	15	11	15	24	EIP ulnar
Average	36.4		9.3	11.1	11.0	10.6	16.2	
Standard deviation	12.7		1.7	2.7	1.7	2.1	11.1	

dER: Distal extensor retinaculum; MCP: Metacarpophalangeal; EIP: Extensor indicis proprius; EDCI: Extensor digitorum communis to the index; M: Male; F: Female.

DISCUSSION

Although EIP has a role in index finger extension, it also possesses utility in tendon transfers. It is most often used in cases of EPL rupture, and many anatomic studies have been performed on extensor tendon variations[1,4,8,14]. The causes of these differences remain obscure, although differences in racial grouping have been suggested. South Asian populations have the highest rate of single-slip EIP and the lowest rate of double-slip EIP when compared to Japanese, Europeans and North Americans[1].

Table 2 Measurements of extensor indicis proprius and extensor digitorum communis to the index tendons, segregated by gender

Sex	Age (yr) ± Std	Circumference at dER (mm) ± Std		Circumference at MCP (mm) ± Std		EIP distance from dER to myotendinous junction (mm) ± Std
		cEDCI	cEIP	cEDCI	cEIP	EIP
M	34.7 ± 11.1	9.5 ± 1.9	11.7±2.8	11.1 ± 1.8	11.0 ± 2.3	18.4 ± 11.8
F	40.2 ±1 5.8	9.1 ± 1.1	9.9 ± 2.0	10.9 ± 1.4	9.7 ± 1.6	11.2 ± 8.0
P value	0.28	0.56	0.09	0.77	0.14	0.11

Std: Standard deviation; dER: Distal extensor retinaculum; MCP: Metacarpophalangeal; EIP: Extensor indicis proprius; EDCI: Extensor digitorum communis to the index; M: Male; F: Female.

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Figure 1 Tendon circumference measurement. Tendon circumference was measured utilizing 4-0 prolene at distal extensor retinaculum and at the metacarpophalangeal joint for both the extensor indicis proprius and extensor digitorum communis to the index tendons. Prolene was used to obtain accurate circumference measurements. The distal extensor retinaculum was marked prior to measurements to ensure repeatability and consistent measurement to the myotendinous junction.

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Figure 2 Interesting case of a split extensor indicis proprius tendon that joined the extensor digitorum communis to the index tendon. A specimen in which the EIP consisted of two slips, one of which arose from the extensor indicis proprius and joined the extensor digitorum communis to the index just proximal to the metacarpophalangeal joint.

We chose to measure EIP and EDCI circumference at the distal edge of the extensor retinaculum because this is where EIP is typically harvested to attain sufficient tendon length for transfer. Given that the EIP has the most distal muscle belly, often in the extensor retinaculum, we hypothesized that the EIP would have a greater circumference than the EDCI at the distal extensor retinaculum. Although the EIP circumference 11.1 mm (± 2.7 mm) was statistically greater than EDCI circumference 9.3 mm (± 1.7 mm) (P = 0.001), this was found to be true in only in 76% (22/29) of specimens. Perhaps this could be attributed to the wide variety in distance between the distal edge of the extensor retinaculum and the muscle belly of EIP, which averaged 16.2 mm (± 11.1 mm), similar to findings in other studies[11].

Although we hypothesized that a smaller distance between the myotendinous junction of EIP and the distal edge of the extensor retinaculum would be associated with a greater difference in circumference between EIP and EDCI, this was not found to be statistically significant (P = 0.510).

In 28/29 specimens with a single insertion for EIP, the EIP was located ulnar to the EDCI at the extensor retinaculum. It was located directly volar in the other specimen. The specimen with a split EIP had both branches ulnar to EDCI. These findings are consistent with the known literature where the vast majority (approximately 99%) of single slip EIP tendons are ulnar to EDCI[15], even when 7% of EIPs had two slips and of these, half had both tendons ulnar[1]. These findings are useful when identifying tendons for transfer with small transverse incisions at the distal extensor retinaculum. Although there are other reports of minimally invasive single incision EIP to EPL transfer[15] with a 3 cm incision placed midway between the course of the EIP and EPL at the level of mid-diaphyseal metacarpal, we believe the frequent anatomic variations in the EDCI and EIP relationship warrant additional incisions for EIP harvest and identification.

Preferred surgical technique

Given the finding of the frequently more ulnar EIP to EDCI tendon at the level of the distal extensor retinaculum, we recommend performing a small transverse as opposed to a longitudinal incision at the extensor retinaculum, allowing for a more cosmetic scar. Here, we share our preferred technique using wide awake local EIP to EPL tendon transfer[16].

Begin by injecting 30 mL of 1% lidocaine with 1 : 100000 epinephrine 2 cm beyond the distal extent of the planned incisions. For incisions, we recommend a small 1 cm transverse incision just ulnar to Lister's tubercle at the distal aspect of the extensor retinaculum over the EIP tendon, a 1cm transverse incision over the index metacarpophalangeal joint, and a 2 cm longitudinal incision over the thumb carpometacarpal joint, where the distal stump of the EPL is often located for transfer. At the distal extensor retinaculum, fully flex the wrist and identify the ulnar EIP tendon. Perform a small 1cm transverse incision at the index MCP joint to transect the more ulnar EIP tendon. The extensor indicis is consistently "free" from junctura tendinae[3,8], and after dissecting the EIP tendon from EDCI, a small Ragnell retractor may be used to harvest the EIP tendon through the 1 cm incision at the distal extensor retinaculum. A transverse incision acknowledging the frequent relationship of the EIP being more ulnar or volar to EDCI at the distal extensor retinaculum avoids the longitudinal incision previously used by the authors for dissection to the myotendinous junction, improving cosmesis with an incision hidden along Langer's lines. Use a single 4-0 Fiberwire (Arthrex, Naples, FL) suture to secure any remaining distal EIP tendon stump to EDCI at the MCP joint to prevent the tendon stump from interfering with range of motion of the MCP joint. Transfer the harvested tendon subcutaneously into the longitudinal thumb incision (underneath dorsal radial branch of radial nerve), leaving the tendon in the extensor retinaculum. Use a tendon weaver to make 3 Pulvertaft weaves at 90 degree angles to each other and set the appropriate tension for the tendon to allow full extension of MCP and IP joints, or just shy of full extension to accommodate for loosening of the transfer. Place a single 4-0 Fiberwire suture before asking the patient to move the thumb. Check full flexion and full extension to ensure appropriate range of motion. Place a 4-0 Fiberwire horizontal mattress suture through each subsequent weave. Splint in thumb spica with thumb fully extended for 4 wk and start the retraining process with a hand therapist. In cases of suspected abnormal anatomy, we recommend following the EIP tendon proximally with an additional incision at the myotendinous junction to evaluate for the most distal muscle belly in order to isolate the correct slip(s) for tendon transfer. Should there be a split tendon, consider using a single slip for the tendon transfer.

Limitations

Although a power analysis was implemented to detect significance for an effect size of 0.6 with 2 mm difference in tendon circumference, it is inadequately powered to capture all variations due to the relatively low incidence of these tendon variations. We performed our dissections from a random selection of cadaveric specimens but there is a chance that it is not representative of the population as a whole. Lastly, there is a chance of measurement error given the small values being analyzed. To counteract this, Prolene, a synthetic monofilament composed of isostatic crystalline stereoisomer of polypropylene was chosen for its intrinsic high memory characteristics and thus decreased risk for error in measurement with small caliber tendons[13]. Considering these limitations, we believe that our study is well designed to accurately depict the relationship between the EIP and EDCI at the distal retinaculum and builds on the existing literature characterizing the complex relationship of dorsal hand tendons.

CONCLUSION

We found that EIP was consistently ulnar to EDCI in 96.5% of specimens at the distal extensor retinaculum. The EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum. This research contributes to the body of knowledge on extensor tendon anatomy and

facilitates the smaller incisions and dissection of EIP needed for tendon transfers.

ARTICLE HIGHLIGHTS

Research objectives

We sought to characterize the arrangement and circumference of the extensor indicis proprius (EIP) tendon with respect to the extensor digitorum communis tendon to the index finger (EDCI) at the level of the extensor retinaculum, where tendon harvest is often performed, and share our preferred technique for EIP to extensor pollicis longus (EPL) transfer.

Research methods

Twenty-nine fresh-frozen cadaveric forearms were dissected. Tendon circumference and relationship of the EIP and EDCI at the metacarpophalangeal (MCP) joint and the distal extensor retinaculum were recorded. Distance from the distal extensor retinaculum to the EIP myotendinous junction was measured.

Research results

EIP was ulnar to the EDCI in 96.5% of specimens (28/29) at the distal edge of the extensor retinaculum. In the remaining specimen, EIP was volar to EDCI. Tendon circumference at the distal extensor retinaculum averaged (9.3 mm ± 1.7 mm) for EDCI and 11.1 mm (± 2.7 mm) for EIP (P = 0.0010). The tendon circumference at the index MCP joint averaged 11.0 mm (± 1.7 mm) for EDCI and 10.6 mm (± 2.1 mm) for EIP (P = 0.33). EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum whereas EIP had a greater circumference in only 31% (9/29) of specimens at the MCP joint.

Research conclusions

The EIP tendon is frequently ulnar to and greater in circumference than the EDCI at the distal extensor retinaculum, suggesting a minimally invasive approach to tendon transfer using transverse incisions hidden in Langer's lines would be effective and safe.

Research perspectives

This research contributes to the body of knowledge on extensor tendon anatomy and facilitates the smaller incisions and dissection of EIP needed for tendon transfers.

Research motivation

Understanding the variability in anatomic relationships is important when harvesting EIP through a small incision. To our knowledge, no studies have examined the relationship and anatomy of the EIP and EDCI at the level of tendon harvest at the distal extensor retinaculum.

Research background

The EIP is a redundant extrinsic extensor of the index finger, commonly used in tendon transfer for EPL ruptures. Many variations of the course and arrangement of the tendons have been previously described. It is important to understand the arrangement and anatomy of the EIP tendon at the level of tendon harvest.

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FOOTNOTES

Author contributions: Zhou J contributed to study design, dissections, statistical analysis, and writing the manuscript; Frey C contributed to study design, dissections, statistical analysis, and writing the manuscript; Segovia N carried out statistical analyses and assisted with manuscript revisions; Yao J contributed to study design and manuscript revisions.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Can immediate postoperative radiographs predict outcomes in pediatric clubfoot?

Duangjai Leeprakobboon

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Abstract

BACKGROUND

The goal of treatment for pediatric idiopathic clubfoot is to enable the patient to comfortably walk on his or her soles without pain. However, currently accepted treatment protocols are not always successful. Based on the abnormal bone alignment reported in this disease, some studies have noted a correlation between radiographic characteristics and outcome, but this correlation remains debated.

AIM

To assess the correlation between immediately postoperative radiographic parameters and functional outcomes and to identify which best predicts functional outcome.

METHODS

To predict the outcome and prevent early failure of the Ponseti's method, we used a simple radiographic method to predict outcome. Our study included newborns with idiopathic clubfoot treated with Ponseti's protocol from November 2018 to August 2022. After Achilles tenotomy and a long leg cast were applied, the surgeon obtained a single lateral radiograph. Radiographic parameters included the tibiocalcaneal angle (TiCal), talocalcaneal angle (TaCal), talofirst metatarsal angle (Ta1st) and tibiotalar angle (TiTa). During the follow-up period, the Dimeglio score and functional score were examined 1 year after surgery. Additionally, recurring events were reported. The correlation between functional score and radiographic characteristics was analyzed using sample and multiple logistic regression, and the optimal predictor was also identified.

RESULTS

In total, 54 feet received approximately 8 manipulations of casting and Achilles tenotomy at a mean age of 149 days. The average TiCal, TaCal, Ta1st, and TiTa angles were 75.24, 28.96, 7.61, and 107.31 degrees, respectively. After 12 mo of follow up, we found 66% excellent-to-good and 33.3% fair-to-poor functional

outcomes. The Dimeglio score significantly worsened in the poor outcome group (P value < 0.001). Tical and TaCal showed significant differences between each functional outcome (P value < 0.05), and the TiCal strongly correlated with outcome, with a smaller angle indicating a better outcome, each 1 degree decrease improved the functional outcome by 10 percent. The diagnostic test revealed that a TiCal angle of 70 degrees predicts an inferior functional outcome.

CONCLUSION

The TiCal, derived from lateral radiographs immediately after Achilles tenotomy, can predict functional outcome at 1 year postoperatively, justifying its use for screening patients who need very close follow-up.

Key Words: Idiopathic clubfoot; Radiograph; Functional outcome; Tenotomy; Prognostic; Tibiocalcaneal angle

Core Tip: Idiopathic clubfoot is an abnormality of bone alignment. Current treatment strategies are associated with recurrence, which results in pain and poor quality of life. Radiography-assisted outcome prediction must be harmless in young children. The lateral tibiocalcaneal angle was directly related to functional outcomes, as a smaller angle was associated with a better outcome. A lateral tibiocalcaneal angle exceeding 70 degrees immediately after Achilles tenotomy predicted an inferior outcome.

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INTRODUCTION

Talipes equinovarus, known as idiopathic clubfoot, is a complexity inside the bone of the foot, with a birth prevalence of approximately 1-3 cases per thousand born[1,2]. The treatment goals are painlessness and a plantigrade walk. Currently, Ponseti's technique, which includes casting, Achilles tenotomy and bracing, is the accepted treatment strategy, but up to 11%-48% recurrence has been found [3-7].

However, Ponseti noted that radiography cannot predict prognosis because it is not associated with clinical appearance[8]. Nevertheless, some reports identified a significant relationship between preoperative radiographs and treatment decisions. For example, a lateral tibiocalcaneal angle > 80 degrees indicates a need for Achilles tenotomy[9]. In 2015, a retrospective study found that a preoperative dorsiflex angle > 16.6 degrees did not require reoperation and was related to recurrence [10]. Furthermore, a lateral tibiocalcaneal angle > 77 degrees and lateral talocalcaneal angle < 29 degrees at the time of brace withdrawal predicts reoperation[11].

The purposes of this study were as follows: To demonstrate the correlation between immediately postoperative radiographic parameters and functional outcome. To identify the radiographic parameter that best predicts functional outcome.

MATERIALS AND METHODS

Population

This work was a retrospective cohort study conducted from November 2018 to August 2022. Any newborn patient who was diagnosed with idiopathic clubfoot was included. Exclusion criteria included syndromic clubfoot, recurrent cases and patients who had received previous treatment. All patients underwent weekly manipulation of their feet according to the Ponseti technique, followed by Achilles tendon tenotomy and long leg cast application. Immediately after this procedure, the surgeon took one radiograph of the lateral foot and ankle.

Radiography and clinical parameters

In an attempt to predict the outcome and prevent early failure of the Ponseti's method, we used a simple radiographic method to predict outcome because radiographic postoperative studies are lacking

and radiographic assessment is not associated with disadvantages[12].

Radiographic parameters included the tibiocalcaneal angle (TiCal), talocalcaneal angle (TaCal), talofirst metatarsal angle (Ta1st) and tibiotalar angle (TiTa) (Figure 1). Foot characteristics were evaluated according to the Dimeglio classification, and functional scores were assessed 1 year after surgery, as described by Ponseti, and interpreted as follows: A total score < 70, 70-79, 80-89, and 90-100 represents poor, fair, good, and excellent outcomes, respectively[13]. Additionally, recurring events were reported if further surgery was needed. Data were analyzed by 2 observers, a fourth-year resident orthopedic training and pediatric orthopedic surgeon, and interrater reliability was confirmed using the kappa statistic.

Statistical analysis

All statistical analyses were performed using STATA 11 statistical software (Stata Corp., College Station, TX, United States). The chi-squared test and Fisher's exact test were used to assess independence between two dichotomous variables. The chi-squared test was applied under the assumption that the sample was large. When more than 20 percent of cells had expected frequencies < 5, the Fisher's exact test was run for small-sized samples. The two-sample *t*-test was used to compare the mean of continuous variables, and the Mann-Whitney U test was used when the variable did not have a normal distribution. Logistic regression by using a penalized maximum likelihood estimation method was used to determine factors associated with functional scores, *P* value < 0.05 was considered statistically significant and the magnitude of association was shown as crude odds ratios (OR), adjusted OR, and 95% confidence intervals (CI).

RESULTS

The study included 54 feet from 35 newborn patients with clubfoot. All feet received manipulation, and a long leg cast was applied approximately 8 times on average. Then, the Achilles tenotomy procedure was performed at an average age of 149 days. Immediately after surgery and cast application, we obtained radiographs and found that the average TiCal, TaCal, Ta1st, and TiTa angles were 75.24, 28.96, 7.61, and 107.31 degrees, respectively. After the last cast was removed, the brace protocol was utilized as usual, and the Dimeglio score significantly worsened in the poor outcome group (*P* value < 0.001), which was clearly evident 6 mo postoperatively. After 12 mo of follow up, 24% of cases required further surgery, 66% of cases had an excellent-to-good functional outcome and 33.3% of cases had a fair-to-poor functional outcomes. Demographic data did not significantly differ between groups, as shown in Table 1.

Table 2 presents the significant differences in the Tical and TaCal angles between each functional outcome (*P* value < 0.05), and the TiCal angle was strongly predictive of outcome, as shown in Table 3. Furthermore, the study shows that a lower TiCal angle corresponded to a better outcome, with an adjusted odds ratio of 0.90 (0.83-0.99). Specifically, each 1 degree decrease improved the functional outcome by 10 percent. The diagnostic test revealed that a TiCal angle of 70 degrees predicts an inferior functional outcome, with 88.9% sensitivity, 41.7% specificity, and 0.56 ROC area (95%CI: 0.42-0.70).

DISCUSSION

Idiopathic clubfoot is the most common multifactorial irreducible foot problem in newborns[2,14]. To date, the Ponseti protocol is widely utilized to treat this condition, in which the deformity is corrected sequentially by Achilles tenotomy and a brace is applied. However, a previous study showed a 33%-41% rate of recurrence[15,16]. Clubfoot is pathogenically characterized by abnormal bone alignment and abnormal radiographic features compared with normal feet, including bony abnormalities from incorrect treatment, whereas radiographic features from correct treatment are obviously better than pre-treatment[17,18].

This study found a correlation between radiographic data, lateral tibiocalcaneal and talocalcaneal angles derived immediately postoperation, and functional outcomes at the 12 mo follow-up. This finding is in agreement with a previous report that supports the use of radiographs for treatment guidance, especially in residual deformity correction, such as complete subtalar release or postero-medial release procedures[19-21].

The tibiocalcaneal angle was the most reliable feature for predicting outcome in the present study, as a smaller angle predicted a better outcome based on the plantigrade ability. We found that a cutoff point of > 70 degrees could predict fair-to-poor functional outcome at walking age with 88.9% sensitivity, similar to the equinus position, which results in a poor quality of life. Similarly, previous studies recommended using this angle to predict risk of relapse and decide the surgical type, such as Achilles tenotomy, soft tissue release, and even reconstructive procedures for recurrent clubfoot, to improve functional outcome, but these studies investigated older children[8,10,11,22,23]. Additionally, a close relationship of clinical and talocalcaneal and talo-1st metatarsal angles was found in some studies[17,24,

Table 1 Demographic data for the excellent/good and fair/poor functional groups

Demographic data	Excellent and good group (*n* = 36)	Fair and poor group (*n* = 18)	Mean different (95%CI)	*P* value
Male, *n* (%)	26 (72.22)	11 (61.11)	-	0.407[b]
Number of casts	8.69 (3.05)	8.33 (3.39)	-0.36 (-2.19, 1.47)	0.6950[a]
Age at tenotomy (d), mean (SD)	144 (53.52)	161.55 (69.11)	17.55 (-16.66, 51.77)	0.3081[a]
Brace compliance, *n* (%)	29 (80.56)	17 (94.44)	-	0.245[c]

[a]Independent samples *t* test.
[b]Pearson chi square test.
[c]Fisher's exact test. SD: Standard error.

Table 2 Mean range of each radiographic angle in clubfeet patients after surgery in lateral view

Angle	Excellent and good group, mean (SD)	Fair and poor group, mean (SD)	Mean different (95%CI)	*P* value[a]
Tibiocalcaneal angle	72.55 (10.36)	80.61 (7.76)	8.05 (2.49, 13.61)	0.0053
Talocalcaneal angle	31.66 (11.92)	23.55 (12.00)	-8.11 (-15.03, -1.18)	0.0225
Talofirst metatarsal angle	7.72 (7.83)	7.38 (5.23)	-0.33 (-4.44, 3.77)	0.8713
Tibiotalar angle	107.72 (11.73)	106.50 (15.53)	-1.22 (-8.80, 6.36)	0.7478

[a]Independent samples *t* test.

Table 3 Correlation of radiographic parameters and functional outcomes

Angle	Functional score, excellent and good group (*n* = 36), fair and poor group (*n* = 18)		
	Crude odds ratio (95%CI)[a]	Adjusted odds ratio (95%CI)	*P* value[b]
Tibiocalcaneal angle	0.90 (0.84-0.97)	0.90 (0.83-0.99)	0.031
Talocalcaneal angle	1.06 (1.00-1.12)	1.04 (0.97-1.11)	0.199
Talofirst metatarsal angle	1.00 (0.92-1.09)	0.99 (0.89-1.10)	0.916
Tibiotalar angle	1.00 (0.96-1.05)	1.01 (0.95-1.07)	0.707

[a]Simple logistic regression.
[b]Multiple logistic regression. CI: Confidence interval.

25].

Although a later study from 2017 discovered that radiographic abnormalities are not indicative of clinical abnormalities and that the Ponseti method can improve foot shape but cannot correct bone deformities, the treatment protocol needs to be based on various data sources[8,26]. Radiography is a criterion to screen patients who need very close follow-up.

This study has the following strengths: (1) We used functional outcome as the end result instead of recurrence because recurrence is a subjective assessment that the surgeon utilizes to determine whether to perform additional interventions; (2) We analyzed only ossified bone to provide more accurate results; and (3) We based our analysis on one lateral view radiograph, which is harmless to patients, as shown in a previous study[12].

Limitations of the study

The small sample analyzed in this study precludes large effect sizes between groups. Furthermore, we calculated the angle based on only ossified bone in a small child for accuracy reasons. Consequently, we may lack information from other nonossified bone.

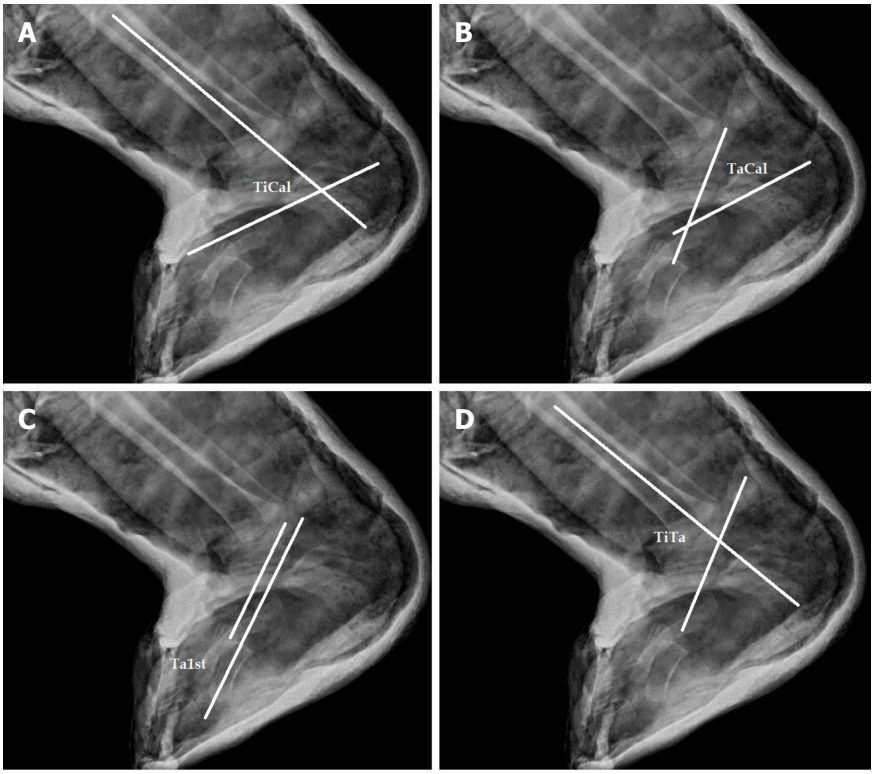

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Figure 1 Radiographic angles. A: The tibiocalcaneal angle was defined as the angle between the axis of the tibia and the axis of the calcaneus; B: The talocalcaneal angle was defined as the angle between the talus axis and the calcaneus axis'; C: Talofirst metatarsal angle was defined as the angle between the axis of the talus and the axis of the 1st metatarsal bone; D: The tibiotalar angle was defined as the angle between the axis of the tibia and the axis of the talus.

CONCLUSION

The tibiocalcaneal angle, derived from lateral radiographs immediately after Achilles tenotomy and casting, can predict functional outcome at 1 year postoperatively and provide a sufficient rationale for screening patients who need very close follow-up.

ARTICLE HIGHLIGHTS

Research background

Idiopathic clubfoot is an abnormal bone alignment and there are currently failure cases resulting from the currently acceptable treatment protocol. Postoperative radiographs are expected to predict outcomes beginning at the prewalking age.

Research motivation

To predict the outcome and early prevention in cases that may fail with Ponseti's method, considering the lack of radiographic postoperative studies and almost none of the disadvantages of radiation taken once, we decided to use the simple radiographic method for outcome prediction.

Research objectives

To assess the correlation between immediately postoperative radiographic parameters and functional outcomes.

Research methods

Patients with idiopathic clubfoot were assessed for radiographic parameters immediately postoperatively, and functional scores were assessed at follow-up.

Research results

The tibiocalcaneal and talocalcaneal angles showed significant differences between each functional outcome, and the tibiocalcaneal angle had a strong effect, with a smaller angle seeming better.

Research conclusions

The tibiocalcaneal angle, derived from lateral radiographs immediately after Achilles tenotomy and cast, can predict functional outcome at 1 year postoperatively.

Research perspectives

A larger population and long-term follow-up of 5 to 10 years would provide a better correlation of the radiographic parameters and functional outcomes.

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FOOTNOTES

Author contributions: Leeprakobboon D solely contributed to this paper.

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Informed consent statement: All study participants or their legal guardian provided informed written consent regarding personal and medical data collection prior to study enrollment.

Conflict-of-interest statement: All author reports no conflicts of interest, financial or otherwise, with regard to the materials or methods used or the findings described in this study.

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Septic arthritis of the hand: From etiopathogenesis to surgical treatment

Konstantin V Lipatov, Arthur Asatryan, George Melkonyan, Aleksandr D Kazantcev, Ekaterina I Solov'eva, Irina V Gorbacheva, Alexander S Vorotyntsev, Andrey Y Emelyanov

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Abstract

BACKGROUND

Septic arthritis of the hand, which is the second most common after damage of the knee joint, remains one of the leading causes of temporary disability. An inflammation can cause dysfunction of the joint, and in the most severe cases, the need for amputation of the finger may arise. The results of their treatment today, especially from a functional point of view, cannot be considered satisfactory. Urgent surgical treatment is extremely important in septic arthritis of the hand, as it helps to prevent cartilage destruction and the development of osteomyelitis.

AIM

To explore the features of the course of septic arthritis of the hand as well as approaches to surgical treatment and its results, depending on the nature of the damage to the articular structures.

METHODS

The results of the treatment of 170 patients with septic arthritis of the hand, which were treated in the period of 2020-2021, were analyzed. Inflammation of the

interphalangeal and metacarpophalangeal joints (MCP) of fingers 1, 2, and 3 was more often noted in 147 (81.6%) joints. The most common cause of arthritis was a penetrating injury as a result of household trauma (101, 59.4%), animal bite (30, 17.6%), and clenched fist injury (15, 8.8%). Septic arthritis with contiguous osteomyelitis was observed in 98 (54.4%) cases. Surgical treatment was completed with drainage and irrigation of the joint. Early mobilization was used to restore function. In patients with osteomyelitis, it was aimed at the formation of neoarthrosis. Arthrodesis was not applied. Long-term results of treatment were assessed in 142 (83.5%) patients within 1 mo to 12 mo after discharge from the hospital [the median was 7 mo (IQR: 4-9)].

RESULTS

The most commonly isolated organism was *Staphylococcus aureus* (35.3%). The median treatment delay in patients without osteomyelitis was 5 d (IQR: 4-7); for septic arthritis with contiguous osteomyelitis, it was 14 d (IQR: 5-21). Radiography for osteomyelitis within 2 wk was uninformative: 41.2% of diagnoses. A single surgical treatment was required in 138 (81.2%) patients, two treatments in 22 (12.9%), and three or more in 10 (5.9%). Total elimination of the infection was achieved in 163 (95.9%) patients. The best functional results of treatment were noted in patients without osteomyelitis. After septic arthritis, Total Active Motion (TAM) for the MCP was 96.2% (IQR: 85.1-98.0), for the proximal interphalangeal joint (PIP) 82.4% (IQR: 54.5-98.5), and for the distal interphalangeal joint (DIP) 69.4% (IQR: 65.4-74.1). In cases with osteomyelitis, it was possible to achieve the formation of neoarthrosis with TAM for MCP-64.2% (IQR: 45.3-90.1), for PIP-62.5% (IQR: 41.8-68.9), and for DIP-59.4% (IQR: 50-62.1). Additionally, the severity of pain during movements did not exceed 1 point.

CONCLUSION

The delay in treatment of patients with septic arthritis of the hand was accompanied by a high incidence of osteomyelitis, especially in the presence of diabetes mellitus. Urgent surgical treatment, along with continued irrigation of the joint and antibiotic therapy, made it possible to eliminate the infection, and early rehabilitation restored the range of motion. The best results were noted in patients without osteomyelitis. With the development of osteomyelitis, a complex of early rehabilitation measures also made it possible to partially restore the range of motion due to the formation of neoarthrosis, without resorting to arthrodesis.

Key Words: Septic arthritis; Osteomyelitis; Hand; Surgical treatment; Neoarthrosis

Core Tip: The timing of surgical treatment initiation is extremely important in septic arthritis of the hand. Prompt and timely surgical intervention can prevent the destruction of cartilage and the development of osteomyelitis. In the presence of osteomyelitis, surgical debridement followed by early rehabilitation aimed at developing neoarthrosis may be an alternative to traditional treatment using arthrodesis. This conception makes it possible to largely preserve the range of active motions in the affected joint.

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INTRODUCTION

It is difficult to overestimate the importance of the hand as a unique anatomical and physiological formation. The hand is important not only from the point of view of aesthetics but is also often decisive in the performance of professional activities. Therefore, any disease or traumatic injury can cause irreparable damage[1,2]. Septic diseases of the hand are characterized by a high prevalence and remain one of the leading causes of temporary disability. Among the pathologies of the hand, septic arthritis of the metacarpophalangeal and interphalangeal joints is characterized by particular severity. An inflammation can cause dysfunction of the joint, and in the most severe cases, the need for amputation of the finger[1,3,4] may arise. The incidence of septic arthritis of the hand differs significantly by region and ranges from 2 to 12 cases per 100000 population per year[5]. Among septic arthritis, septic arthritis of

the hand takes second place in prevalence (15%-20%) after lesions of the knee joint, and among hand infections it occurs in 5%-18% cases[3,6]. Pathogenesis, clinical manifestations, and approaches to the treatment of septic arthritis of the hand have quite significant differences from inflammation of large joints. The causes of their occurrence are most often the direct penetration of the infection as a result of traumatic injury or the spread of infection from the surrounding soft tissues during felon, tenosynovitis, *etc*. In the absence of timely and complete treatment, cartilage destruction and osteomyelitis will develop in a short time[7-9]. A diagnosis of septic arthritis of the hand is based on clinical data, as well as the results of instrumental and laboratory research. Such clinical manifestations as pain, edema, hyperemia, and limitation of range of motion (ROM) are typical but do not allow us to establish the stage of the inflammatory process, including cartilage destruction and osteomyelitis[10]. The most commonly used radiography is also uninformative in the early stages. All these substantiate the expediency of using computed tomography and magnetic resonance imaging, which have high diagnostic value[1,3,11]. The microbial landscape in septic arthritis of the hand is not well understood. The leading role of *Staphylococcus aureus* (*S. aureus*) in this pathology has been reported. At the same time, data regarding the frequency of isolation of methicillin-resistant *S. aureus* (MRSA) differ significantly (from 0% to 73%)[10,12-14].

Treatment of septic arthritis of the hand is based on a combination of surgical methods and antibiotic therapy[10,15,16]. A number of authors note that persistent inflammation after surgical debridement determines the need to perform repeated surgical intervention within 24-48 h[2,17,18]. Articular cartilage destruction and osteomyelitis are considered by most experts as indications for arthrodesis[4, 10,17,19]. The possibility of neoarthrosis formation after resection of the destroyed joint is not considered. Some authors, characterizing their own observations, testify that arthrodesis was not performed in patients with osteochondral destruction. However, they do not report long-term functional results of the treatment [15].

The duration of antibiotic therapy remains a subject of discussion. A significant number of authors are supporters of long-term (at least 1 mo) administration of antibiotics[20-22]. However, in a study performed by Gjika *et al*[23], it was shown that a shorter 2-wk course of antibiotic therapy was as effective as a 4-wk course. The most important moment in the treatment of septic arthritis of the hand is the beginning of rehabilitation as a factor contributing to the restoration of movements and a decrease in joint stiffness. Some authors refer to supporters of early rehabilitation (1 d after surgery), while others consider it necessary to ensure peace for 7-14 d[5,16,18,24].

Thus, although septic arthritis of the hand is a common pathology, many questions regarding its etiology, pathogenesis, and treatment approaches remain insufficiently explored. There is still no answer to the question of whether there is a real alternative to arthrodesis in the presence of osteochondral destruction of the joint.

MATERIALS AND METHODS

Population

The results of the examination and treatment of 170 patients (180 joints) who were hospitalized with a diagnosis of septic arthritis of the hand from 2020 to 2021 were retrospectively analyzed. The average age of the patients was 49 years (IQR: 34-65). There were 116 men (68.2%) and 54 women (31.8%). Damage to the joints of the right hand was observed in 103 (60.6%) patients, and damage to the left hand was observed in 67 (39.4%). Most often, inflammation of the joints of 1, 2, and 3 fingers was diagnosed (detected: 147 (81.6%) joints). Septic arthritis of the metacarpophalangeal joint (MCP) was noted in 55 (30.6%) cases, proximal interphalangeal joint (PIP) in 54 (30%), distal interphalangeal joint (DIP) in 45 (25%), and interphalangeal joint of the first finger (IP of the thumb) in 26 (14.4%) (Figure 1).

Exogenous infection was detected in 164 (96.5%) patients, and endogenous (the source of infection was not found) was detected in 6 (3.5%). Among the causes of septic arthritis, various types of household trauma were most often noted-101 (59.4%), animal bites-30 (17.6%), and clenched fist injury-15 (8.8%) (Figure 2).

The nature of the clinical course of arthritis was assessed based on the duration of symptoms: Acute-less than 3 wk and chronic-3 wk or more[25]. An acute course was observed in 156 (91.8%) patients, and a chronic course was observed in 14 (8.2%).

While a specialized classification of septic arthritis of the hand needs further specification, the classification of septic arthritis of large joints worked out by Tan *et al*[26] is widely used in surgery. Isolated septic arthritis was noted in 11 (6.1%) cases, septic arthritis with soft-tissue extension but no osteomyelitis in 71 (39.4%), and septic arthritis with contiguous osteomyelitis in 98 (54.4%).

Among comorbidities, arterial hypertension was most often observed (36 patients; 21.2%), followed by diabetes mellitus (16 patients; 9.4%) and postinfarction cardiosclerosis (7 patients; 4.1%).

All patients underwent surgical treatment during the first day after hospitalization. It included the excision of all nonviable tissues (soft tissues, and in the case of osteomyelitis, both bone and cartilage structures) and ended with drainage and irrigation of the joint cavity. The drains were removed after the inflammation subsided, usually after 3-5 d. Persistent inflammation served as the basis for repeated

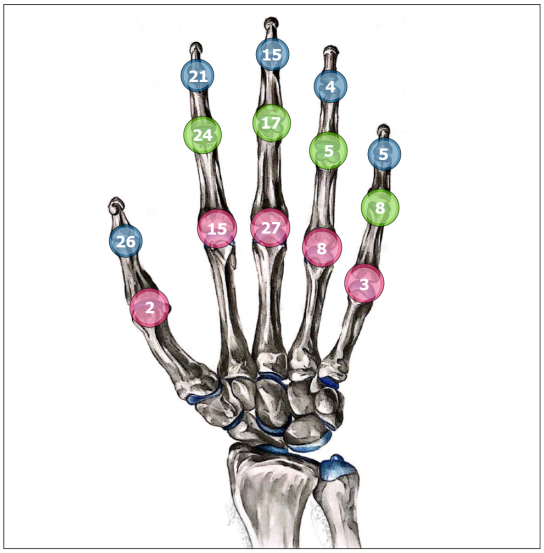

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Figure 1 Distribution of 180 small joints involved in 170 episodes of septic arthritis.

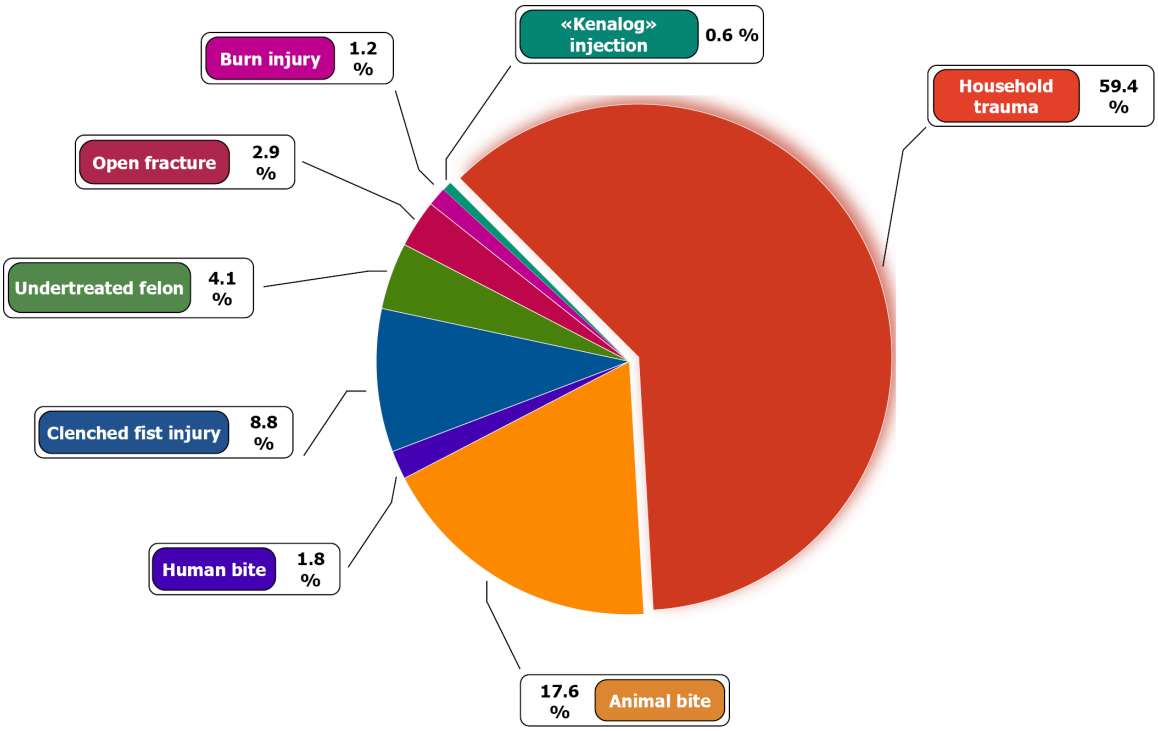

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Figure 2 Causative factors of septic arthritis of the hand.

surgical treatment within 24-48 h. Although the conventional surgical approach for septic arthritis with contiguous osteomyelitis is the need for arthrodesis (either primary or delayed), a different approach was used in these observations. The concept of the formation of neoarthrosis was fundamental, and was achieved through early mobilization, starting 5-7 d after the removal of the affected bone and cartilage structures.

Immobilization of the hand was carried out for 3-5 d using a developed design that allows axial extension of the affected finger (Figure 3). Subsequently, rehabilitation activities began.

Antibacterial therapy at the inpatient stage included intravenous administration of antibiotics such as amoxicillin/clavulanate, ceftriaxone, ciprofloxacin, and clindamycin. The results of microbiological research were taken into account. Patients who developed osteomyelitis after discharge continued to receive oral antibiotic therapy for 2 wk.

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Figure 3 Immobilization of the hand using a developed design that allows axial extension of the affected finger.

The long-term results of the performed treatment were evaluated in 142 (83.5%) patients within 1 mo to 12 mo after discharge from the hospital [the median was 7 mo (IQR: 4-9)]. The evaluation parameters included totalelimination of the infection as well as the volume of active movements of the affected joint (ROM). For this, the Total Active Motion (TAM) system was used. TAM is described by the American Society for Surgery of the Hand as the sum of active MCP, PIP, and DIP arc of motion in degrees of an individual digit. This calculation can then be compared to the TAM of the contralateral hand[27]. If necessary, control radiography or computed tomography was performed.

The severity of chronic pain during movement was assessed using a 10-cm visual analog scale (VAS), where 0 is no pain, and 10 cm is pain that is as bad as it could possibly be. In the analysis, centimeters were converted into points, where 1 cm equaled 1 point on the pain scale.

When examining patients, along with general clinical methods, radiography, computed tomography, microbiological examination with identification of microbial flora and determination of its sensitivity to antibiotics, as well as morphological examination of tissues removed during surgical treatment were used.

Statistical analysis

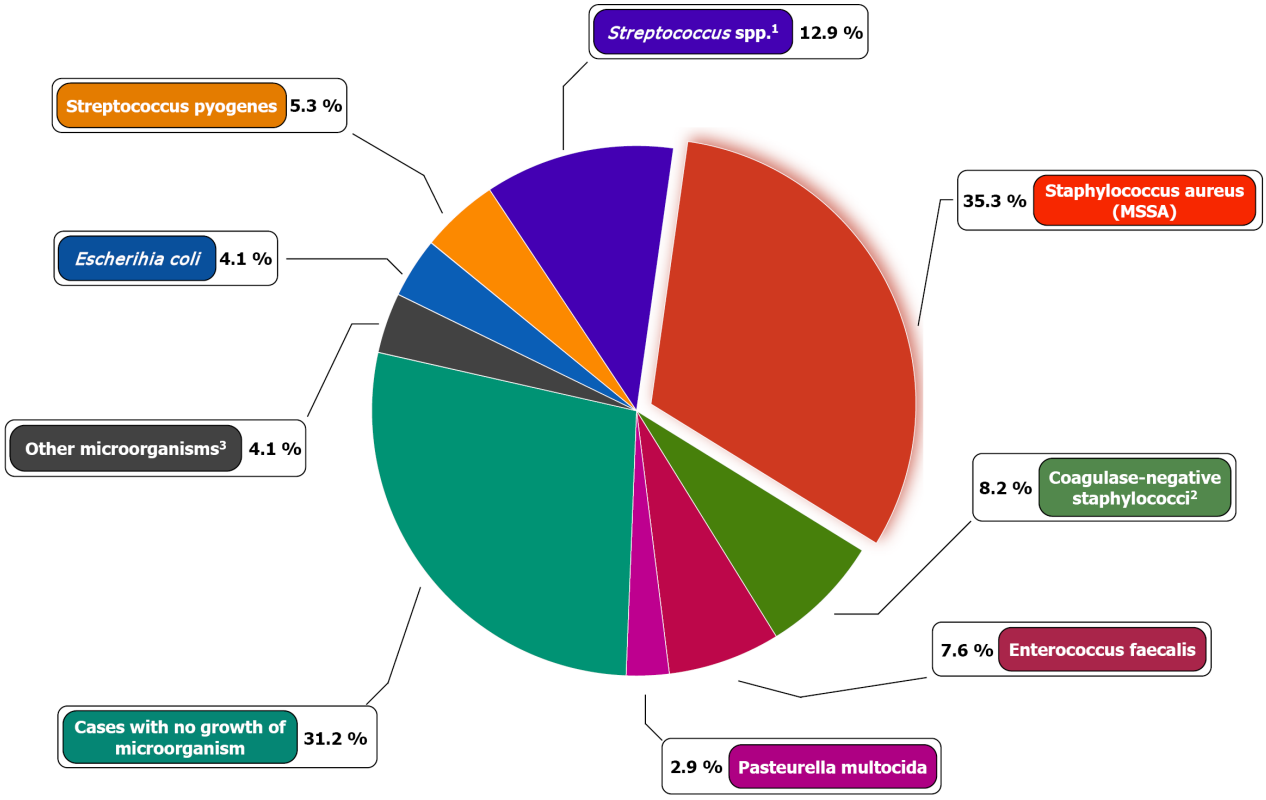
Statistical processing was carried out by methods of collecting and grouping factual material, calculating the median (Me) and IQR. The normality of the distribution was determined using the Shapiro-Wilk normality test. The significance of difference for nonparametric indicators was determined using the Mann-Whitney *U* test. Differences in indicators at $P < 0.05$ were considered significant. The study was reviewed by our biostatistic expert

RESULTS

Men predominated among the sick (68.2% *vs* 31.8% of women). The most common inflammation was MCP of the middle finger (15%), IP of the thumb (14.4%), PIP of the index finger (13.3%), and DIP of the index finger (11.7%). Septic arthritis of the MCP of the middle finger in all cases was the result of a clenched fist injury. At the same time, damage to the joint capsule and the extensor tendon of the finger was observed. Defects in the treatment of felon as a cause of septic arthritis DIP were identified in 7 (4.1%) patients.

The clinical course of septic arthritis in most patients (91.8%) was regarded as acute. However, local inflammation prevailed. An increase in body temperature was noted only in 55 (32.4%) patients; the median was 37.2 °C (IQR: 37.2-37.6). An increase in the number of leukocytes in the peripheral blood was observed in 82 (48.2%) patients; the median was 11.1 × 10^9/L (IQR: 10.2-13.6).

As a result of microbiological analysis, the bacterial flora was identified in 117 (68.8%) cases (Figure 4). In other plates the growth of microflora was absent. Among the isolated microorganisms, *S. aureus* was the most common (35.3%). A feature of the observations was that *MRSA* was not detected in any case. Monoinfection was noted in 98 (57.6%) cases, and polymicrobial infection was detected in 19



[1]*Streptococcus* spp. consisted of *Streptococcus mitis*, *Streptococcus anginosus*, and *Streptococcus agalactiae*.

[2]Coagulase-negative staphylococci consisted of *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*.

[3]Other microorganisms consisted of *Klebsiella pneumoniae*, *Bacillus cereus*, *Proteus mirabilis*, *Acinetobacter baumannii*, *and Enterobacter aerogenes*.

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Figure 4 Microorganisms cultured from patients with septic arthritis of the hand.

(11.2%).

Another feature of the presented observations was a large number of cases of septic arthritis with contiguous osteomyelitis: 98 (54.4%) cases. To explain this fact, the duration of the delay in the start of treatment in various anatomical types of septic arthritis was analyzed. The median treatment delay in patients with septic arthritis without osteomyelitis was 5 d (IQR: 4-7). Septic arthritis with contiguous osteomyelitis was significantly longer and lasted for 14 d (IQR: 5-21). The diagnosis of osteomyelitis was confirmed by the results of intraoperative revision, morphological examination, and radiography (Figure 5). At the same time, radiographic data did not always make it possible to diagnose osteomyelitis in a timely manner. Among all cases with proven osteomyelitis (n = 98) with a treatment delay of up to 14 d (n = 51), it was detected on radiographs only in 21 (41.2%) cases. If the delay in treatment exceeded 14 d (n = 47), then radiographic signs of osteomyelitis were much more common and were reported in 39 (83%) cases. In 8 (17%) observations, even in these terms, radiographs did not allow a correct diagnosis.

The course of septic arthritis in patients with diabetes mellitus (n = 16) was characterized by particular severity. Fourteen (87.5%) of them developed osteomyelitis. The median treatment delay was 6 d (IQR: 4-28).

Surgical treatment has become a fundamental moment in the treatment of septic arthritis. A single surgical treatment was performed in 138 (81.2%) patients. The need for two surgical treatments was noted in 22 (12.9%) patients. Three or more treatments were required in 10 (5.9%) patients. Thus, repeated operations were performed in 32 (18.8%) patients. There was a certain relationship between the cause of septic arthritis and the need to perform repeated surgical treatment. The highest frequency of repeated surgical interventions was noted in patients with diabetes mellitus: 56.3%.

The duration of antibiotic therapy depended on the anatomical form of arthritis and the effectiveness of the treatment. In septic arthritis without osteomyelitis, the duration of antibiotic therapy averaged 7 d (IQR: 5-7). Septic arthritis with contiguous osteomyelitis was longer and lasted for 23 d (IQR: 21-25). This included inpatient and subsequent outpatient antibiotics.

In the majority of patients (163, 95.9%), it was possible to achieve elimination of infection and healing the wounds. However, 7 (4.1%) patients required rehospitalization for surgical treatment due to the ongoing septic process. Among them, there were 3 patients initially hospitalized with a diagnosis of septic arthritis of the hand without osteomyelitis and 4 with a diagnosis of septic arthritis with

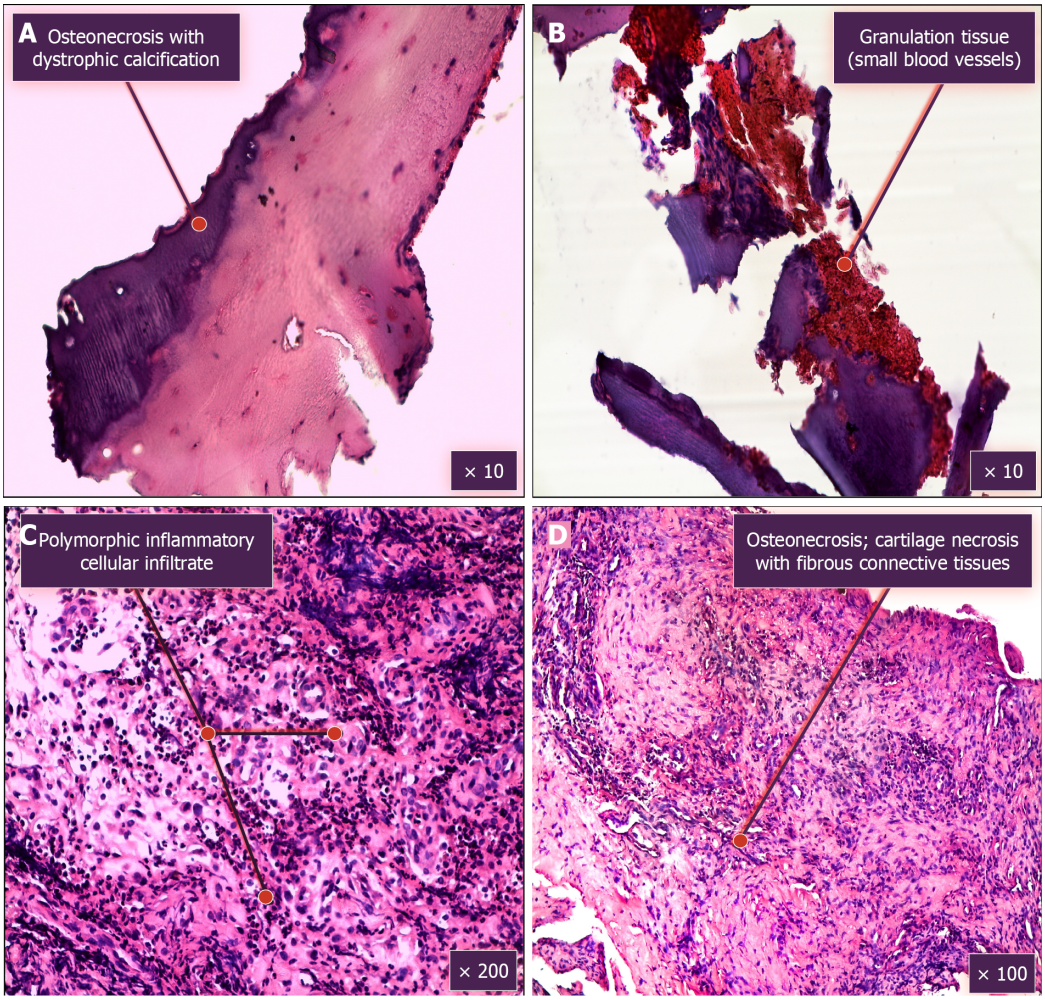

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Figure 5 Morphological examination of tissues removed during surgical treatment (hematoxylin and eosin staining). A: Osteonecrosis with dystrophic calcification; B: Granulation tissue (small blood vessels); C: Polymorphic inflammatory cellular infiltrate; D: Osteonecrosis; cartilage necrosis with fibrous connective tissues.

contiguous osteomyelitis.

The best functional results were noted in the treatment of septic arthritis without osteomyelitis. The TAM assessment showed that the range of active movements of the finger was maximal after suffering septic arthritis of the MCP, and its median was 96.2% (IQR: 85.1-98.0) on the ROM of the contralateral finger. Slightly worse rates were reported for lesions of the proximal interphalangeal [median, 82.4% (IQR: 54.5-98.5)] and distal interphalangeal [median, 69.4% (IQR: 65.4-74.1)] joints. If we consider the recovery of ROM in a particular joint, then it was significantly better in the MCP [median, 97.6% (IQR: 84.6-100.0)] ($P < 0.05$). The worst indicators were characterized by the DIP [median, 62.1% (53.6-67.9)]. The median ROM of PIP was 84% (IQR: 68.2-98.5). The severity of pain during movement (according to the VAS scale) was minimal and did not exceed 1 point on a ten-point scale.

In cases of septic arthritis with contiguous osteomyelitis, the formation of neoarthrosis allowed only partial restoration of the range of active movements. The median TAM with MCP destruction was 62.7% (IQR: 48.1-87.5), with destruction of PIP was 60.5% (IQR: 51.8-71.8), and with DIP destruction was 63.2% (IQR: 61.5-71.7). The ROM in these joints was as follows: MCP-64.2% (IQR: 45.3-90.1), PIP-62.5% (41.8-68.9), and DIP-59.4% (50.0-62.1) (Figures 6-8). The severity of pain during movement was insignificant, although it was statistically significantly higher than pain in patients with septic arthritis without osteomyelitis. It was 0.86 points (IQR: 0.72-1.45) for MCP, 1.05 points (IQR: 0.71-1.55) for PIP, and 0.4 points (IQR: 0.3-0.55) for DIP (Table 1, Supplementary material).

DISCUSSION

The occurrence of septic arthritis of the hand, as a rule, was the result of a penetrating injury to the joint. The predominance of men with septic arthritis was explained by their frequent traumatization. The

Table 1 Summary of total active motion and range of motion

Outcome	Patients without osteomyelitis, median (IQR)	Patients with osteomyelitis, median (IQR)	*P* value
TAM, %			
MCP	96.2 (85.1-98.0)	62.7 (48.1-87.5)	0.01072
PIP	82.4 (54.5-98.5)	60.5 (51.8-71.8)	0.00695
DIP	69.4 (65.4-74.1)	63.2 (61.5-71.7)	0.03662
ROM, %			
MCP	97.6 (84.6-100.0)	64.20 (45.30-95.05)	0.03362
PIP	84.0 (68.2-98.5)	62.5 (41.8-68.9)	0.01017
DIP	62.1 (53.6-67.9)	59.4 (50.0-62.1)	0.00960
Pain, VAS, cm			
MCP	0.40 (0.20-0.55)	0.86 (0.72-1.45)	< 0.00100
PIP	0.98 (0.75-1.50)	1.05 (0.71-1.55)	< 0.00100
DIP	0.20 (0.10-0.45)	0.40 (0.30-0.55)	< 0.00100

The values are given as the median and IQR. TAM: Total active motion; ROM: Range of motion; MCP: Metacarpophalangeal joint; PIP: Proximal interphalangeal joint; DIP: Distal interphalangeal joint; VAS: Visual analogue scale.

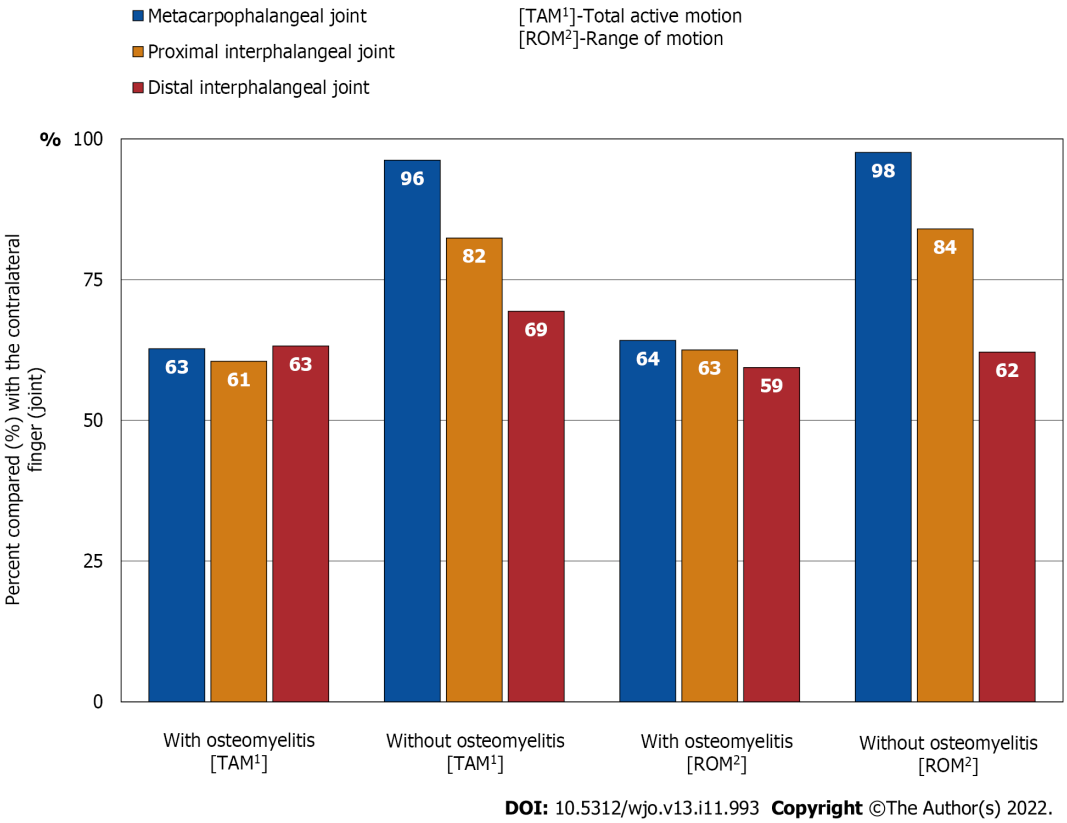

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Figure 6 Summary of total active motion and range of motion.

frequency of lesions of different joints of the hand was different. The most frequent involvement in the inflammatory process of MCP of the middle finger (15%), IP of the thumb (14.4%), and PIP (13.3%) and DIP (11.7%) of the index finger can be explained by the high frequency of damage. *S. aureus* has become a characteristic causative agent of joint infection. A feature of these observations was the fact that its polyantibiotic-resistant form, *MRSA,* was not isolated. The clinical course of septic arthritis of the hand in most cases was characterized as acute with a predominance of local inflammation.

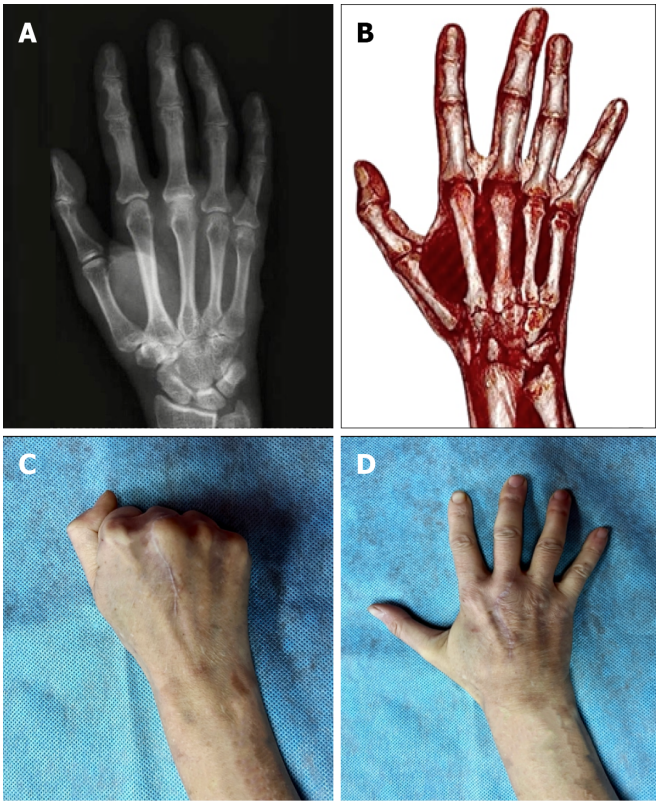

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Figure 7 Outcomes of septic arthritis with osteomyelitis of the metacarpophalangeal joint, third finger (right hand). A: Preoperative radiography; B: 3D-reconstruction (CT) 5 mo after operative intervention; C and D: Long-term outcomes of the function recovery of the metacarpophalangeal joint.

Patients with septic arthritis with contiguous osteomyelitis were characterized by a significant delay in the start of treatment associated with late seeking medical help. The radiography performed during the first 14 d after the onset of the disease was uninformative, and must be taken into account in clinical practice. The course of septic arthritis of the hand in patients with diabetes mellitus was characterized by the greatest severity. This was evidenced by the high incidence of osteomyelitis in these patients (87.5%) with a relatively small delay in the start of treatment (the median was 6 d). Thus, timely treatment of septic arthritis of the hand is one of the most important factors in the prevention of osteomyelitis.

Surgical treatment, which ended with drainage and irrigation of the joint supplemented by antibiotic therapy, eliminated the inflammatory process. Some patients (18.8%) had a need for repeated surgical treatments. Most often, this concerned patients with diabetes mellitus, as well as victims of human and animal bites. In these cases, highly virulent microflora from the oral cavity entered the tissues.

Antibacterial therapy for septic arthritis without osteomyelitis was characterized by a short course (the median was 7 d), differing from the longer duration in osteomyelitis (the median was 23 d).

In 7 (4.1%) patients, after discharge from the hospital, a recurrence of the septic process was noted, which required readmission for surgical treatment. In 3 of them, septic arthritis with soft-tissue extension but no osteomyelitis was initially diagnosed, and signs of osteomyelitis were revealed during rehospitalization. Perhaps this situation was associated with an underestimation of objective data during the initial hospitalization, or with defects in subsequent outpatient treatment. Another 4 patients were initially diagnosed with osteomyelitis, and in all cases there was a severe lesion of the soft tissue of the finger. Of these, 2 patients had to undergo finger amputation as a result, including a patient with severe diabetes mellitus (Supplementary Table 1).

The key to success in restoring joint function was early rehabilitation. Arthrodesis was not used in patients with osteomyelitis after surgical debridement with removal of affected bone and cartilage structures. A complex of early rehabilitation measures contributed to the formation of neoarthrosis with a significant restoration of the volume of active movements. Painful arthrosis as one of the grounds for arthrodesis was not observed in any case. The functional results of the treatment of septic arthritis of the hand with osteomyelitis were slightly worse than those in cases without osteomyelitis. However, they also testified to the possibility of restoring more than 50% of the ROM in the joint without significant pain.

Contraindications to the start of early rehabilitation were related to patients who had damage to the flexor/extensor tendons that did not allow recovery of joint function. In these cases, arthrodesis was achieved using prolonged immobilization of the finger in a functionally advantageous position. Patients

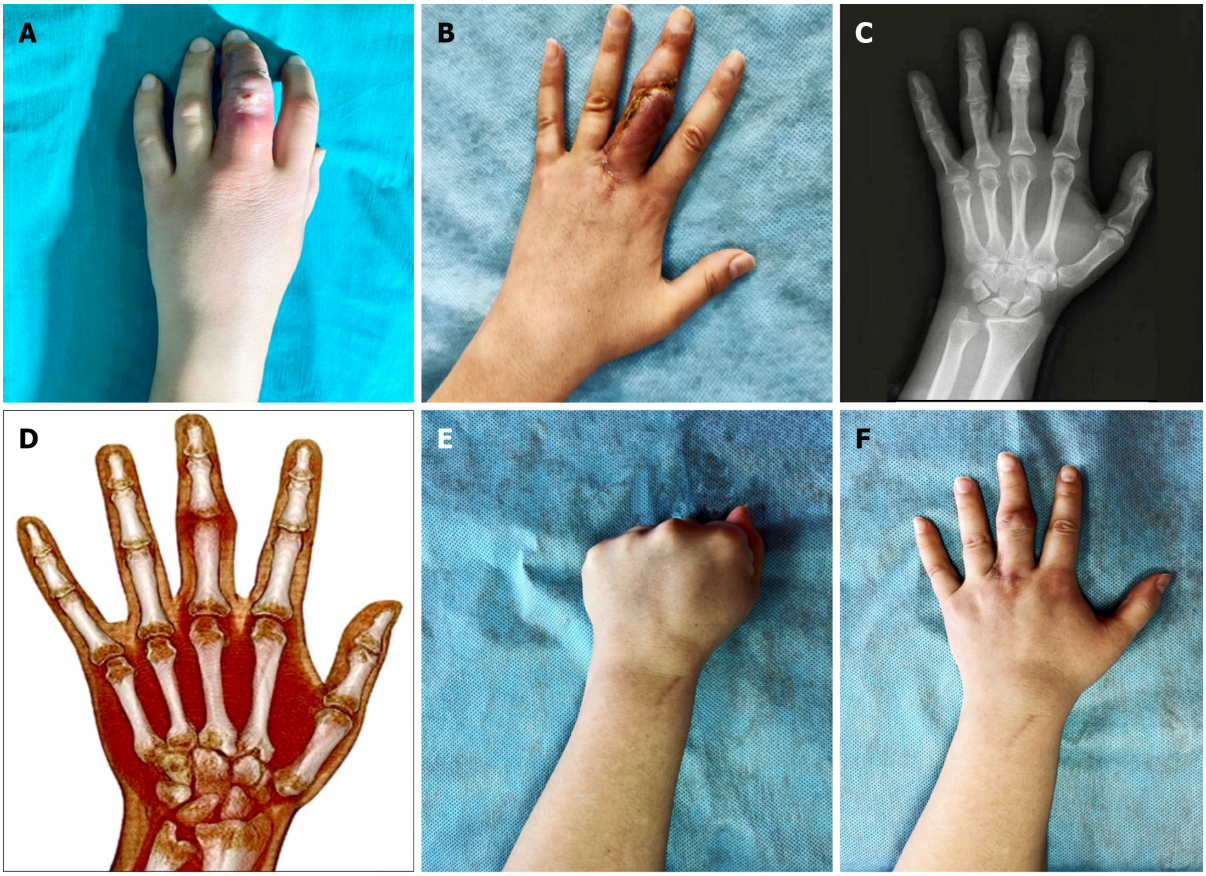

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Figure 8 Treatment of septic arthritis with osteomyelitis of the proximal interphalangeal joint, third finger (left hand). A: Clinical presentation at admission; B: Short-term outcomes after operative intervention; C: Preoperative radiography; D: 3D-reconstruction (CT) 4 mo after operative intervention; E and F: Long-term outcomes of the function recovery of the proximal interphalangeal joint.

who violated the prescribed rehabilitation regime and systematically failed to follow the recommendations of a specialist were excluded from the research.

The main limitations are related to the fact that the research is retrospective. Not in all cases was it possible to estimate the extent of damage to paraarticular soft tissues, if any. Also, insufficient information was received on the condition of the flexor/extensor tendons of the finger, the presence and extent of their possible damage. And this is of fundamental importance in predicting the possibility of restoring the function, and choosing the nature and extent of rehabilitation measures. With an overall significant number of patients included in the research, the number of patients with concomitant diabetes mellitus is relatively small. Therefore, the data concerning this category of patients need to be clarified. A retrospective research also created significant difficulties in assessing the quality of rehabilitation after discharge of patients from the hospital. While rehabilitation, as you know, is the most important factor in restoring the function of the hand after septic arthritis.

CONCLUSION

To sum up, the duration of delay in treatment of patients significantly correlated with the incidence of osteomyelitis. In patients with diabetes mellitus, osteomyelitis developed much faster, which must be taken into account in clinical practice. Timely surgical treatment, along with continued irrigation of the joint and antibiotic therapy, made it possible to eliminate the infection, and early rehabilitation allowed restoring the ROM. The best results were noted in patients without osteomyelitis. With the development of osteomyelitis, a complex of early rehabilitation measures also made it possible to partially restore the ROM due to the formation of neoarthrosis, without resorting to arthrodesis.

ARTICLE HIGHLIGHTS

Research background

Septic arthritis of the hand, which is the second most common after damage of the knee joint, remains one of the leading causes of temporary disability. The results of their treatment today, especially from a functional point of view, cannot be considered satisfactory.

Research motivation

Dissatisfaction with the results of the treatment of septic arthritis of the hand, including a significant number of cases of joint stiffness and even amputations of the fingers, followed by the loss of the ability of patients to engage in their usual work activities, which is a severe psychological trauma, motivated us to find ways to solve this problem.

Research objectives

To explore the etiology and clinical course of septic arthritis of the hand; to analyze the timing of the development of osteomyelitis with a delay in the treatment of patients; and to compare approaches to surgical treatment and rehabilitation depending on the nature of the pathological process.

Research methods

The results of treatment of 170 patients with septic arthritis of the hand were retrospectively analyzed. The causes of the disease and the nature of the microbial flora were explored. The frequency of various forms of septic arthritis of the hand and approaches to surgical treatment were analyzed.

Research results

The most common pathogen was *S. aureus*. The form of septic arthritis was largely determined by the duration of treatment delay. In the presence of osteomyelitis, it was maximal. In patients with diabetes mellitus, osteomyelitis developed much earlier. Comprehensive treatment made it possible to eliminate the infection. Functional outcomes were better in patients without osteomyelitis. With the development of osteomyelitis, surgical debridement and early rehabilitation made it possible to partially restore the range of motion without resorting to arthrodesis.

Research conclusions

Timely surgical treatment of septic arthritis of the hand allows reducing the number of cases of osteomyelitis. Early rehabilitation is the key to success in restoring hand function after surgery. The development of osteochondral destruction does not exclude the possibility of partial restoration of function due to the formation of neoarthrosis.

Research perspectives

To optimize approaches to the surgical treatment of septic arthritis of the hand and postoperative rehabilitation, it is necessary to develop a specialized classification of this disease, taking into account the involvement in the pathological process of not only the elements of the joint, but also the paraarticular soft tissues and flexor/extensor tendons of the finger.

FOOTNOTES

Author contributions: Lipatov KV performed conceptualization and manuscript writing, review, and editing; Asatryan A and Melkonyan G performed methodology and writing of the original draft; Kazantcev AD performed visualization and manuscript writing, review, and editing; Solov'eva EI and Gorbacheva IV performed investigation and writing of the original draft; Vorotyntsev AS and Emelyanov AY performed formal analysis and supervision.

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Patient preference for trigger finger treatment

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Abstract

BACKGROUND

Trigger finger is a common disorder of the hand that can cause disabling symptoms. Treatment options range from conservative management with observation and splinting, to surgical release, but there is currently not a consensus on a treatment algorithm.

AIM

To determine patient preference for the treatment of trigger finger using an online survey.

METHODS

An online crowdsourcing platform, Amazon Mechanical Turk, was used to recruit participants for this study. Participants were led through a scenario in which they were diagnosed with trigger finger. They were then asked to rank their preference of treatment options from the following: Observation, splinting, corticosteroid injection, surgery. The results of the surveys were then analyzed using R software.

RESULTS

Of 323 participants completed the survey. 7 participants were excluded because they failed to correctly answer the attention question, leaving 316 participants whose results were included. As a first choice for treatment 117 (37%) of the included participants chose observation, 86 (27%) chose splinting, 61 (19%) chose corticosteroid injection, and 52 (16%) chose surgery. The mean rank for observation was 2.26, for splinting was 2.30, for corticosteroid injection was 2.53, and for surgery was 2.91. The ranking of each treatment option was statistically different (P value < 0.05) from the others except for observation and splinting.

CONCLUSION

The practice of shared decision making with patients is imperative to providing the best care possible. The results from this study, especially the preference for less invasive treatment, may help providers better frame discussion around treatment options of trigger fingers. This in turn, may increase patient satisfaction

in the treatment of trigger finger.

Key Words: Trigger finger; Trigger digit; Hand surgery; Shared decision making

Core Tip: Given the lack of current consensus on ideal management of trigger fingers, it is imperative for providers to pursue shared decision making with their patients. The results from this study may help providers better frame discussion around treatment options of trigger fingers. This, in turn, should lead to increased patient satisfaction.

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INTRODUCTION

Trigger finger, or stenosing flexor tenosynovitis, is a disorder of the hand which causes catching, or 'triggering', of the finger with extension of a flexed digit. This in turn can lead to difficulties with activities of daily living and interfere with patient's work. It is one of the most common causes of hand disability, effecting between 2%-3% of the worldwide population[1]. The variability of symptoms is large, with mild symptoms being pain, and more severe symptoms including flexion contractures of the involved digit(s). The specific etiology of trigger finger has yet to be determined but multiple theories exist[1]. Treatment options range from conservative management with observation or splinting, to one of the most common options, corticosteroid injection, to surgical intervention with percutaneous or open release, with no clear guidelines on an algorithm[2]. The choice of treatment depends on patient and surgeon preference. There is currently a plethora of research indicating that patients seek to be more actively involved in their care with the use of a shared decision-making framework[3-5]. The goal of this study was to determine patient preferences regarding trigger finger in an effort to better prepare providers for shared decision-making conversations with their patients.

MATERIALS AND METHODS

An online, survey based, descriptive study was performed through the use of a crowdsourcing website, Amazon Mechanical Turk (AMT). Participants for this study were randomly recruited through AMT. Studies have shown that AMT produces results similar to conventional surveying techniques and the population surveyed is representative of the United States internet population[6-8].

AMT workers must be older than 18 years of age to participate on the platform. Survey participants are screened through AMT to ensure that the same individual cannot complete multiple responses. AMT screens participants to ensure quality responses. Additionally, an attention check question was included to verify the quality of the responses. If a survey participant failed the attention check, their response was excluded.

If a participant completed the survey and adequately responded to the attention check, they were compensated ($0.20 *per* unique response) through the AMT platform for their time.

Attention check question

In an effort to ensure that participants were paying close attention to the prompts, questions, and giving meaningful opinions about the prior, an attention check question was inserted into the survey as follows.

"Attention check. Please select answer 3 if you are paying attention".

Respondents who did not answer this question correctly were excluded from the study.

Survey questions

The authors devised the survey in an effort to simulate a real clinical scenario. The participants were presented with the following scenario and questions. It begins as follows:

Scenario I: Trigger finger is a common problem affecting the hand. Patient's report pain and a clicking sensation with motion of the finger. The affected finger can catch or lock when trying to make a fist. Symptoms can limit the ability to grasp or hold objects. (A short 8 s video was made available to the respondents *via* a hyperlink that showcased an example of a trigger finger). Assume that your doctor has diagnosed you as having trigger finger.

Your doctor discusses the following options for treatment: (1) Observation: 50% of patients with trigger finger will get better without any treatment, most within one year[9]; (2) Splint: A restrictive splint keeping the finger straight will be worn on the involved finger. You are told this treatment option resolves symptoms 55% of the time[10]; (3) Cortisone injection: A very small steroid injection will be administered in the office. Some patients experience temporary pain from the injection. Symptoms resolved after one injection for 45% of patients, after two injections 60% of patients, and after three injections 76% of patients[11,12]; and (4) Surgery: Open release of the structure that causes the trigger resolves symptoms > 90% of the time[2].

Question 1: Which treatment option would you initially choose?

Observation

Splinting

Cortisone injection

Surgery

Participants were then asked to rank the remaining treatment options based on how they would prefer to be treated for their trigger finger.

Data analysis

Results from the survey were pooled and mean ranking was calculated using Microsoft Excel Online (Redmond, WA). The statistical review was then completed by a biomedical statistician. To assess the variance of mean ranking of each treatment type a Friedman Rank Sum Test was run. Additionally, a pairwise Wilcoxon Rank Sum tests with a Bonferroni adjustment for multiple comparisons was run to allow analysis of the difference in rankings between treatment types. This analysis was completed using R software (Boston, MA).

RESULTS

A total of 323 participants completed the survey *via* AMT. 7 participants were excluded because they failed the attention check question, leaving 316 participants who were included in the study, as seen in Figure 1.

Following the prompt asking which treatment option they would initially choose, 117 (37%) participants opted for observation as their first preferred method of treatment *vs* 86 (27%), 61 (19%), and 52 (16%) participants who responded with splinting, a cortisone injection, and surgery, respectively, as their first preferred method of treatment. Participants were then asked to rank what their second, third, and fourth preferred methods of treatment would be.

These results can collectively be seen in Table 1.

The mean ranking for observation was 2.26, for splint 2.30, for cortisone injection 2.53, and for surgery 2.91. The Friedman Rank Sum of this data was then calculated and the Chi-Squared was 50.5 with a P value less than 0.00001. These results can be seen in Table 2.

A pairwise comparison using Wilcoxon Rank Sum Tests was then performed revealing significant differences (P value < 0.05) in all treatment choices relative to one another, except for observation *vs* splint. These results can be seen in Table 3.

DISCUSSION

Epidemiology

As previously noted, trigger finger has an estimated lifetime incidence in 2%-3% of the population[1]. It most often affects middle-aged women (2-6 times as likely as men) in their dominant hand[13,14]. The ring finger is the most commonly affected digit, followed by the middle finger, index finger, and little finger (excluding the thumb)[15]. The constellation of diseases that constitute metabolic syndrome, specifically diabetes, hypertension, and dyslipidemia, have all been shown to be risk factors[15]. The incidence is also increased in patients with other hand conditions, including carpal tunnel syndrome, de Quervain's tenosynovitis, and Dupuytren's contracture[16]. Diabetes mellitus puts patients at elevated risk of developing trigger finger, with lifetime incidence in this subset of the population estimated at 10%[17]. The risk of developing trigger finger, as well as the severity of symptoms, is positively correlated with elevated glycosylated hemoglobin levels, specifically HbA1c levels greater than 7%[18].

The diagnosis of trigger finger is relatively straightforward. Patients report a locking or catching sensation with active range of motion of a digit. There may be pain with motion and motion of the digit

Table 1 Patient preference for treatment of trigger finger

	Observation	Splint	Cortisone injection	Surgery
1st Choice	117 (37%)	86 (27%)	61 (19%)	52 (16%)
2nd Choice	69 (22%)	96 (30%)	93 (29%)	58 (18%)
3rd Choice	61 (19%)	86 (27%)	97 (31%)	72 (23%)
4th Choice	69 (22%)	48 (15%)	65 (21%)	134 (42%)
Sum	316	316	316	316

Table 2 Descriptives of rank for each treatment option

	N	Mean ranking	Standard deviation
Cortisone injection	316	2.53	1.02
Splint	316	2.30	1.03
Surgery	316	2.91	1.12
Observation	316	2.26	1.17

Table 3 Pairwise comparison using Wilcoxon Rank Sum Tests (*P* value)

	Cortisone injection	Splint	Surgery	Observation
Cortisone injection				
Splint	0.0426[a]			
Surgery	< 0.00001[a]	< 0.00001[a]		
Observation	0.0093[a]	1.0000	< 0.00001[a]	

[a]$P < 0.05$.

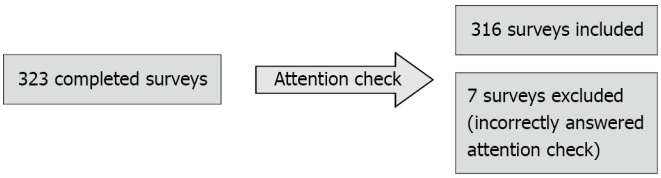

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Figure 1 Study participants. A total of 323 participants completed the survey *via* Amazon Mechanical Turk. 7 participants were excluded because they failed the attention check question, leaving 316 participants who were included in the study.

may be diminished[19]. The physician can observe the phenomena described by the patient or feel the catching at the level of the A1 pulley or detect crepitus at this level. The patient often reports pain with palpation at the A1 pulley. Subluxation of the extensor tendon at the dorsal aspect of the metacarpophalangeal (MCP) joint secondary to a sagittal band rupture and a locked metacarpal phalangeal joint are rare but are occasionally confused with trigger finger. The pathophysiology of trigger finger is felt to be the result of thickening and narrowing of the tendon sheath–and not in the tendon itself or tenosynovium[19,20]. This size mismatch occurs at the level of the A1 pulley. Thickening at the A1 pulley restricts motion of the flexor tendon.

No standard protocol exists for treatment of trigger finger[21,22]. Treatment options include splinting, corticosteroid injection and surgery[23]. In addition to these interventions, observation (no treatment) is an option. The reported success rates for each option vary considerably. There are only a few reports on the natural history of untreated trigger finger. McKee *et al*[9], in 2018, reported the results of 343 patients with a diagnosis of trigger finger who received no treatment, 178 patients (52%) had complete spontaneous resolution. Of the 178 patients who had complete spontaneous resolution, 50% did so within 8 mo of initial consultation and 90% had complete resolution within one year[9]. The

authors hypothesized that improvement resulted from "some remodeling over time of the pulley" and decreased inflammation from rest and lifestyle modification. Schofield and Citron reported on the natural history of adult trigger thumb in 30 patients enrolled in a prospective study[24]. (According to the authors) five patients insisted on treatment, triggering resolved in the remaining patients without treatment after an average of 6-8 mo, within a range of 2-15 mo.

Not all patients are willing to wait but would like to "do something." For those who want to do something but are not ready for surgery, splinting and cortisone injections are options. Several splinting designs and techniques have been described[25-29]. Colbourn *et al*[28] reported improvement in 28 patients who wore a custom-made thermoplastic splint which limited motion at the MCP joint for 6 wk [28]. Rodgers *et al*[25] reported the results of splinting the distal interphalangeal (DIP) joint in meat packing plant laborers, some of whom also were given a cortisone injection. At a mean one year follow up 81% were treated successfully[25]. Tarbhai *et al*[27] compared splinting of the MCP joint *vs* splinting of the DIP joint in a prospective randomized study of 30 subjects[27]. Success was defined as complete or partial relief of triggering. Success rate with splinting of the DIP joint was 47%, a lower success rate than reported by Rodgers *et al*[25]. Success rate with blocking splint of the MCP joint was 77%. Teo *et al* [26] compared splinting of the MCP joint with splinting of the proximal interphalangeal (PIP) joint. Both splints were effective in reducing pain and disability and improving triggering symptoms, but the PIP splint was more effective[26]. Collectively, splinting of the affected digit, in various forms, appears to be a viable treatment option.

Corticosteroid injection into the flexor tendon sheath was first described by Howard *et al*[30] in 1953. Reported success rates vary[2]. Wojahn *et al*[11] investigated the long-term effectiveness of a single corticosteroid injection for trigger finger in 366 patients with a minimum 5 year follow up[11]. 45% of patients had long term success following one injection. Most failures (84%) occurred within the first two years following injection. Dala-Ali *et al*[31] reported results in patients who received up to 3 cortisone injections[31]. Studying 90 trigger digits in 61 patients the reported a 34% success rate with one injection, 63% success rate with 2 injections and 66% success rate with 3 injections. Dardas *et al*[12] investigated the effectiveness of repeat cortisone injections for trigger fingers[12]. Second injections provided long term success in 39% of trigger fingers and third injections provided a similar 39% success rate. The authors reported a hypothetical success rate of 82% after 3 injections. Rozental *et al*[20] looked at prognostic indicators of recurrence following cortisone injection[20]. Insulin dependent diabetes, younger age and involvement of multiple digits were associated with higher rate of treatment failure. Grandizio *et al*[32] also noted that younger age was a risk factor for persistent triggering after a cortisone injection[32]. However, in their study diabetes was not a risk factor for failure.

Many patients, when given the option of cortisone injection, want to know how soon they might see improvement. Seigerman *et al*[33] investigated time to improvement after cortisone injection in a study involving 452 patients and found that most patients experience relief of pain and triggering at 3 wk following cortisone injection[33]. They reported that the majority of patients had some pain relief within the first week after cortisone injection. Improvement in trigger lagged behind pain relief.

When non-operative modalities fail, surgery is an option. While percutaneous procedures and endoscopic surgery are options, the most common surgical intervention is release of the A1 pulley *via* an open incision. The success rate is high, with success rates reported at > 95%, and the procedure is considered low risk but complications can and do occur[34]. Everding *et al*[23] in a retrospective review of 795 digits release in 543 patients reported complications in 12%[23]. Most common complications were persistent pain, swelling, persistent or recurrent triggering. Reoperation rate was 2.4% including revision release and investigation and debridement. The rate of infection following trigger finger release is low but increased rate of infection is reported if surgery is performed within 90 d of cortisone injection[35,36].

Percutaneous release of the first annular pulley is a procedure that has been increasing in popularity. The biggest advantage of this procedure is its less invasive nature and lower cost compared to open release. The biggest disadvantage is the lower success rate, reported at around 94%, often due to incomplete release of the annular pulley[37].

Augmentation of percutaneous release with sonographic guidance is a recent technique that has increases the success rate of percutaneous release. One factor limiting wider acceptance of sonographic guidance is the high cost[37]. More research is needed to assess the cost effectiveness of sonographic guidance.

Recommendations for a treatment algorithm are reported in the literature, but consensus lacks. Amirfeyz *et al*[38] stated that there was weak evidence to support use of a splint and that a single cortisone injection may be offered as initial treatment, but surgery should be next if injection fails[38].

Cost of treatment can affect recommendations that a provider makes. Zhuang *et al*[39] evaluated cost effectiveness of cortisone injections *vs* open trigger finger release and reported that, from a healthcare payer perspective, offering 3 cortisone injections before surgery is a cost-effective strategy[39]. Kerrigan and Stanwix examined cost of treatment and concluded that the least costly treatment would be 2 injections before surgery[40].

The published papers that review results of various treatment options, and studies that examine costs associated with treatment for trigger finger, often fail to consider the patient's perspective. In our investigation participants were asked to assume they were diagnosed as having a trigger finger. They were

given a hyperlink that allowed them to see an 8 s video which demonstrated a trigger finger. They were then presented with 4 options for treatment: Observation, use of a splint, cortisone injection and surgery. A plurality (37%) chose observation as their first method of treatment and 27% chose splinting as their choice. Thus, more than half selected a non-invasive modality as their first choice. Analysis revealed that patients do have a preference between treatment options, except when choosing between observation and splinting.

This contrasts most current recommendations on treatment which recommend corticosteroid injection as a first line treatment. This information can inform physicians when seeing a patient who presents with a trigger finger that there may be a reluctance by the patient to undergo an invasive intervention (cortisone injection or surgery). The job of the treating physician is not to persuade the patient to pursue a particular treatment modality but rather to educate, to explain, to discuss, to answer questions, and to listen and respond. The results of this study provide the treating physician with a very general idea of what patients may want when learning they have a trigger finger.

Limitations

The use of an online survey inherently limits patient knowledge on treatment options, including duration of treatment, success rates, and complications. All of these factors are likely to affect a patient's selection of treatment.

No demographics were collected from the participants. It has previously been shown that the AMT worker population is representative of the general United States internet population is similar studies[6-8,41,42]. However, the internet population may not be the same as the population treated for trigger finger.

It was unknown if any study participants previously had trigger finger. They were given a prompt and information to review as well as a video of a trigger finger. An individual's perspective on treatment may change if they experience the symptoms of a disorder, as opposed to simply reading about it.

The severity of trigger finger symptoms varies widely. Our survey did not indicate to participants the severity of their symptoms which may affect the treatment they chose to pursue.

The inclusion of a pay-per-response model could lead to a selection bias as individuals may have not viewed our particular pay as high enough to proceed with the survey.

Participants were not offered an option for percutaneous A1 pulley release. Given the less invasive nature of this procedure compared to open release, patients may be more likely to choose this option.

CONCLUSION

The practice of shared decision making with patients is imperative to providing the best care possible. The results from this study, especially the preference for less invasive treatment, may help providers better frame discussion around treatment options of trigger fingers. This in turn, may increase patient satisfaction in the treatment of trigger finger.

ARTICLE HIGHLIGHTS

Research background

Trigger finger is one of the most common hand disorders that can lead to debilitating symptoms.

Research motivation

To provide increased insight to providers treating patients with trigger finger to better allow shared decision making.

Research objectives

To determine patient preference for the treatment of trigger finger.

Research methods

An online survey was perfomed using a crowdsourcing website. Participants were led through scenarios regarding the symptoms of trigger finger and treatment options. They were then asked questions regarding their preferred treatment.

Research results

Of 316 participants results were included. 37% of the participants chose observation as their first choice, 27% splinting, 19% corticosteroid injection, and 16% surgery. The mean rank of each treatment option was statistically different from the others, except for observation and splinting.

Research conclusions

Patients may have more of a preference for less invasive treatment of trigger finger. This information can help providers better frame discussions around shared decision making with patients.

Research perspectives

Further research is needed to better understand patient factors that effect treatment choice.

FOOTNOTES

Author contributions: Blough C and Kuschner S designed the research study; Blough C and Najdawi J performed the research study and analyzed the data; Blough C and Kuschner S prepared the manuscript; all authors have read and approve the final manuscript.

Institutional review board statement: This study was exempt from IRB review as described in 45 CFR part 46. Participants were made aware of the voluntary nature of this survey and the data was collected in a way that the subjects' identity could not be ascertained by the researches.

Informed consent statement: An online, survey based, descriptive study was performed through the use of a crowdsourcing website, Amazon Mechanical Turk (AMT). Participants for this study were randomly recruited through AMT.

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SYSTEMATIC REVIEWS

Viral infections in orthopedics: A systematic review and classification proposal

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Abstract

BACKGROUND

Although the impact of microbial infections on orthopedic clinical outcomes is well recognized, the influence of viral infections on the musculoskeletal system might have been underestimated.

AIM

To systematically review the available evidence on risk factors and musculoskeletal manifestations following viral infections and to propose a pertinent classification scheme.

METHODS

We searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), the Reference Citation Analysis (RCA), and Scopus for completed studies published before January 30, 2021, to evaluate risk factors and bone and joint manifestations of viral infection in animal models and patient registries. Quality assessment was performed using SYRCLE's risk of bias tool for animal studies, Moga score for case series, Wylde score for registry studies, and Newcastle-Ottawa Scale for case-control studies.

RESULTS

Six human and four animal studies were eligible for inclusion in the qualitative synthesis. Hepatitis C virus was implicated in several peri- and post-operative complications in patients without cirrhosis after major orthopedic surgery. Herpes virus may affect the integrity of lumbar discs, whereas Ross River and Chikungunya viruses provoke viral arthritis and bone loss.

CONCLUSION

Evidence of moderate strength suggested that viruses can cause moderate to severe arthritis and osteitis. Risk factors such as pre-existing rheumatologic disease contributed to higher disease severity and duration of symptoms. Therefore, based on our literature search, the proposed clinical and pathogenetic classification scheme is as follows: (1) Viral infections of bone or joint; (2) Active bone and joint inflammatory diseases secondary to viral infections in other organs or tissues; and (3) Viral infection as a risk factor for post-surgical bacterial infection.

Key Words: Viral infection; Musculoskeletal system; Bone and joint manifestations; Chikungunya; Zika; Hepatitis C virus; Herpesviridae; Ross River virus; Cross-reactivity; Classification

Core Tip: Viral infections can include multiple orthopedic manifestations, thus resulting in significant distress. In addition, the outcome of orthopedic surgeries may be influenced by certain chronic viral infections such as hepatitis C virus. There is evidence of autoimmune-mediated mechanisms, immunosuppression, and perhaps direct viral infection provoking this, although the precise mechanisms have yet to be fully understood. In this review, a classification scheme was proposed. However, further research is needed to unveil the relative contributions of the identified mechanisms and develop novel preventative and treatment strategies.

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INTRODUCTION

Fracture-related and periprosthetic joint infections (PJIs) represent dreadful complications of orthopedic surgery[1]. Although the impact of microbial infections has been well documented, the influence of viral infections on orthopedics might have been underestimated[2]. The first investigation into the probable cause of bone reactions brought on by viral infections was conducted in 1962 by Marcowa[3], who examined the tick-borne encephalitis virus's ability to cause mice to develop tibial osteitis histologically and radiographically. The potential cause of bone reaction due to viral infections was firstly studied in 1962 by Marcowa[3], who histologically and radiographically evaluated tick-borne encephalitis virus, which induced tibial osteitis in mice. Since then, evidence has suggested that viral agents, such as parvovirus B19, hepatitis B, C virus, Human immunodeficiency virus (HIV), and alphavirus, cause viral arthritis with an estimated incidence of 1% of all acute arthritides[4].

Furthermore, an elevated risk of total hip arthroplasty (THA) revision has been documented in HIV patients 90 days post-procedure[5]; whereas sepsis, pneumonia, microbial joint infection, and revision surgery are more ubiquitous in hepatitis C virus (HCV)/hepatitis B virus (HBV) patients after total joint arthroplasty[5]. In addition, orthopedic manifestations of Alphaviridae have been observed[6], with Chikungunya virus (CHIKV), Ross River virus (RRV), and Sindbis virus being implicated and with viral ribonucleic acid (RNA) being present in joints for months post-infection[6]. Flaviviridae are also relevant as arthralgia occurs in 23%-80% of Zika virus infections[7]. In addition, a decrease in Alkaline

Phosphatase (ALP) production by osteoblasts post-infection tends to delay their maturation[8].

Arthritis is a significant pain generator in HIV patients and is mediated by the premature degenerative joint disease through non-specific chronic synovitis and thickening of the 'vessels' wall/tubuloreticular structures[9]. HIV further accelerates bone degeneration by altering the sealing zone and increasing osteoclast-mediated bone resorption[10]. Finally, Parvovirus B19, a deoxyribonucleic acid (DNA) virus, can cause mono- or polyarthropathy with a preponderance in adult female patients (80%)[11] and with a duration of symptoms varying from 2 months to 4 years[11].

Additionally, it would be reasonable to broadly categorize the orthopedic signs and symptoms of viral infections into three somewhat similar groups. More precisely, manifestations can be provoked by the inflammatory response or direct infection during the acute phase of the illness. This could be the case in Flaviviridae members, such as the Zika virus and Alphaviridae member RRV[7,8]. In addition, the Chikungunya virus (CHIKV) causes orthopedic manifestations mainly *via* autoimmune mechanisms such as cross-reactivity[6]. Lastly, certain viral infections could predispose to microbial infections due to immunosuppression. Examples would be HIV and HCV/HBV[5]. Of note, in the case of HIV, this was more commonly documented in the pre-highly active antiretroviral therapy (HAART) era[5].

In this present systematic review, we sought to systematically evaluate the risk factors for developing persistent arthritis after a viral infection and the impact of viral infections on musculoskeletal clinical outcomes. Lastly, we sought to categorize the musculoskeletal manifestations of viral infections according to their causative mechanism and offer insight into novel treatment strategies.

MATERIALS AND METHODS

This review included human and animal model studies exploring bone and joint manifestations secondary to human viral infections. Observational studies, papers that did not report clinical outcomes, rheumatological articles, and papers that assessed patients under 18 years of age were excluded. Moreover, case series with less than ten subjects were discarded to increase the validity and credibility of our reporting. We searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), the Reference Citation Analysis, and Scopus for completed studies published before January 30, 2021. We also considered the trial registries of ClinicalTrials.gov, the EU clinical trial register, and the Australian New Zealand Clinical Trials Registry to search for completed yet unpublished studies. The search terms for MEDLINE were 'clinical trials', 'case series,' 'viral infection,' and 'bone'/joint'. KT and KS conducted the literature search independently without any language restrictions. Articles were deduplicated and examined for eligibility using title and article screening. Subsequently, a full-text evaluation of the remainder of the articles was performed. Any discrepancies between authors in the study selection procedure were resolved through discussion. KT and KS independently extracted relevant information from the included full-text articles, including any risk factors for persistent musculoskeletal manifestations.

Quality assessment

Two reviewers (KT and DK) assessed the quality of the included studies using SYRCLE's risk of bias tool[12] for animal studies, Newcastle-Ottawa Scale for case-control studies[13], Wylde score for Registry Studies[14], and Moga score for case series[15]. For the included animal studies, the following domains were considered: sequence generation, baseline characteristics (*i.e.*, sex, age, weight), allocation concealment, random housing, identical housing conditions, blinding of caregivers, random outcome assessment, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, other bias (*i.e.*, contamination, pooling drugs, the influence of funders, units of analysis errors, design risk, new animals added for dropouts). Regarding case-control studies, we assessed the adequacy of case definition, representativeness, control selection and definition, comparability of cases and controls based on design analysis, ascertainment of exposure on the same method for both cases and controls, and non-response rates. For registry studies, we evaluated the following domains: consecutive patients, representativeness, percentage of follow-up, and minimization of potential confounding. In addition, we checked the quality of the included case studies against the 18-criteria checklist included in the Moga score[15].

Outcome assessment

The primary outcome measure of the present systematic review was bone and joint manifestations after direct viral infections other than those associated with abnormal autoimmune responses. The secondary outcomes included the general impact of viruses on clinical features and the study of any risk factors for developing persistent musculoskeletal manifestations following viral infections.

RESULTS

The literature search yielded 995 potentially relevant records. After removing duplicates, the remaining 985 articles were screened for eligibility. Following title and abstract evaluation, 84 articles were eligible for inclusion. The full texts were assessed, and ten articles were included for systematic review (Figure 1). Of these papers, two addressed treatment strategies, and three dealt with arthroplasties in patients with HCV. In addition, six papers involved humans looking at Chikungunya, HCV, and RRV [16-25].

Quality assessment

For the included animal studies, the domains of follow-up, minimization of potential confounding, representativeness, baseline characteristics (*i.e.*, sex and age), other bias (*i.e.*, contamination, pooling drugs, influence of funders, unit of analysis errors, design risk, new animals added for dropouts) and adequate definitions of cases, selection and definition of controls, ascertainment of the same exposure to control and cases, and comparability of cases and controls were considered to be at low risk of bias (Supplementary Table 1). Moreover, the following domains were judged to be at unclear risk of bias: sequence generation, allocation concealment, random housing, blinding of caregivers, random outcome assessment, blinding of outcome assessors, incomplete outcome data, and selective outcome reporting (Supplementary Table 1). Furthermore, the domains of identical housing conditions were found to be at an unclear risk of bias (Supplementary Table 1). Regarding the case-control studies, the Newcastle-Ottawa score was used, and the only domain found to have an unclear risk of bias was the non-response rate for both included papers (Supplementary Table 2). On the contrary, the adequacy and representativeness of cases and the selection and definition of controls had a low risk of bias (Supplementary Table 2). Lastly, the comparability of cases and controls based on design, and the ascertainment of exposure, were deemed to be at low risk of bias (Supplementary Table 2). Furthermore, following an appraisal of the two included registry studies, representativeness was deemed adequate because the articles were multicenter with sufficient follow-up (Supplementary Table 3). Lastly, the case series of Alpantaki *et al* [25] and Soden *et al*[22] were evaluated utilizing the Moga score (Supplementary Table 4), with the former study reaching a sum of 13 and the latter achieving a sum of 10 (Supplementary Table 4).

Arthroplasties and major orthopedic surgeries in patients with HCV infection

Three studies related to HCV infection were identified[18-20]. In particular, Best *et al*[18] published a retrospective cohort study in 2015 looking at non-cirrhotic HCV patients subjected to total hip and knee arthroplasty. Half of the included cases were subjected to total hip arthroplasty (THA) (approximately 50% males), and the rest to total knee arthroplasty (TKA) (40% males) (Table 1). Likewise, Chowdhury *et al*[19] published a retrospective study in 2017 to assess the effect of HCV infection 90 days after TKA, THA, and spine surgery. This study included 2262 patients, half HCV positive (Table 1). Moreover, Pour *et al*[20] investigated HCV-positive patients relative to matched controls with a 1:2 ratio in 2011 and included individuals who underwent THA and TKA from 1995-2006 in the US (Table 1). Risk factors in the article published by Best *et al*[18] included length of hospital stay (LOHS), age, gender, comorbidities, post-operative bleeding, thrombocytopenia, transfusion reaction, cardiac complications, respiratory and renal complications, as well as osteomyelitis, and infection. In the study of Chowdhury *et al*[19], age, race, readmission, and death within 30 or 90 days post-operatively were identified as outcome measures/risk factors (Table 1). Lastly, those identified by Pour *et al*[20] were age, gender, BMI, preoperative platelets, complication rate, and LOHS (Table 1). Best *et al*[18] noted that patients from the HCV-positive group presented fewer comorbidities such as diabetes mellitus, hypertension, cardiovascular disease, and osteoporosis as well as a shorter LOHS (5.3 ± 3.4 compared with 5.4 ± 5.1 days in the non-HCV group, $P < 0.001$)[18]. In the above study, the overall complication rate was higher in the HCV group with prosthetic joint infection (OR was 9.5 [95%CI 8.3 to 10.8], $P < 0.001$)[18]. More specifically, acute renal failure and peripheral vascular complications showed an OR of 8 (95%CI 7.4 to 8.6, $P < 0.001$) and 4.8 (95%CI 4.3 to 5.4, $P < 0.001$), respectively[18]. It is underlined that stratification of the 'patients' cohort into THA and TKA revealed a significant difference in the comorbidities of these patients[18]. Other complications noted in the HCV group were deep venous thrombosis and pulmonary embolism, pneumonia, post-operative bleeding, and a higher blood transfusion rate[18]. Similar results were presented by Pour *et al*[20], who noted a statistically significant difference when the complications of revision hip or knee arthroplasty were compared between the two study groups ($P < 0.05$)[20]. When comparing the results of Best and Pour's studies, the only difference was the LOHS [18, 20]. Furthermore, Chowdhury *et al*[19]; reported higher readmission and mortality rates in the HCV group after THA, TKA, lumbar interbody fusion, decompression, and discectomy.

Orthopaedic manifestations induced by low-grade viruses

The role of a Herpes virus infection in intervertebral disc degeneration was studied by Alpantaki *et al* [25]. More precisely, 16 consecutive patients (8 males) with a mean age of 40 years undergoing discectomy within six months of lumbar disc herniation were included. Those individuals constituted the study group, while two patients with thoracolumbar burst fractures formed the control group[25].

Table 1 Study characteristics of articles dealing with hepatitis C virus patients undergoing total knee arthroplasty/total hip arthroplasty or other major orthopedic surgery

Author (year)	Study design	Inoculated groups and number of subjects	Risk factors/outcome measures	Outcomes	Follow-up
Best (2014)	Retrospective cohort study of non-cirrhotic HCV positive individuals and HCV negative patients who underwent TKA/THA in the USA from 1990-2007	Group 1: 26444 HCV patients, 14452 subjected to THA (51.2% males) and 11992, to TKA (36.5% males); Group 2: 8336822 HCV negative patients, 2968679 subjected to THA (42.6% males), and 5370202 subjected to TKA (36.2% males)	Gender, Age, LOHS, Comorbidities, post-operative bleeding, thrombocytopenia, transfusion reaction, cardiac complications, peripheral vascular complications, urinary complications, acute renal failure, myocardial infarction, pulmonary embolism, pneumonia, deep venous thrombosis, blood transfusion, osteomyelitis, and infection	LOHS, age, rates of total complications, and post-operative bleeding	Not specified
Chowdhury (2017)	Retrospective registry study with a propensity-matched cohort including HCV patients and uninfected participants who have undergone TKA, THA, and spine procedures in the USA between 2006-2014	Group 1: 1131 (52% males) with HCV; Group 2: 95161 (56% males) non-HCV individuals, and after propensity score matching, 1131 non-HCV patients were matched to the HCV group, and the cohort consisted of 2262 patients	Mortality within 30- or 90-d, readmission, and complications within 30 and 90 d	Mortality assessment, complication, and readmission rate evaluation	Up to 30 and 90 d post-operatively or upon complication
Pour (2011)	Retrospective case-control study with a control group matched at a 2:1 ratio with asymptomatic HCV patients subjected to THA and TKA from 1995-2006 in the USA	Group 1: n = 39 (29 males) HCV patients who have undergone THA; Group 2: n = 80 (60 males) patients who have undergone THA (control group); Group 3: n = 32 (15 males) HCV patients subjected to TKAGroup 4: 64 (30 males) patients subjected to TKA (control group)	Age, gender, BMI, need for transfusion, preoperative PLTS, LOHS, and the complication rate	Complication assessment (wound, mechanical, fracture, reoperation, revision); Length of hospital stay	101 mo (range 66-140) for the HCV patients subjected to THA; 94 mo (range 45-131 mo) for the control group subjected to THA, 117 months (range 67-150 mo) for the HCV patients subjected to TKA; 98 mo (range 49-133 mo) for the control group subjected to TKA

TKA: Total knee arthroplasty; THA: Total hip arthroplasty; HCV: Hepatitis C virus; LOHS: Length of hospital stay; PLTS: Platelets; BMI: Body mass index.

Moreover, material from the herniated or fractured disc and peripheral blood samples were sampled intraoperatively. Polymerase chain reaction (PCR) detected Herpesviridae DNA in 13 study group subjects[25].

Regarding blood samples, seropositivity of patients was assessed with IgM and IgG assays for HSV-1 and Cytomegalovirus (CMV)[25]. Moreover, the surrounding tissues of the herniated disc were tested by qRT-PCR for mRNA levels of TNF-α and IL-6[25]. Herpes simplex virus type-1 (HSV-1) DNA was detected in 9/16 subjects, and CMV DNA was found in 6 subjects, while 2/16 subjects had a co-infection with both species[25]. On the contrary, DNA from HSV-2, Varicella-Zoster Virus, Epstein-Barr Virus, Human Herpes Virus 6, 7, and 8 were not found in any participants, and the control group tested negative for Herpesviridae DNA[25]. In addition, the IgG serological tests were positive in 13/16 subjects with PCR positivity for viral DNA, whereas all subjects were negative for IgM antibodies, indicating the absence of an acute reaction at the time of surgical excision[25]. Furthermore, IL-6, TNF-a, and viral mRNA in the study group were two to three times higher than in the control group[25]. This is the only indication that the Herpesviridae evoke disc herniation in individuals, regardless of age or sex [25].

Ross River Virus infection causes viral arthritis

We note that almost all Alphaviruses can cause joint manifestations. For instance, the RRV is detectable in the serum within 7-10 days after the initial symptoms, with synovial fluid infiltration by mononuclear cells being a common phenomenon throughout the disease. Soden *et al*[22] assessed synovial membrane biopsies of inflamed knees weeks after the initial symptoms of RRV infection (Table 2), whereas Chen *et al*[16] studied the effects of the RRV on human osteoblasts, bone loss in an established murine model, and viral arthralgia. Soden *et al*[22] also used RT-PCR to detect viral RNA from synovial membrane biopsy samples that were histologically evaluated with standard H&E staining, immunohistochemistry, and TRIzol treatment[22]. Chen *et al*[16] included 21-d-old male and female C57BL/6 WT mice inoculated with 10^4 PFU RRV T48 strain (Table 2). This study replicated bone infection and implemented μCT to assess bone loss in WT mice (Table 2). In addition, it compared the RANKL/osteoprotegerin

Table 2 Study characteristics of the included articles dealing with the Ross River Virus

Author (year)	Study design	Inoculated groups and number of subjects	Outcomes	Follow-up
Chen (2014)	*In vitro* and *in vivo* animal interventional study	For the *in vitro* experiment: 21-day-old male and female C57BL/6 WT mice were inoculated in the thorax with 10^4 PFU of RRV. Those mice received 500 μg of anti-IL-6 antibody injections on days 0 and 2, 4, 6, 8 post-infection. For the *in vivo* investigation: Serum samples from 14 Ross River virus patients (7M and 7F) were obtained, and serum from 13 healthy individuals (7M). Synovial fluid samples from 12 RRV-induced polyarthritis patients (6M) were retrieved and from 6 healthy individuals (3M).	The animal part of the study investigated whether RRV replicates in the bone (murine model) and viral titers were measured. μCT imaging was used to assess the impact of the infection on bone architecture and loss. The role of IL-6 on bone loss was evaluated. The human part of the study looked at OPG, RANKL, and TRAP5b levels in RRV-positive patients.	Not specified
Soden (2000)	Prospective observational study involving humans	Biopsy tissue from inflamed knees from 12 patients was retrieved.	Histological examination of the synovial membrane. RT-PCRto look for the presence of viral RNA	The follow-up was performed at 3-mo intervals until 6 m following symptom resolution

RANKL: Receptor activator of nuclear factor kappa beta (NF-kB ligand); TRAP5b: Tartrate-resistant acid phosphatase serum band 5 (TRAP5b); WT: Wild type; RT-PCR: Reverse transcription-polymerase chain reaction; μCT: Micro-computed tomography; RRV: Ross River virus; M: Male; F: Female; IL-6: interleukin 6.

(OPG) levels in the serum of healthy and RRV-infected individuals (Table 2). Soden *et al*[22] detected RRV RNA in the synovial membrane in 2 subjects 5 weeks after the onset of symptoms, with almost all subjects presenting with detectable histological abnormalities, including minor lining layer hyperplasia, vascular proliferation, and mononuclear cell infiltration[22]. This study proved that RRV affects the joints by directly triggering an inflammatory reaction and is also detectable weeks after the initial symptoms[22]. Chen *et al*[16] detected high viral titers in the femur, tibia, patella, and foot, mainly in osteoblastic bone cells. Notably, high viral levels were detected until day 21 post-infection[16]. By day 15, post-infection μCT imaging showed an evident bone loss in the tibial epiphysis, metatarsal joints, and vertebrae, accompanied by a decrease in trabecular thickness and a reduction in the growth plate [16]. By contrast, these findings were not noticed in the control group[16]. Lower OPG and higher RANKL levels were observed in the study group, while serum TRAP5b levels were also higher[16]. These findings indicate increased osteoclastogenesis in humans, similar to that observed in a murine model[16]. It is worth noting that the RRV also has a tropism for osteocytes[16].

Chikungunya evokes bone and joint manifestations

Four studies looking at CHIKV alphavirus joint manifestations fulfilled our eligibility criteria (Table 3). Chang *et al*[23] recruited 907 clinically and laboratory-confirmed CHIKV-infected patients. Of these, 38 presented with chronic knee arthritis and were deemed eligible for selection. Furthermore, a control group with ten location-matched individuals was considered (Table 3). Chen *et al*[21] studied bone loss after CHIKV infection by recruiting 14 CHIKV patients (6 males) and a control group consisting of 7 healthy individuals (3 males) (Table 3). The second part of the experiment included 25 day-old C57BL/6 mice infected with CHIKV-mCherry (Table 3). Goupil *et al*[24] studied bone and cartilage loss during CHIKV infection by employing two groups of mice featuring IRF 3/7 with deficient type 1 interferon response and adult wild-type C57BL/6. The study group consisted of 11 IRF mice and the control group of 9 C57BL/6 mice[24]. Hawman *et al*[17] studied the persistence of the viral RNA and its role in 'joint pathology. Two groups of 3-wk-old C57BL/6J WT mice and $Rag1^{-/-}$ with a lack of T and B cells were formed, and a control group was also included. Chang *et al*[23] collected synovial fluid samples for viral culture and performed qRT-PCR and mass spectrometry for the detection/quantification of viral genome and proteins, respectively (Table 3). Moreover, serum samples were analyzed for CRP, IgM, IgM-RF, anti-cyclic citrullinated peptide (anti-CCP), and selected cytokine and chemokine levels[23]. Chen *et al*[21] collected serum from the 3rd to the 22nd post-infection week and compared the RANKL/OPG of the 14 CHIKV patients and the seven healthy participants. In the second part of the study, 25 d old C57BL/6 mice were infected with CHIKV-mCherry (20 μL of 10^5 PFU at the ventral side of the foot), and a control group was injected with saline (Table 3)[21]. They were followed up on the 1st, 3rd, 7th, and 15th days post-infection[21]. Goupil *et al*[24] injected IRF 3/7 mice with IFN-1 deficiency, and C56BL/6 WT mice, with 2 × 10^4 PFU CHIKV SVO 476-96 at the caudoventral aspect of the hindfoot[24]. In addition, intact hindlimbs were collected from both groups and scanned *via* μCT to evaluate differences in the morphology of joints and the trabecular bones post-infection[24]. Furthermore, histopathological analysis was performed using hematoxylin, eosin, and Mason's Trichrome staining [24]. Hawman *et al*[17] utilized CHIKV patients' serum to inoculate $Rag1^{-/-}$ mice which lacked T and B cells, and WT mice with CHIKV SL 15649 in the left rear footpad[17]. Viral titers were measured, and

Table 3 Study characteristics of the included articles dealing with Chikungunya virus infection

Author (year)	Virus information	Study design	Inoculated groups and number of subjects	Outcome measures	Follow-up
Chang (2017)	Colombian patients infected by CHIKV	Case-control study of 38 participants with CHIVK and chronic arthritis and 10 location-matched controls without CHIKV or arthritis	Group 1: Out of 907 patients who were clinically (424) and laboratory (483) confirmed for CHIKV, 38 individuals with chronic arthritis post-infection were selected; Group 2: 10 matched controls without CHIKV/arthritis were considered	Synovial fluid samples were analyzed by PCR, and mass spectrometry for viral proteins. No virus could be detected.	Not specified
Chen (2015)	Chikungunya virus from infected patients' serum. CHIKV-mCherry strain was also used	*In vitro* study utilizing serum from 14 CHIK patients and 7 healthy individuals; *In vivo* animal study utilizing 25 d-old C57BL/6 mice infected with CHIKV/mCherry	Group 1: Serum from 14 CHIKV patients (8F 6M) was collected between the 3rd and 22nd week post-infection; Group 2: Serum from 7 (4F and 3M) healthy individuals was also used; Group 1: 25 d-old mice were infected with 20 μL 10^5 PFU CHIKV-mCherry in the ventral side of the foot. Group 2: Consisted of the control group of mice.	For the *in vitro* study: Serum RANKL/OPG ratio was measured; For the *in vivo* study: Day 3 post-infection peak swelling was measured until day 10. Levels of RANKL and OPG were measured inside the joint during days 1, 3, 7 and 15 post-infection.	Days 1, 3, 7, and 15 post-infection
Goupil (2016)	Chikungunya virus SVO 476-96	*In vivo* animal study featuring IRF 3/7 C57BL/6 mice (M and F > 8 wk old) and C57BL/6J mice (> 8 wk old only F)	Group 1: 11 IRF mice were intradermally injected with 2×10^4 PFU; Group 2: 9 control C57BL/6j mice were injected with 2×10^4 PFU	Intact hindlimbs were collected and scanned μCT to evaluate the difference between the morphology of two types of mice (joint, trabecular bone). Histopathological evaluation was also performed. On day 5, post-infection 4 mice were euthanized due to being lethargic, and 6 mice died due to rapid progression of the illness	For the IRF mice 1, 2, 3, 5, 6, 7th day post-infection;For the C57BL/6J mice 7, 14, 21st day post-infection
Hawman (2013)	Chikungunya SL15649 from serum sample	*In vivo* animal study featuring 3-week-old C57BL/6J mice and congenial rag_/- mice	Group 1: 55 mice were inoculated in the left rear footpad with 10^3 PFU (10 μL). MAbs (200 μg each of CHK-152 and CHK-166) were administered intraperitoneally on days -1 and 3 for prophylaxis studies. For therapeutic studies, MAbs were administered on days 21 and 25 post-infection; Group 2: Control mice were subject to mock-infection	Duration of CHIKV infection in tissues was assessed, and associated histopathological changes were evaluated	Day 3 and weeks 1, 2, 4, 6, 12, 16

CHIKV: Chikungunya virus; PCR: Polymerase chain reaction; WT: Wild type; RT-PCR: Reverse transcription polymerase chain reaction; μCT: Micro-computed tomography; M: Male; F: Female; IL-6: Interleukin 6; PFU: Plaque-forming unit; MAbs: Monoclonal antibodies.

histopathological analysis was performed[17]. Chang *et al*[23] found no evidence of viral infection, and therefore it was concluded that either CHIKV is exclusively found in synovial tissue cells or it provokes arthritis through autoimmune mechanisms. Chen *et al*[21] found higher RANKL levels in the CHIKV patients and almost the same OPG levels (Table 3) in the CHIKV and control groups. This finding indicated an osteoclastic condition during the infection. From a clinical point of view, edema was greatest on the third day of CHIKV-mCherry mice follow-up, which was eventually resolved by day 10 [21]. Moreover, the pro-osteoclastic microenvironment was created early after the acute infection as RANKL/OPG was elevated from day one and remained high thereafter[21]. In addition, CHIKV was replicated in a murine bone and induced bone loss of 25% relative to uninfected mice[21]. The immune response resulted in arthritis on the 3rd post-infection day, featuring elevated MCP-2/CCL8 and increased cellularity[21]. Goupil *et al*[24] found that C57BL/6J mice on the 7th post-infection day suffered from moderate dermatitis/dermal edema, extensive degeneration/necrosis of skeletal muscles, minimal periostitis, mononuclear/neutrophilic synovitis, and equivocal cartilage necrosis. On day 14 post-inoculation, mild to moderate dermatitis was observed, as well as extensive skeletal muscle degeneration/necrosis with early evidence of regeneration, extensive periostitis, and persistent synovitis with distal joint involvement[24]. On day 21 post-infection, the following findings were documented: minimal/mild dermatitis, resolving necrosis/inflammation of muscles (immature fibrosis), extensive periostitis with periosteal bone proliferation, subacute lymphoplasmacytic synovitis, synovial hypertrophy/fibrosis, and cartilage necrosis[24]. The tendons showed variable mild peritendonitis from day seven and minimal myocyte necrosis in the contralateral feet[24]. When the IRF type mice were assessed by Goupil *et al*[24], the following findings were observed by the fourth day post-infection: multifocal mild to moderate epidermic necrosis, mild neutrophilic dermatitis/edema, rare vascular necrosis, mild myofiber degeneration, periosteal necrosis, and minimal inflammation of

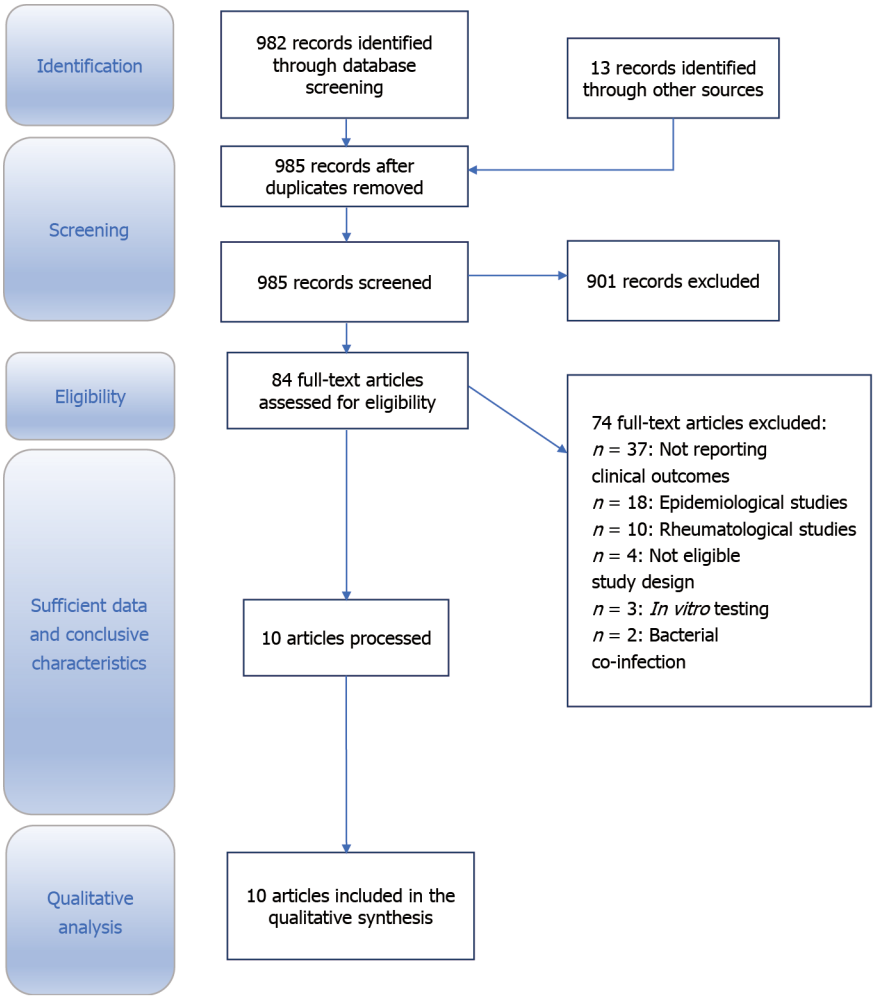

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Figure 1 The flow diagram.

tendons and cartilage. At the same time, the synovium presented with multifocal degeneration/necrosis affecting a few joints. Subsequently, extensive synovitis in multiple joints was documented[24]. By day 7, these findings worsened with extensive epidermal necrosis, extensive vascular necrosis, moderate myofiber degeneration/necrosis, bone marrow and periosteum necrosis, articular cartilage necrosis, and fibrinosuppurative synovitis in the majority of joints[24]. The tendons only presented mild inflammation[24]. It was concluded that the bone and joint manifestations resulted from acute viral infection rather than autoimmune-mediated mechanisms[24]. Hawman *et al*[17] documented that viral inoculation of Rag1$^{-/-}$ mice that lacked T and B cells resulted in higher virus titers. In addition, the histopathological analysis presented more intense synovitis, arthritis, and tendonitis[17]. These findings support the notion that joint manifestations of CHIKV infection directly result from the infection rather than the host's immune system[17]. It should be noted that the authors of the included studies proposed possible treatment strategies for CHIKV infection. In particular, Chen *et al*[21] used an inhibitor of monocyte chemoattractant protein (MCP) (*i.e.*, Bindarit) twice daily intraperitoneally (100 mg/kg) in mice which reduced joint swelling and bone loss but not viral titers[21]. Hawman *et al*[17], on the other hand, proved that tissue-specific administration of monoclonal antibodies reduced the viral RNA in these tissues.

DISCUSSION

It is undeniable that viral infections pose a substantial yet unclear impact on the musculoskeletal system. Most aspects have not yet been studied sufficiently, mainly due to the lack of technological advancements until the 21st century. In light of the above, a systematic review was designed to delineate the risk factors and orthopedic clinical outcomes secondary to viral infections. More specifically, the effects of chronic HCV infection on TKA and THA, as well as the role of Herpesviridae on lumbar disc degeneration, were addressed. Moreover, the musculoskeletal effects of the Chikungunya virus and

RRV-mediated chronic arthritis were examined.

The impact of viruses on clinical musculoskeletal outcomes

HCV is a significant cause of orthopedic complications such as an oligoarthritis of large and middle joints or rarely a rheumatoid arthritis-like illness[26]. A higher level of post-operative complications and a higher mortality rate were noted in the HCV group despite the patients being younger and having fewer medical comorbidities[18]. Nevertheless, the hospitalization of HCV patients was shorter, perhaps due to them being transferred to different units to have their complications addressed[18]. A possible explanation would be the circulating autoantibodies leading to decreased lymphoproliferation. As a result of lymphoproliferation, predisposition to infection, leukocytoclastic vasculitis[27], and glomerulonephritis[27,28] develop. In addition to the above features of HCV patients, a hypercoagulability profile was observed[18].

It should be noted that HCV has been shown to induce thrombocytopenia and impaired platelet function[29,30,31], predisposing to higher rates of bleeding[18]. Pour *et al*[20] also documented increased reoperation rates, higher mechanical complications, and hospital stays in the HCV group. To be more precise, complications included periprosthetic femoral fractures, femoral implant loosening, and hip dislocation secondary to migration of acetabular implant that required a revision of the THA [20]. On the other hand, chronic HCV disease was associated with multiple extrahepatic manifestations such as diabetes mellitus and thyroiditis, thrombocytopenia, glomerulonephritis, inflammatory myositis, arthralgia, mixed connective tissue disease, leukocytoclastic vasculitis, and lymphadenopathy. These can be attributed to circulating autoantibodies that could alter the physiological process of healing[20]. In addition, low-key inflammation can alter the function of platelets, further compounding the pathophysiologic mechanism[20]. Another aspect worth mentioning is the potential difference in the socio-economic level of HCV-infected individuals and that of healthy participants[20]. Furthermore, ancillary liver effects were investigated by Chowdhury *et al*[19], and it was thought that they were implicated in immunosuppression and impaired wound healing. These findings confirm the significance of HCV infection in post-operative outcomes and highlight the importance of including HCV testing in the preoperative workup.

Regarding the potential of Herpesviridae being a possible cause of disc degeneration, Alpantaki *et al* [25] studied 16 patients undergoing discectomy six months after lumbar disc herniation subjected to Herpesviridae DNA testing[25]. Positivity for at least one species (most commonly HSV) was found in 13[25]. Possible mechanisms implicated in disc degeneration could be the vascular channels formed during fetal development that remain patent until the 4th-6th year of life, as well as migrating macrophages and retrograde axoplasmic transport[25]. However, it remains unclear whether degeneration is solely secondary to the upregulation of inflammatory cytokines or whether viral-induced cell death could also contribute[32]. In addition, it has been postulated that Herpesvirus 6 could cause Langerhans' Histiocytosis[33]. This rare disease affecting children of 1 to 4 years of age has predominantly bone involvement, and, more often than not, the first presentation of the disease is a pathological fracture[33].

Furthermore, CHIKV has a cyclical pattern of epidemics from 7 to 20 years and affects countries neighboring the Indian Ocean, Central Africa, China, Italy, and France. After transmission *via* a mosquito bite, the virus multiplies locally and is then transferred to the whole host body *via* lymphoid organs and the bloodstream. Mononuclear cell infiltration and viral replication in muscles and joints cause severe pain and arthritis. Although CHIKV infection is self-limiting, arthritis/arthralgia occurs for a particular amount of time due to the immune response or an active viral reservoir in joints[34]. In 2018, a systematic review and meta-analysis of 2415 individuals suffering from CHIKV infection in the US revealed that 52% of the patients appeared to have persistent arthritis 10 to 72 weeks after the primary infection[35]. It has been thought that arthritis may develop due to epigenetic modifications of macrophages which present a more aggressive cell behavior[36]. Another possible cause could be the concomitant presence of seronegative rheumatoid arthritis, although this has been doubted by Chen *et al* [21]. Moreover, Chen *et al*[21] noted that Alfaviridae, such as RRV, could infect primary human osteoblasts and cause the production of inflammatory cytokines, thus promoting osteoclastogenesis[37-39]. In addition, when analyzed with μCT, it was clear that Alfaviridae could also lead to bone loss. Interestingly, after treatment with IL-6 inhibitors, bone loss was blocked, thus highlighting the central role of inflammation in pathogenesis[16]. Finally, it is essential to stress the impact of CHIVK-mediated arthritis as 82% of chronically infected patients present with arthritis that substantially impacts their quality of life[23].

The proposed clinical and pathogenetic viral infection classification system

In the current review, we have proposed a classification system for the pathogenesis of viral infection (Table 4 and Figure 2). Regarding the first proposed category addressing the viral infections of bones and joints, we noted that the Alphavirdae member RRV replicated in murine bones[16]. To address this proposed mechanism further, we note that human osteoblasts could be infected with RRV and produce inflammatory cytokines such as IL-6. In addition, in the inflamed knees of affected patients, RRV RNA was present five weeks after the onset of symptoms[22]. However, some patients presented symptoms in the absence of detectable viruses[22], and this finding is partially congruent with the initial

Table 4 Proposed viral classification scheme

Proposed pathogenetic mechanism	Viruses involved	Evidence supporting the proposed mechanism
Direct infection and subsequent inflammation	Ross Rover and Zika viruses	RRV causes arthritis with its RNA coinciding with the appearance of symptoms; Evidence of human osteoblasts being primarily infected
Inflammation primarily through autoimmune mechanisms such as cross-reactivity	CHIKV	CHIKV causes arthritis in the absence of evident infection. Other supporting information includes rheumatoid factor negative RA and exclusive presence in the synoviocytes. Animal studies implicate a potential role of primary infection
Systemic manifestations resulting in immunosuppression	HCV and HIV	Greater rates of microbial infections in HCV patients post-surgery. Greater rates of infections post-surgery pre-HAART. High rates of mechanical and medical comorbidities

RRV: Ross River virus; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus; CHIKV: Chikungunya virus; HAART: Highly active antiretroviral therapy; RA: Rheumatoid arthritis; hOBs: Human osteoblasts.

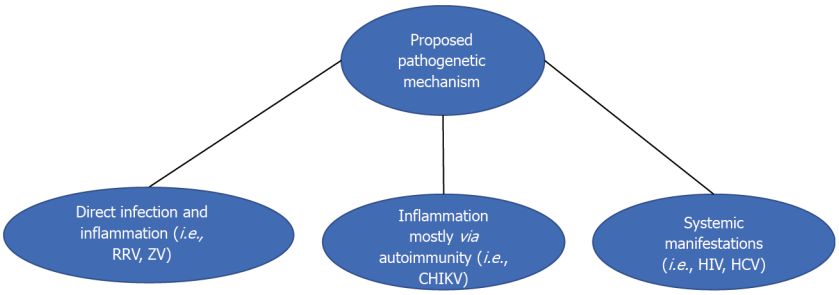

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Figure 2 Graphical demonstration of the proposed viral pathogenetic mechanism. RRV: Ross River virus; CHIKV: Chikungunya virus; HIV: Human immunodeficiency virus; HCV: Hepatitis C virus; ZV: Zika virus.

hypothesis that RRV provokes orthopedic manifestations through primary infection and inflammation [22].

Regarding the second proposed category, active bone and joint inflammatory diseases occur secondary to viral infections in other organs or tissues. CHIKV indeed causes arthralgia/arthritis without being directly detectable[23]. No evidence of it was found *via* RT-PCR, mass spectrometry, and culture of synovial fluid, thus agreeing with the initial hypothesis of it causing arthritis principally *via* cross-reactivity and suggesting immunomodulatory agents in its treatment[23]. Although, productive infection of musculoskeletal cells was reported by Chen *et al*[21]. In addition, Hawman *et al*[17] presented animal evidence revealed persistent viral infection, but safe extrapolations to human biology cannot be made based on this finding.

Lastly, the third proposed category included viral infection as a risk factor for post-surgical bacterial infection. To elaborate, we reported that HCV predisposes to immunosuppression[18] with associated increased post-surgical complications in HCV patients[19], in addition to compromised liver function and wound healing[19]. Pour *et al*[20] confirmed this finding as wound complications requiring antibiotics/wound debridement were noticeably more common in HCV patients post-surgery.

Risk factors for chronic disease – The appearance of rheumatologic diseases

The persistence of the viral genome or proteins in host cells could represent the major risk factor for chronic manifestations after the initial infection. However, no data prove any association between Epstein-Barr and rheumatoid arthritis[40]. In the setting of CHIKV infection, joint manifestations resemble inflammatory arthropathies[41], and their severity depends on the levels of cytokines. We highlight that further studies should be performed to clarify that[42].

Study limitations and implications for future research

We recognize that the lack of a consistent definition of virus-induced rheumatoid arthritis and the wide variety of musculoskeletal manifestations secondary to viral infections complicates the picture for clinicians and health policymakers. In addition, the limited number of studies addressing the above issues and the uncertainty introduced by the moderate-to-low quality of evidence of the included articles further contribute to this vagueness. It has been shown that some tropism exists for cells such as osteocytes, synovial cells, and chondrocytes. However, the pathophysiology of the infection or inflammation, the underlying processes, and the reasons for lingering symptoms are still unknown. Towards this direction, we advocate that future research should aim for the development of novel treatment

options based on the underlying mechanisms.

The role of COVID-19 on the musculoskeletal system

It is highlighted that all articles relating to COVID-19 were excluded as the vast majority were based on expert opinions and observational studies with limited follow-up and sample size. However, some aspects of this pandemic should be commented on. First, it is unknown whether osteoporosis and osteonecrosis are two common findings after COVID-19 infection, but the potential role of corticosteroid administration as a part of the therapeutic regime cannot be overlooked[43]. Another clinical finding worth mentioning is the higher incidence of late (*i.e.*, a few weeks following COVID-19 diagnosis) spinal epidural abscesses. This could be explained by 'patients' immunosuppression or the occurrence of nosocomial superinfection[44]. Finally, the binding of COVID-19 spike protein to functional receptors of ACE2, also expressed in human bone marrow, could be a possible explanation for the decreased bone matrix and early muscle disorders[45]. Although the above considerations represent some early indications of the potential connection of COVID-19 with orthopedic clinical outcomes, we underline that a safe conclusion cannot be drawn, given the limited available literature and considerable risk of bias.

CONCLUSION

Viral infections pose a major concern for microbiologists and orthopedic surgeons, given the high incidence of chronic arthritis and its detrimental effect on patients' quality of life[23]. While the literature on this topic was sparse and heterogenous, the negative influence of viruses on orthopedic surgical outcomes is evident[18-20]. We highlight that arthralgia, myalgia, and transient arthritis could result from viral infection or secondary immune processes, although each mechanism's contribution is still relatively unclear. Therefore, we advocate that the present systematic review raises awareness of the implications of viral infections in orthopedics and acts as a guide for orthopedic surgeons to classify them in a clinical and pathogenetic fashion.

ARTICLE HIGHLIGHTS

Research background

While the influence of microbial infections on orthopedic clinical outcomes is well documented, the impact of viral infections on the musculoskeletal system has been inadequately investigated.

Research motivation

Although microbial infections have been studied extensively in orthopedics, the impact of viral infections on orthopedics has not been sufficiently investigated. In addition, we are unaware of any classifications relating to viral infections in the orthopedic literature.

Research objectives

In this article, we looked at the risk factors for persistent arthritis development after a viral infection and the impact of viral infections on orthopedic clinical outcomes. In addition, we categorized orthopedic manifestations of viral infections relative to their causative mechanism.

Research methods

An extensive literature search was performed to identify completed studies published before January 30, 2021. MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), the Reference Citation Analysis, and Scopus were searched for articles evaluating risk factors and bone/joint manifestations of viral infection in animals and humans. In addition, we assessed the quality of the included articles utilizing SYRCLE's risk of bias tool for animal studies, the Moga score for case series, the Wylde score for registry studies, and the Newcastle-Ottawa Scale for Case-control studies.

Research results

Ten articles were included in the systematic review. Of these, two dealt with treatment strategies and another three with arthroplasties in patients with hepatitis C virus (HCV). In addition, six articles addressed human beings investigating Chikungunya, HCV, and RRVs. After major orthopedic surgery, HCV was implicated in several peri- and post-operative complications. Herpes virus may affect the integrity of lumbar discs, whereas Ross River and Chikungunya viruses negatively influence bones and/or joints, resulting in viral arthritis and bone loss.

Research conclusions

Viral infections pose a significant burden in orthopedics due to the significant impact on patient quality of life. We have demonstrated a connection between viral infections and orthopedic surgical outcomes. We highlight that arthralgia, myalgia, and transient arthritis could result from viral infection or secondary immune processes, although each mechanism's contribution is still relatively unclear. We advocate that the present systematic review raises awareness of the implications of viral infections in orthopedics and acts as a guide for orthopedic surgeons to classify them in a clinical and pathogenetic fashion.

Research perspectives

We recommend that a consistent definition of virus-induced rheumatoid arthritis be developed. Furthermore, we suggest that further high-quality articles investigating novel treatment options based on the underlying mechanisms be conducted.

FOOTNOTES

Author contributions: Drago L and Kavarthapu V were involved in the study's conceptualization; Tsikopoulos K and Sidiropoulos K conducted the literature research and extracted relevant information; Tsikopoulos K and Kitridis D assessed the quality of the included studies; Christofilos SI and Meroni G were involved in the generation of tables and writing the paper; Drago L, Kavarthapu V, and Romanò CL supervised the paper and revised the paper accordingly.

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SYSTEMATIC REVIEWS

Patient-reported dissatisfaction following second side in staged bilateral total knee arthroplasty: A systematic review

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Abstract

BACKGROUND

Around one third of patients who undergo total knee arthroplasty (TKA) will eventually have the contralateral knee replaced. Overall patient satisfaction after staged bilateral total knee arthroplasty procedures performed on different days is reportedly similar to unilateral TKA. Nevertheless, in our anecdotal experience patients often report less satisfying outcomes following the second side. A cursory review of available literature tended to confirm that observation. We sought therefore to consolidate all of the available data on this issue to further investigate this phenomenon.

AIM

To consolidate available published data revealing satisfaction scores among patients following staged bilateral TKA, and to evaluate the phenomenon of less satisfying results following TKA2.

METHODS

A systematic review of available literature reporting on satisfaction with TKA1 and TKA2 after staged bilateral knee arthroplasty was undertaken using PubMed, Google Scholar, and Embase. From 427 records, five full-length articles met criteria for inclusion in the meta-analysis. The data were then extracted and assessed on the basis of the *Reference Citation Analysis* (https://www.referencecitationanalysis.com/).

RESULTS

A total of 1889 patients with an average age of 68 (range: 38–92) underwent staged bilateral TKA with outcomes reported at 1 year following each TKA with a mean

21.9 mo between surgeries (range: 2 d to 14.5 years). Overall satisfaction with both knees was 83.70% (1581) and dissatisfaction with both knees was 2.75% (52). In the remaining 13.56% (256) who were dissatisfied with one side, 61.0% were dissatisfied with TKA2, and 39.0% were dissatisfied with TKA1. Patient-reported outcome scores for TKA2 were frequently lower than TKA1 even in patients reporting overall satisfaction with both knees.

CONCLUSION

At 1-year follow-up, there was a 50% greater risk of dissatisfaction with TKA2 among the 13.56% of patients reporting dissatisfaction in one knee after staged bilateral TKA. Whether the interval between procedures or long-term follow-up changes these results requires further investigation.

Key Words: Staged; Staggered; Sequential; Bilateral arthroplasty; Total knee arthroplasty; Patient-reported outcomes

Core Tip: Total knee arthroplasty (TKA) is one of the most popular and successful treatments for end stage arthritis worldwide. Around one third of patients who undergo TKA will eventually have the contralateral knee replaced. Anecdotal experience has shown that patients tend to report decreased satisfaction following the second TKA procedure (TKA2). The primary aim of this review article was to assess patient satisfaction following TKA2 after staged bilateral knee arthroplasty. Ideally, quantifying reported dissatisfaction as well as reporting associated factors.

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INTRODUCTION

Total knee arthroplasty (TKA) is a highly effective procedure for the treatment of end stage arthritis and is the most common arthroplasty procedure performed worldwide[1,2]. As such, it is important to investigate patient satisfaction and quality of life following surgery. Patient-reported outcomes and scoring systems have become essential measurement tools, particularly given the limited correlation that functional outcome scores and other direct measurement data have with patient satisfaction[3,4]. Patient scoring systems were first introduced in the 1990's to investigate function in the context of quality of life and have since been used clinically, and in research, to reaffirm patient wellness in surgical healthcare[4,5]. Although a majority of patients report satisfactory outcomes following TKA, an estimated 10%-20% report being dissatisfied in the absence of clinical complications[1,2,6-8]. Investigation into factors predicting dissatisfaction tend to revolve around failure to meet expectations, recall bias, and physiologic rationale for hypersensitivity to pain[3,5]. Previous studies have also demonstrated associations with variables such as patient gender, patient age, history of rheumatoid arthritis, as well as patient personality traits[3]. There is also evidence that a history of any previous arthroplasty - not necessarily a previous knee replacement - lowered the expectations for the outcome of TKA[9].

In patients who have undergone total knee replacement, 25% or more will go on to have the contralateral side replaced[2,6,10]. Much of the literature on bilateral knee replacement focuses on pain improvement, functional outcomes, safety, efficiency, and cost-effectiveness of simultaneous bilateral TKA (one anesthesia event) compared to staged or staggered TKA (two anesthesia events)[2,7,11]. Unlike unilateral TKA, there is very limited data on patient satisfaction following staged TKA, particularly comparing one side to the other. In our anecdotal experience, many patients who have undergone staged bilateral knee replacement report less satisfying results with the second side (TKA2). Review of available literature on this issue revealed some data that tended to confirm this observation[7,12]. Reported reasons included failure to meet the anticipated improvements of pain and function compared to the first side (TKA1), slower return to activity, and inability to engage in full activity. Still, others provide no specific reasons for preferring TKA1 over TKA2, with some reporting uncertainty about their satisfaction with TKA2[7-9,11,13]. To consolidate these data, and better understand the phenomenon of unilateral dissatisfaction following staged bilateral TKA, we performed a systematic review of available literature reporting on both patient-reported outcomes and satisfaction.

MATERIALS AND METHODS

We queried PubMed, Embase, and Google Scholar for articles using: "staged" or "staggered" or "sequential" and "bilateral arthroplasty" and "patient-reported outcomes." PRISMA guidelines were followed for inclusion and exclusion of articles as shown in Figure 1. This review was submitted for registration with PROSPERO (ID: 299833). Only full-text articles with an English version available were included. Additional inclusion criteria were individually reported Oxford Knee Scores (OKS) as a patient reported outcome measure, and/or a satisfaction score for each knee, with follow-up of at least 1 year. Exclusion criteria included abstracts only, follow-up information missing, individual scores for each knee missing, and simultaneous knee replacement. The initial search returned 427 records; 397 had been excluded after screening, leaving 30 full-text articles. Of these, five articles explicitly reported information comparing outcome data between TKA1 to TKA2 for each patient. To determine the disparity in satisfaction between sides, we recorded the satisfaction scores of TKA1 and TKA2 or the OKS of TKA1 and TKA2 for patients that reported unequal satisfaction.

Patients who reported being uncertain about one knee and dissatisfied with the other were grouped according to the dissatisfied knee. Patients who reported being uncertain with one knee and satisfied with the other were grouped according to the uncertain knee. Patients with an OKS score difference below the minimal clinically important difference (MCID) for only one knee were considered dissatisfied with that knee; patients with an OKS score difference between knees that exceeded the MCID for the study, were considered dissatisfied with knee with the lower OKS. The use of the OKS to predict satisfaction was based on previous literature[14].

STATISTICS

Weighted values were used to calculate the average age and interval between surgeries.

The Q = W/S method was used to test for normality. Frequency data from each study were used to calculate the relative risk (RR) of TKA2 dissatisfaction in patients who reported unequal satisfaction after bilateral TKA. The RR was used under the assumption that unilateral dissatisfaction is relatively rare (< 10% of patients) and that using the odds ratio may result in an inflated rate of dissatisfaction with TKA2. Statistical significance was set at $P < 0.05$, chi-square analysis was used to determine the significance of the resultant RR. The Mann-Whitney *U* test was used to compare the RR of TKA2 dissatisfaction between studies. Calculations were performed using SPSS V.27 (IBM Corp., Armonk, NY, United States).

RESULTS

A total of 1889 patients from five studies underwent staged bilateral TKA with patient reported outcomes and satisfaction recorded at 1 year following each TKA. Two of the five studies (85% of patients) explicitly reported satisfaction. The most common PROMs used were the OKS, the Western Ontario and McMaster Universities Osteoarthritis Index, and short form 12 (SF-12). The average age was 68 years with a range of 38 to 92. The time interval between surgeries was not standardized; the largest study reported the widest interval range of 2 d to 14.5 years between sides, with an average interval of 21.9 mo. Table 1 summarizes the details of the five studies. The results of bias assessment with MINORS criteria are displayed in Table 2. Overall satisfaction with both knees across all studies was 83.70% (1581), and dissatisfaction with both knees was 2.75% (52). Two hundred fifty-six patients (13.56%) reported unequal satisfaction between knees. Assessing each study individually, two cohorts, Suzangar *et al*[4] and Abram *et al*[5], demonstrated a significantly increased relative risk of dissatisfaction with TKA2 *vs* TKA1. Comparing frequencies between studies, chi-square N-1 comparison showed a difference between Clement *et al*[6] and Abram *et al*[5], in the reported frequency of dissatisfaction with TKA1 and TKA2. No other differences were found within or among studies. The pooled data demonstrated a significant increase in the relative risk of dissatisfaction with TKA2 *vs* TKA1 among patients who reported unequal satisfaction (RR = 1.49, $P < 0.01$) shown below in Figure 2. Table 3 summarizes the results.

DISCUSSION

The goal of this review was to consolidate available published data revealing satisfaction scores among patients following staged bilateral TKA, and to evaluate the phenomenon of less satisfying results following TKA2. The overall satisfaction rate for unilateral TKA and bilateral staged TKA is reported at 80%-89% with minimum 2-year follow-up[5,15,16]. Similar to previous reports, we calculated overall satisfaction with both sides of 83.70% after accounting for 52 patients (2.75%) who were dissatisfied with

Table 1 Study information, all studies included for analysis had a minimum follow-up of 1 year after each total knee arthroplasty

Ref.	Participants, *n* (weight %)	Male, *n*	Female, *n*	Mean age, range	Interval between TKAs, mo (range)	PROMs	Conclusions
Suzangar *et al* [4], 2019	1001 (53.0%)	459	542	68.7	25.6 (0.1-174.0)	Satisfaction	More dissatisfaction after TKA2
Clement *et al*[6], 2019	454 (24.0%)	219	235	68.0	16.8 (7.2-44.4)	Satisfaction, OKS	No difference between knees
Abram *et al*[5], 2016	250 (13.2%)	84	166	66.0	23.0 (2.0-74.0)	OKS, WOMAC	Lower TKA2 OKS
Scott *et al*[9], 2014	70 (3.7%)	29	41	71.7	7.8 (2.0-25.0)	Satisfaction, OKS	No difference between knees
Tucker *et al*[10], 2021	114 (6.0%)	31	83	66.5	16.2 (11.4-22.8)	OKS	Females less satisfied than males
Pooled	1889 (100.0%)	822 (43.5%)	1067 (56.5%)	68 (38 to 92)	21.9 (0.1-174.1)		

Age reported in years. OKS: Oxford knee score; TKA1: First side total knee arthroplasty; TKA2: Second side total knee arthroplasty; WOMAC: Western Ontario and McMaster universities.

Table 2 MINORS assessment

Ref.	A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoint appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss of follow-up less than 5%	Prospective calculation of the study size	Total
Suzangar *et al*[4], 2019	2	2	2	1	N/A	2	2	1	12
Clement *et al*[6], 2019	2	2	2	2	N/A	2	2	1	13
Abram *et al*[5], 2016	2	1	2	2	N/A	2	2	2	13
Scott *et al* [9], 2014	2	2	2	1	N/A	2	2	1	12
Tucker *et al*[10], 2021	2	2	2	2	N/A	2	2	1	13

The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score is 16 for non-comparative studies. N/A: Not applicable.

both sides (not included in tables). The remaining 13.56% of the included patients that were unilaterally dissatisfied varied widely by interval between surgeries, age, indications (osteoarthritis, inflammatory, and post-traumatic arthritis were all represented to unknown degrees) and inclusion/exclusion criteria. Although the studies included in this review reported significant differences in the rates of unilateral dissatisfaction, the proportion of patients reporting a preference for TKA1 over TKA2 was similar. Based on pooled data we found that the risk of an unsatisfying result with one side after staged bilateral TKA is about 50% greater for TKA2 (RR = 1.56) at the 1-year follow-up. We also predicted that the interval between TKA1 and TKA2, and the potential influence of recall bias based on the interval between surgeries and follow-up time, could be associated with unilaterally decreased satisfaction after staged bilateral TKA. Although we only included studies reporting results at 1 year, we could not account for the variation in surgical intervals. Therefore, there was not enough data shared among the included studies to determine additional variables associated with our results.

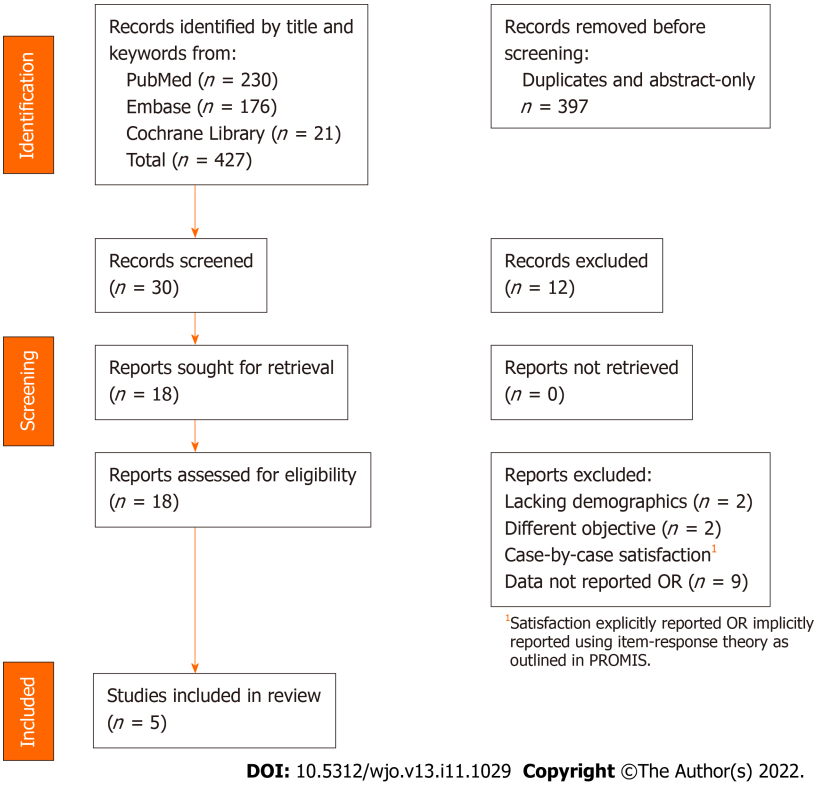
Correlation between Satisfaction and PROMs

Experience with shoulder arthroplasty literature has shown variable strengths of correlation to satisfaction using the Oxford Shoulder Score (moderate correlation, 0.311) and Quick DASH (weak

Table 3 Patients in each study reporting unequal satisfaction between knees after staged bilateral total knee arthroplasty

Ref.	Dissatisfied with TKA1, *n*	Dissatisfied with TKA2, *n*	Study RR	95%CI LL	95%CI UL	Study significance
Suzangar *et al*[4], 2019	61	91	1.49	1.18	1.88	0.025
Clement *et al*[6], 2019[a]	21	19	0.90	0.49	1.66	0.757
Abram *et al*[5], 2016[a]	15	32	2.0	1.11	3.61	0.021[1]
Scott *et al*[9], 2014	4	8	2.0	0.63	6.34	0.239
Tucker *et al*[10], 2021	0	5	12.0	0.67	215.26	0.090[1]
Pooled	101 (39.5%)	155 (60.5%)	1.49	1.17	1.90	0.001

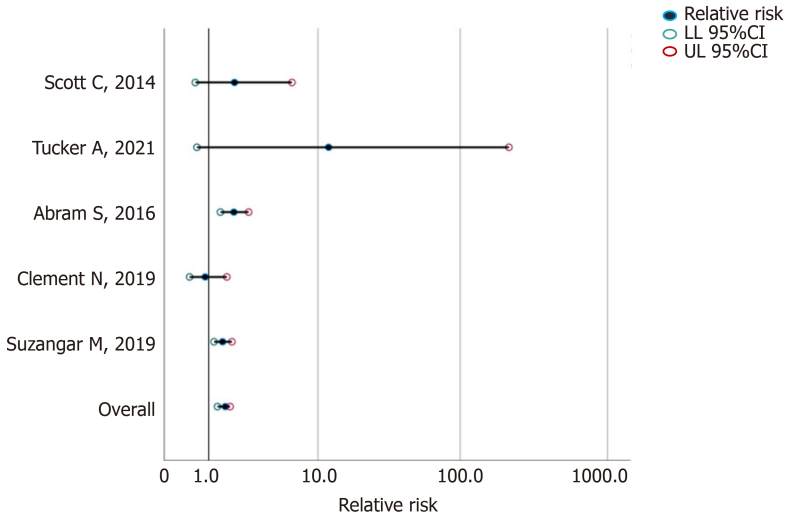
[1]Based on number of patients with OKS score differences between knees exceeding MCID; calculation assumes skewness of distribution < 2.
[a]Pairwise comparison of proportions with Chi square N-1 statistic 17.847, $P < 0.0001$.
Those that more satisfied with TKA2 are classified as "Dissatisfied with TKA1"; those that preferred TKA1 over TKA2 are classified as "Dissatisfied with TKA2" ($n = 256$, 13.6%). LL: Lower limit; TKA1: First side total knee arthroplasty; TKA2: Second side total knee arthroplasty; UL: Upper limit. Significance of the RR of dissatisfaction with TKA2 for each study with significance value set at $P < 0.05$.



DOI: 10.5312/wjo.v13.i11.1029

Figure 1 PRISMA flow chart.

correlation, -0.292)[17]. Unlike the Oxford Shoulder Score, the OKS has been shown to be a reliable, reproducible proxy for detecting patient satisfaction. Clement and colleagues further demonstrated the OKS is a highly accurate model for predicting patient satisfaction (AUC = 0.86)[14]. In patients with bilateral knee arthritis undergoing staged bilateral TKA, the most painful knee is typically replaced first. Unsurprisingly, TKA2 tends to have higher initial OKS scores, smaller gains postoperatively (often attributed to the ceiling effect, where the difference in the patient score and maximum score can be less than the minimum clinically important difference), followed by higher scores than TKA1 at 1 year and beyond[18-22]. However, the differences in OKS scores and satisfaction are reported in the context of high overall satisfaction, and do not readily explain the differences among patients that are dissatisfied with one side, nor the preference for one side over the other in this subgroup. The OKS may be an accurate screening tool for satisfaction, but its use in determining individual reasons for dissatisfaction



DOI: 10.5312/wjo.v13.i11.1029

Figure 2 Relative risk of unsatisfactory outcome following total knee arthroplasty 2. The studies are ordered along the vertical axis according to power from least (top) to greatest (bottom); the relative risk is given in a log10 scale along the horizontal axis. LL: Lower limit; UL: Upper limit.

has not been validated.

Factors affecting satisfaction

Pain was perhaps the most consistently reported factor that strongly correlated with satisfaction after surgery, and there is evidence suggesting the surgical interval and follow-up interval may have a role in actual pain perceived and recall of perceived pain, respectively[3,13,18,22,23]. An interval greater than 1 year has been associated with higher TKA2 satisfaction scores, while intervals less than 6 mo negatively impact TKA2 scores[12,13]. An interval less than 6 mo has also been associated with increased post-operative pain in the first 48 h based on analgesic requirements, suggesting a physiologic rationale for the potential recall bias[3,18]. Conversely, Gabr *et al*[8] found no difference in TKA2 pain or function scores after stratifying patients by intervals greater than or less than 6 mo. However, they reported TKA2 pain scores gathered beyond 1 year continued to improve with time, even exceeding those of TKA1[11]. Similarly, Clement *et al*[6] reported an increased interval from TKA1 correlated with increased TKA1 dissatisfaction, along with higher unilateral dissatisfaction with TKA1 over TKA2. Although their findings are contrary to ours, they were similarly unable to determine consistency in factors related to the preferred side in cases of unilateral dissatisfaction. Expectations and perceptions are also associated with satisfaction to varying degrees[23]. High rates of unmet postoperative expectations for activity and pain levels in TKA patients have been reported despite overall satisfaction (83% expected pain-free recovery, 43% met expectations, 52% expected to be fully active after surgery, and 20% achieved this)[22]. Negative psychosocial factors are shown to exaggerate negative clinical predictors and independently influence surgical outcomes, while general perceptions of the hospital stay have been strongly correlated with TKA satisfaction at 1 year[3,20,21,24]. In a study by Scott *et al*[9], expectations were lowered in younger individuals and those with high expectations before TKA1, and unilateral dissatisfaction occurred most frequently after TKA2[12]. Above average satisfaction was reported for TKA1 (93%) and TKA2 (87%) in the patients, but satisfaction with either side did not correlate within individuals. These findings further display the multifactorial subjectivity of satisfaction, the difficulty in discerning modifiable risk factors for dissatisfaction, and corroborate our experience and the results of this review.

Limitations

This study was primarily limited by the amount of available evidence reporting individual satisfaction and associated patient-specific variables in those who underwent staged bilateral knee arthroplasties. TKA is the most common arthroplasty procedure worldwide[1]. Considering that 25%–30% of patients undergoing TKA will also have a contralateral TKA within 5 years, there is a substantial portion of the population not accounted for in this review of only 1889 total patients[2,6]. The article by Suzangar *et al*[4] accounted for over half of the included patients and stochastically dominated the data. The second largest study, by Clement *et al*[6], was 50% smaller and showed no difference in dissatisfaction between sides while being appropriately powered. Unlike the larger studies, the smaller studies included here did not show a difference in the risk of dissatisfaction between TKA1 and TKA2. They might have found a difference had the study been powered to do so. Additionally, treatment of Likert data as categorical or continuous is arguable, as is the granularity and balance of the scale (how many points, and whether the mid-point of the scale should be neutral and balanced by equal-opposite positive and

negative responses). We treated Likert scales as continuous data, and therefore patients who reported "uncertain" on a 4-point scale were classified as dissatisfied with the uncertain side. Finally, we acknowledge the inherent limitations in use of the OKS as a satisfaction proxy which likely added an element of error, albeit statistically insignificant[9,18]. Nevertheless, the purpose of this review was to consolidate all of the available data to better study the phenomenon of unequal satisfaction following staged bilateral TKA. The OKS has been shown to be accurate for predicting satisfaction, and we believe including the study by Tucker *et al*[10] improved the statistical power and potentially reduced the bias imparted by larger studies[3,9,12,14].

CONCLUSION

In patients undergoing staged bilateral TKA, we calculated a 50% increased risk of dissatisfaction with TKA2 compared to TKA1 (RR = 1.56) but could not establish risk factors causally linked to this phenomenon. Reasons for unilateral dissatisfaction appear to be multifactorial and are inconsistent between and within patients. Patient education preoperatively about the possibility and probability of differences in subjective outcomes may help temper expectations and could potentially improve overall patient satisfaction.

ARTICLE HIGHLIGHTS

Research background

Total knee arthroplasty (TKA) is a highly effective procedure for the treatment of end stage arthritis, and is the most common arthroplasty procedure performed worldwide. Although many patients report satisfaction with their outcomes, an estimated 10%–20% report being dissatisfied in the absence of clinical complications. This is significant given that in patients who have undergone total knee replacement, 25% or more will go on to have the contralateral side replaced in the future. Unlike unilateral TKA, there is very limited data on patient satisfaction following staged TKA, particularly comparing one side to the other.

Research motivation

Our motivation arose from the anecdotal experience that patients who have undergone bilateral knee replacement in a staged fashion indicate that the second side (TKA2) had a less satisfying outcome compared to the first side (TKA1). Our initial cursory reviews of the literature also seemed to confirm this experience. However, little is known about the factors associated with these reports. To better understand the phenomenon of unilateral dissatisfaction, the goal of this study was to perform a systematic review on currently available literature investigating patient reported outcomes and satisfaction following staged bilateral TKA.

Research objectives

The primary aim of this review article was to consolidate available published data revealing satisfaction scores among patients following staged bilateral TKA and to evaluate the phenomenon of less satisfying results following TKA2. Ideally, quantifying reported dissatisfaction as well as trending associated factors.

Research methods

A systematic review of available literature reporting on satisfaction with TKA1 and TKA2 after staged bilateral knee arthroplasty was undertaken using PubMed, Google Scholar, and Embase. Among 427 records, five articles meeting inclusion criteria were included in the meta-analysis. Statistical analysis was performed to calculate relative risk of TKA2 dissatisfaction and compare the relative risk of TKA2 dissatisfaction between studies.

Research results

In the five included studies, a total of 1889 patients with an average age of 68 years underwent staged bilateral TKA with patient reported outcomes and satisfaction recorded at 1 year following each TKA. Average time between surgeries was 21.9 mo. Overall satisfaction with both knees was 83.70 % (1581), and dissatisfaction with both knees was 2.75% (52). In the remaining 13.56% (256) who were dissatisfied with one side, 61.0% were dissatisfied with TKA2, and 39.0% were dissatisfied with TKA1. Patient-reported outcome scores for TKA2 were frequently lower than TKA1 even in patients reporting overall satisfaction with both knees.

Research conclusions

In patients undergoing staged bilateral TKA, we calculated a 50% increased risk of dissatisfaction with TKA2 compared to TKA1. Although we were unable to establish risk factors linked to this phenomenon, there is high suspicion that the factors are multifactorial and often patient specific.

Research perspectives

Future directions include investigating the effects of time between surgeries and scheduled long-term follow-up.

FOOTNOTES

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