ISSN 2218-5836 (online)

World Journal of *Orthopedics*

World J Orthop 2024 February 18; 15(2): 101-200

Published by Baishideng Publishing Group Inc

World Journal of Orthopedics

Contents

Monthly Volume 15 Number 2 February 18, 2024

World Journal of Orthopedics

Monthly Volume 15 Number 2 February 18, 2024

Contents

META-ANALYSIS

LETTER TO THE EDITOR

World Journal of Orthopedics

Monthly Volume 15 Number 2 February 18, 2024

Contents

ABOUT COVER

AIMS AND SCOPE

The primary aim of *World Journal of Orthopedics* (*WJO*, *World J Orthop*) is to provide scholars and readers from various fields of orthopedics with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJO mainly publishes articles reporting research results and findings obtained in the field of orthopedics and covering a wide range of topics including arthroscopy, bone trauma, bone tumors, hand and foot surgery, joint surgery, orthopedic trauma, osteoarthropathy, osteoporosis, pediatric orthopedics, spinal diseases, spine surgery, and sports medicine.

INDEXING/ABSTRACTING

WJO is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJO* as 1.9. The *WJO*'s CiteScore for 2022 is 2.6.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
ISSN 2218-5836 (online)

LAUNCH DATE
November 18, 2010

FREQUENCY
Monthly

PUBLICATION DATE
February 18, 2024

PUBLISHING PARTNER
The Minimally Invasive Spine Surgery Research Center Of Shanghai Jiaotong University

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

Xin Gu

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

PUBLISHING PARTNER's OFFICIAL WEBSITE
https://www.shtrhospital.com/zkjs/info_29.aspx?itemid=647

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 101-104

DOI: 10.5312/wjo.v15.i2.101

ISSN 2218-5836 (online)

EDITORIAL

Mitochondrial dysfunction in type 2 diabetes: A neglected path to skeletal muscle atrophy

Jian-Jun Wu, Hui-Min Xian, Da-Wei Yang, Fan Yang

Specialty type: Orthopedics

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

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

P-Reviewer: Abu Yousuf M, Bangladesh; Wada R, Japan

Received: September 21, 2023
Peer-review started: September 21, 2023
First decision: November 28, 2023
Revised: December 1, 2023
Accepted: January 11, 2024
Article in press: January 11, 2024
Published online: February 18, 2024

Jian-Jun Wu, Hui-Min Xian, Fan Yang, Department of Cardiology, The Second Affiliated Hospital of Harbin Medical University, Harbin 150001, Heilongjiang Province, China

Da-Wei Yang, Department of Orthopedic Surgery, The Fourth Affiliated Hospital of Harbin Medical University, Harbin 150001, Heilongjiang Province, China

Fan Yang, State Key Laboratory of Component-based Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Tianjin 30000, China

Corresponding author: Fan Yang, MD, MMed, PhD, Associate Research Scientist, Occupational Physician, Postdoc, Department of Cardiology, The Second Affiliated Hospital of Harbin Medical University, No. 246 Xuefu Road, Nangang District, Harbin 150001, Heilongjiang Province, China. yangfana@sina.com

Abstract

Over the course of several decades, robust research has firmly established the significance of mitochondrial pathology as a central contributor to the onset of skeletal muscle atrophy in individuals with diabetes. However, the specific intricacies governing this process remain elusive. Extensive evidence highlights that individuals with diabetes regularly confront the severe consequences of skeletal muscle degradation. Deciphering the sophisticated mechanisms at the core of this pathology requires a thorough and meticulous exploration into the nuanced factors intricately associated with mitochondrial dysfunction.

Key Words: Mfn-2; Oxidative stress; Mitochondria metabolism; Skeletal muscle atrophy; Diabetes

Core Tip: Type 2 diabetes mellitus (T2DM) poses a substantial global health challenge. Attaining optimal glycemic control is crucial for mitigating complications and mortality associated with T2DM. However, recent research has unveiled a frequently overlooked complication: The progressive atrophy of skeletal muscle. Mitochondria, pivotal for cellular energy production, uphold a delicate equilibrium in their fusion and fission processes. Investigating the interplay between mitochondrial dysfunction and skeletal muscle atrophy in T2DM is imperative for advancing our comprehension of diabetes. Findings from cellular and animal models suggest that targeting mitochondrial dynamics, particularly through the modulation of Mfn-2, holds promise as a therapeutic strategy to counteract muscle atrophy induced by diabetes. This approach underscores a novel intersection in the management of diabetic complications, forging a connection between metabolic control and muscular health.

Citation: Wu JJ, Xian HM, Yang DW, Yang F. Mitochondrial dysfunction in type 2 diabetes: A neglected path to skeletal muscle atrophy. *World J Orthop* 2024; 15(2): 101-104
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/101.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.101

INTRODUCTION

Type 2 diabetes mellitus (T2DM) represents a relentless and chronic hyperglycemic disorder that has emerged as a grave global public health concern, imposing a substantial burden on both afflicted individuals and healthcare systems[1]. The immense financial toll, surpassing £800 billion annually, covering expenses for T2DM diagnosis, treatment, and care, highlights the urgent need to address this swiftly escalating epidemic[2]. Recent studies indicate that among the numerous factors linked to T2DM, age, place of residence, education level, social status, family income, smoking, body mass index, family history, and physical exercise exert the most significant adverse effects on quality of life (QoL)[3]. Beyond the immediate metabolic disturbances, the insidious nature of T2DM engenders a spectrum of incapacitating complications, marked by their gradual onset and often inconspicuous progression, that exert a significant detrimental impact on both the life expectancy and QoL of individuals grappling with diabetes.

SKELETAL MUSCLE ATROPHY AND MITOCHONDRIA IN T2DM

Glycemic control is pivotal for reducing complications and mortality in T2DM. Emerging research in diabetes highlights skeletal muscle atrophy as a critical aspect of diabetic pathophysiology[4,5]. Skeletal muscle, characterized by high metabolic activity and dense mitochondrial networks, is integral for movement and health, efficiently generating ATP for muscle contraction and metabolic regulation. Diabetes-induced impairment in muscle cell energy production can lead to muscle atrophy and reduced physical function, making mitochondrial function preservation vital for both athletic performance enhancement and QoL improvement in chronic disease management.

Mitochondrial dynamics play a crucial role. Mitochondrial fusion, regulated by GTPases such as (mitofusins (Mfns) and optic atrophy protein 1 (Opa1), and fission, mediated by dynamin-related protein 1 and fission protein 1 (Fis1), undergo significant changes in T2DM[6]. Notably, T2DM patients exhibit downregulation of Mfn2 and Opa1 in skeletal muscles, correlating with reduced mitochondrial mass and density, suggesting aberrant mitochondrial dynamics as an early biomarker for metabolic diseases. Animal models with Mfn2 dysfunction show decreased substrate metabolism, whereas Mfn2 and Opa1 overexpression improves mitochondrial respiratory efficiency and glucose oxidation[7]. This paradoxical interplay between mitochondrial adaptation and dysfunction in diabetic muscles highlights the dual role of mitochondria in energy production and oxidative stress, contributing to muscle atrophy. This balance with reactive oxygen species underscores the complex nature of mitochondrial functions in metabolic regulation.

MFN-2: REGULATING MITOCHONDRIAL DYNAMICS AND POTENTIAL THERAPEUTIC TARGET

Deficiency in Mfn-2 exacerbates the division of mitochondria in cardiomyocytes, impairing cardiac and mitochondrial health, while its overexpression in vascular smooth muscle cells induces apoptosis. These observations underscore the complex and varied roles of Mfn-2 in cellular processes. Maintaining a balance between mitochondrial fusion and fission is essential for cellular homeostasis; disruptions leading to increased fragmentation are linked to various cellular dysfunctions, including a heightened propensity for mitochondrial-related apoptosis.

Innovative research avenues are exploring interventions targeting Mfn-2 and mitochondrial dysfunction. Notably, antioxidative treatments and exogenous hydrogen sulfide have shown potential in counteracting high glucose-induced injuries, mediated through Mfn-2 facilitated endoplasmic reticulum-mitochondria contacts[8]. These advancements present hopeful therapeutic avenues, especially for addressing mitochondrial dysfunction in skeletal muscle injuries related to diabetes.

Additionally, the diterpenoid derivative 15-oxospiramilactone (S3) emerges as a significant player in enhancing mitochondrial dynamics. It targets the mitochondrial enzyme USP30, integral for modulating MFN1 and MFN2, thereby boosting their activity and fostering mitochondrial fusion. Importantly, the ability of S3 to restore mitochondrial function in cells deficient in Mfn1 or Mfn2 underscores its therapeutic potential in treating insulin resistance-related diseases[9].

TOWARD THERAPEUTIC STRATEGIES FOR MODULATING MFN-2 AND MITOCHONDRIAL DYNAMICS

In the realm of diabetes research, a significant focus lies in understanding the correlation between cellular metabolism and the pathophysiology of the disease, emphasizing the role of mitochondria in skeletal muscle atrophy. The mitochondrion, vital for cellular energy, is central to this research, especially regarding Mfn-2-mediated mitochondrial fusion in skeletal muscle. This is particularly relevant in T2DM, where studying skeletal muscle tissues from affected individuals can shed light on the downregulation of Mfn-2 in diabetic conditions. Moreover, exploring type 1 diabetes, specifically the impact of high-fat diets on Mfn-2 in skeletal muscle, is crucial for a comprehensive understanding of diabetes and its effects on skeletal muscle health.

CONCLUSION

The intricate interplay between T2DM and skeletal muscle atrophy, with a focus on the pivotal role of mitochondrial dynamics and Mfn-2, underscores the urgency of developing targeted therapeutic strategies to address these complex metabolic challenges.

ACKNOWLEDGEMENTS

We express our profound appreciation to Academician Bo-Li Zhang and Professor Jun-Hua Zhang from Tianjin University of Traditional Chinese Medicine for their invaluable support and generous contributions. Their expertise and insightful guidance have been instrumental in the success of our research. We also extend our heartfelt thanks to Professor Bo Yu for his engaging discussions and critical technical advice, which have greatly enhanced the progress of our work. Additionally, our warmest gratitude goes to Ms. Lin Wang, whose dedication, passion, and exceptional qualities of warmth, charm, humor, and compassion have continuously inspired and supported us throughout this project.

FOOTNOTES

Co-first authors: Jian-Jun Wu and Hui-Min Xian.

Co-corresponding authors: Da-Wei Yang and Fan Yang.

Author contributions: Wu JJ, Xian HM, Yang DW, and Yang F drafted the manuscript; all authors contributed to the critical review of the manuscript, and have read and approved the final manuscript; Wu JJ and Xian HM contributed equally to this work as co-first authors. Yang DW and Yang F contributed equally to this work as co-corresponding authors. The decision to designate Wu JJ and Xian HM as co-first authors as well as Yang DW and Yang F as co-corresponding authors is based on multiple factors. First, this research was conducted as a collaborative endeavor, and the designation of co-first/co-corresponding authorship accurately reflects the distribution of responsibilities and the considerable effort required to complete the paper. This ensures effective communication and management of post-submission matters, thereby enhancing the paper's quality and reliability. Second, the research team comprises individuals with diverse expertise and skills from various fields, and appointing co-authors best represents this diversity. This approach fosters a more comprehensive and profound examination of the research topic, enriching readers' understanding by presenting multiple expert perspectives. Third, Wu JJ and Xian HM as well as Yang DW and Yang F made equally substantial contributions throughout the research process. Designating them as co-first/co-corresponding authors acknowledges their equal involvement, while also honoring the collaborative spirit and teamwork that characterized this study.

Supported by the Foundation of State Key Laboratory of Component-based Chinese Medicine, No. CBCM2023107; National Natural Science Foundation of China, No. 81901853; and Specially Funded Scientific Research Project of the Fourth Affiliated Hospital of Harbin Medical University, No. HYDSYTB202126.

Conflict-of-interest statement: All the authors have no conflict of interest related to the manuscript.

Country/Territory of origin: China

ORCID number: Da-Wei Yang 0000-0002-7217-9383; Fan Yang 0000-0003-4676-3778.

S-Editor: Lin C
L-Editor: Wang TQ
P-Editor: Zhao YQ

REFERENCES

1 **Nguyen BP**, Pham HN, Tran H, Nghiem N, Nguyen QH, Do TTT, Tran CT, Simpson CR. Predicting the onset of type 2 diabetes using wide and deep learning with electronic health records. *Comput Methods Programs Biomed* 2019; **182**: 105055 [PMID: 31505379 DOI: 10.1016/j.cmpb.2019.105055]

2 **Kopitar L**, Kocbek P, Cilar L, Sheikh A, Stiglic G. Early detection of type 2 diabetes mellitus using machine learning-based prediction models. *Sci Rep* 2020; **10**: 11981 [PMID: 32686721 DOI: 10.1038/s41598-020-68771-z]

3 **Alam Miah MB**, Yousuf MA. Analysis the significant risk factors on type 2 diabetes perspective of Bangladesh. *Diabetes Metab Syndr* 2018; **12**: 897-902 [PMID: 29803509 DOI: 10.1016/j.dsx.2018.05.012]

4 **ChuX**, Feng B, Ge J, Guo L, Huo Y, Ji L, Jia Q, Jiang S, Li Y, Liu F, Liu X, Liu Y, Lu B, Lv A, Wang Y, Weng J, Zeng Q, Zhang Y, Zhou J. Chinese Physicians Association Cardiovascular Medicine Physicians Branch, Chinese Expert Consensus on the Risk Assessment and Management of Panvascular Disease in Patients with Type 2 Diabetes Mellitus Expert Panel. Chinese expert consensus on the risk assessment and management of panvascular disease inpatients with type 2 diabetes mellitus (2022 edition). *CardiolPlus* 2022; **7**: 162-177 [DOI: 10.1097/cp9.0000000000000029]

5 Zuo X, Yao R, Zhao L, Zhang Y, Lu B, Pang Z. Campanumoeajavanica Bl. activates the PI3K/AKT/mTOR signaling pathway and reduces sarcopenia in a T2DM rat model. *AcupunctHerbMed* 2022; **2**: 99-108 [DOI: 10.1097/HM9.0000000000000027]

6 **Wang S**, Zhao H, Lin S, Lv Y, Lin Y, Liu Y, Peng R, Jin H. New therapeutic directions in type II diabetes and its complications: mitochondrial dynamics. *Front Endocrinol (Lausanne)* 2023; **14**: 1230168 [PMID: 37670891 DOI: 10.3389/fendo.2023.1230168]

7 **Ni HM**, Williams JA, Ding WX. Mitochondrial dynamics and mitochondrial quality control. *Redox Biol* 2015; **4**: 6-13 [PMID: 25479550 DOI: 10.1016/j.redox.2014.11.006]

8 **Yang F**, Yu X, Li T, Wu J, Zhao Y, Liu J, Sun A, Dong S, Zhong X, Xu C, Lu F, Zhang W. Exogenous H(2)S regulates endoplasmic reticulum-mitochondria cross-talk to inhibit apoptotic pathways in STZ-induced type I diabetes. *Am J Physiol Endocrinol Metab* 2017; **312**: E190-E203 [PMID: 27998959 DOI: 10.1152/ajpendo.00196.2016]

9 **Yue W**, Chen Z, Liu H, Yan C, Chen M, Feng D, Wu H, Du L, Wang Y, Liu J, Huang X, Xia L, Liu L, Wang X, Jin H, Wang J, Song Z, Hao X, Chen Q. A small natural molecule promotes mitochondrial fusion through inhibition of the deubiquitinase USP30. *Cell Res* 2014; **24**: 482-496 [PMID: 24513856 DOI: 10.1038/cr.2014.20]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 105-109

DOI: 10.5312/wjo.v15.i2.105

ISSN 2218-5836 (online)

EDITORIAL

Deep learning automation of radiographic patterns for hallux valgus diagnosis

Angela Hussain, Cadence Lee, Eric Hu, Farid Amirouche

Specialty type: Mathematical and computational biology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

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

P-Reviewer: Mijwil MM, Iraq

Received: November 30, 2023
Peer-review started: November 30, 2023
First decision: December 7, 2023
Revised: December 22, 2023
Accepted: January 4, 2024
Article in press: January 4, 2024
Published online: February 18, 2024

Angela Hussain, Cadence Lee, Eric Hu, Department of Orthopaedic Surgery, University of Illinois College of Medicine, Chicago, IL 60612, United States

Farid Amirouche, Department of Orthopaedics Surgery, University of Illinois at Chicago, Chicago, IL 60612, United States

Farid Amirouche, Department of Orthopaedic Surgery, Northshore University Health System, Skokie, IL 6007, United States

Corresponding author: Farid Amirouche, PhD, Professor, Department of Orthopedics Surgery, University of Illinois at Chicago, 835 S. Wolcott Ave, Room E270, Chicago, IL 60612, United States. amirouch@uic.edu

Abstract

Artificial intelligence (AI) and deep learning are becoming increasingly powerful tools in diagnostic and radiographic medicine. Deep learning has already been utilized for automated detection of pneumonia from chest radiographs, diabetic retinopathy, breast cancer, skin carcinoma classification, and metastatic lymphadenopathy detection, with diagnostic reliability akin to medical experts. In the *World Journal of Orthopedics* article, the authors apply an automated and AI-assisted technique to determine the hallux valgus angle (HVA) for assessing HV foot deformity. With the U-net neural network, the authors constructed an algorithm for pattern recognition of HV foot deformity from anteroposterior high-resolution radiographs. The performance of the deep learning algorithm was compared to expert clinician manual performance and assessed alongside clinician-clinician variability. The authors found that the AI tool was sufficient in assessing HVA and proposed the system as an instrument to augment clinical efficiency. Though further sophistication is needed to establish automated algorithms for more complicated foot pathologies, this work adds to the growing evidence supporting AI as a powerful diagnostic tool.

Key Words: Artificial intelligence; Hallux valgus; Deep learning; Automated radiography

Core Tip: This editorial summarizes and outlines the original paper "Automated decision support for Hallux valgus treatment options using anteroposterior foot radiographs". We summarize the scope of the deep learning process and compare it to existing artificial intelligence studies used in clinical diagnostic studies. We additionally describe its limitations and impact in the field of automated diagnostic tools.

Citation: Hussain A, Lee C, Hu E, Amirouche F. Deep learning automation of radiographic patterns for hallux valgus diagnosis. *World J Orthop* 2024; 15(2): 105-109
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/105.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.105

INTRODUCTION

Artificial Intelligence (AI) and deep learning have emerged as potential assets in the realm of diagnostic and radiographic medicine, significantly impacting the quality and efficiency of healthcare[1]. Automated systems have demonstrated their value in various medical domains, such as AI-derived pneumonia detection from chest radiographs, diabetic retinopathy assessment, breast cancer diagnosis, skin carcinoma classification, and metastatic lymphadenopathy detection[2]. The diagnostic reliability of some AI systems has been found to parallel that of medical experts, marking a transformative era in medical imaging and analysis[3].

This study by Kwolek *et al*[4], featured in the *World Journal of Orthopedics*, represents a supportive contribution to the application of AI in orthopedic diagnostics. The authors employed an automated and AI-assisted technique to determine the hallux valgus angle (HVA), a critical parameter in assessing HV foot deformity. Leveraging the capabilities of the U-net neural network, the authors constructed an algorithm tailored for pattern recognition of HV foot deformity from anteroposterior high-resolution radiographs. The authors evaluated the performance of their deep learning algorithm by comparing it to expert clinician manual assessments and also considered clinician-clinician variability. The study found that the AI tool demonstrated sufficient accuracy in assessing the HVA when compared to clinician readings and circumvented the issue of clinician-clinician variability. Since the proposed system was effective, the authors suggest that it may have an eventual role in supporting clinical efficiency or efficiency in the evaluation of HV deformities.

While acknowledging the success achieved in this study, the authors emphasize the need for further sophistication in automated algorithms to address more intricate foot pathologies. Automated algorithms like the one presented here are not well-adapted to perform analysis for patients outside the narrow scope of a specific pathology. In this case, exclusion of patients with pathologies such as osteoarthritis, pes cavus, Charcot foot, or other joint deformities limits the clinical application of the proposed algorithm. Especially considering the simple diagnostic nature of assessing HVA, clinician discretion is still important for evaluating concomitant foot deformities or pathologies.

As a general commentary, the integration of AI in medical imaging has significant implications for patients and physicians. The use of AI-assisted diagnostics may lead to enhanced accuracy and efficiency in medical practice, potentially leading to quicker and more precise treatment decisions[5]. Patients may benefit from improved diagnostic capabilities, resulting in more timely interventions and potentially more accurate diagnoses. Physicians may experience a shift in their roles, with AI serving as a valuable supportive tool in diagnostic processes. There is a growing fear that AI may eventually have the power to overtake the clinician's role in diagnosing certain pathologies. Still, at this stage, AI simply serves as a tool for augmenting efficient delivery of care[6]. The proposed AI system in this study does not replace clinical expertise but rather complements it, offering a tool that can handle repetitive tasks efficiently and contribute to diagnostic accuracy[3]. This study reinforces the growing evidence supporting AI as a powerful diagnostic tool in orthopedics. As AI continues to evolve, its impact on the quality of healthcare, patient outcomes, and the workflow of medical practitioners will transform a new era in the integration of technology with traditional medical practices.

The HV is one of the most common forefoot conditions and is defined as an angular deviation of more than 15 degrees of the hallux with respect to the first metatarsal bone[7,8]. Risk factors for the development of HV include female sex, increased age, body mass index, pes planus, hammertoe, and ill-fitting footwear[8,9]. Though the exact biomechanical etiology is unclear, recent literature suggests that HV is likely due to soft tissue contracture and attenuation leading to malalignment at the bone articulations[7]. When evaluating HVA, it is important to evaluate the bony tissue within the foot. The first ray osseous components are composed of the first metatarsal and medial cuneiform with stability dependent on several static and dynamic structures at the first metatarsophalangeal (MTP) and tarsometatarsal joints, making the first ray intrinsically unstable[10]. In the early stages of HV deformity, the prevailing theory posits a weakening of medial support structures of the first toe. This weakening manifests as a medial displacement of the first metatarsal accompanied by a lateral deviation and pronation of the big toe. Consequently, a gradual varus deformity takes shape at the first MTP joint. As the metatarsal head undergoes medial shift and rotation in the frontal plane, its position relative to the sesamoid apparatus is altered. Consequently, the first metatarsal head rests on the medial sesamoid, while the lateral sesamoid is in the first intermetatarsal (IMA) space. Concurrently, the developed deformity at the MTP joint permits the hallux flexor and extensor tendons to bow laterally, causing further deformity. Simultaneously, the displaced abductor hallucis flexes and pronates the phalanx, contributing to the distortion. The increased prominence at the first MTP joint stems from the increased prominence of the first metatarsal head[9,10]. The HVA is commonly measured by plain radiograph. The widely-accepted method to measure HVA consists of an angle constructed between

the center longitudinal axis of the first metatarsal and the axis of the hallux. The angle has typically been determined through use of a protractor by use of the physician but more recently has been determined with assistance from technology[11].

In this article of *World Journal of Orthopedics*, Kwolek *et al*[4] demonstrated a novel approach to HVA and IMA measurements by utilizing deep-learning computer automated methods. By comparing the measurements obtained by their trained U-Net neural network to measurements performed manually by clinicians, they sought to demonstrate the algorithm's clinical efficacy. The study was conducted with a cohort of 133 patients, comprising 265 preoperative radiographic images, with the sole inclusion criteria being weight-bearing symptomatic HV. The authors excluded radiographs with other underlying pathologies that could complicate a read (*i.e.*, severe osteoarthritis, joint deformation, Charcot foot). The U-Net neural network was first trained using anteroposterior foot radiographs with labeled bones and segmental separation. Rather than utilizing binary segmentation of bones with bone extraction, the authors opted for a multi-class segmentation that only selects three bones (1MT, 2MT, and hallucial PP) to calculate HVA/IMA ultimately. This was done to limit the difficulties with reliably training the model despite radiographic noise/artifacts and complex bone structure in the anteroposterior view. Following training and validation of the model, the algorithm was used to automate the measurement of the HVA/IMA in 84 radiographs. In those same radiographs, HVA/IMA was measured manually multiple times by clinicians who were blinded to clinical outcomes. The measurements between AI clinicians and clinician clinicians were compared.

Kwolek *et al*[4] found that there was a significant correlation (HVA: 0.96-0.99; IMA: 0.78-0.95) between the AI-generated measurements and clinician measurements of HVA/IMA. They found that the ratio of operative decisions made based on AI recommendations compared to clinician decisions was almost 0.80, which is equal, if not higher, than the ratio among different clinicians. The authors state that these results are strongly suggestive of a successful achievement that would ultimately save time for the radiologist and orthopedic surgeon while producing clinically actionable results.

A limitation of this study includes the standardization of initial training of the U-Net neural network, as the dataset largely relied on measurements of three segmented bones, which may not be reliable in patients with varying anatomy. In addition, radiographs were selected on the basis that there was no secondary bone pathology present. These limited data sets may not be reflective of the general patient population suffering from HV. These concerns largely coincide with the literature regarding the implementation of AI in clinical practice. These include the dependence on high-quality training data, which requires extensive and clinically relevant datasets[12]. In addition, there are ethical concerns with making clinical decisions based on deep learning technology when not all of the logical bases of the system are understood. Finally, concerns have been raised regarding the clinician's lack of acceptance and trust in AI innovations, as well as their lack of awareness and familiarity with the technology to be used readily in clinical practice[13].

Despite this, the study does well to demonstrate an efficient metric that has produced promising results. The study design is strong, and the authors were able to create a standardized neural network that can reliably make clinically meaningful decisions at the same rate, if not better, than clinicians. Despite the potential limitations of AI implications, it is hard to ignore the potential benefits of the clinical implications that the authors posit.

CONCLUSION

The featured study by Kwolek *et al*[4] supports the integration of AI into orthopedic diagnostics, specifically in the assessment of HV foot deformity. The authors utilized a U-net neural network to determine the HVA. This has implications on the diagnosis of foot pathologies, but also the use of automated tools in healthcare in general.

However, the study also acknowledges the need for further sophistication in automated algorithms to address complex foot pathologies. Considering the rate of concomitant procedures performed during hallux alignment surgery, it is important to note that HV does not always occur in isolation[14]. The authors of this study needed to exclude concomitant pathologies such as osteoarthritis, pes cavus, Charcot foot, and joint deformities, which do not yield a clinically-accurate patient population. The proposed automated system was effective in determining the HVA, a somewhat simple measurement, but only for foot radiographs where no other foot pathologies were noted. Further algorithm optimization is needed for this tool to become clinically relevant.

Additionally, while we have previously discussed the potential for AI to increase clinical efficiency, the value of reduced diagnostic time may be marginal in the case of measuring HVA. The conventional method used to acquire HVA takes 12.3 s ± 0.6 s to measure, and even as short as 5.9 s ± 0.2 s with the point-connection method[15]. While automation of this measurement may be convenient, the marginal time saved by the algorithm may not outweigh the limitations that currently exist with this model. The automated process may save an expertly trained clinician a number of seconds or minutes, but that time would be needed to screen the radiographs for exclusion criteria previously mentioned.

Finally, as with any deep-learning algorithm, the outputs are subject to bias in training data and patient demographic inputs[16]. The study would be strengthened with the use of a larger, more diverse dataset, potentially utilizing a multi-center approach, to ensure that the automated system was able to process patient radiographs from a wide range of demographics, including age, sex, race, and lifestyle.

In summary, while the study supports the exciting topic of AI as a powerful diagnostic tool in medicine, many limitations need to be addressed before the algorithm presented here reaches clinical relevance. The deep-learning system would benefit from training with a broader variety of pathologies and a larger sample size of more diverse patient demographics. Nevertheless, this work by Kwolek *et al*[4] is an important reminder of the potential impacts of automated systems in medicine.

ACKNOWLEDGEMENTS

The views expressed in this article are solely those of the authors and do not necessarily reflect the position or policy of the affiliated institutions.

FOOTNOTES

Co-first authors: Angela Hussain and Cadence Lee.

Author contributions: Hussain A and Lee C contributed equally to this work as co-first authors; Hussain A, Lee C, Hu E, and Amirouche F contributed to this paper; Amirouche F and Lee C designed the concept and outline; Hussain A, Hu E, and Lee C contributed to the writing and review of literature; Amirouche F was responsible for oversight and coordination; and all authors contributed to the editing of the manuscript.

Conflict-of-interest statement: The authors have declared that no conflicts of interest exist.

Country/Territory of origin: United States

ORCID number: Cadence Lee 0000-0002-5437-4273; Farid Amirouche 0000-0002-3002-4199.

S-Editor: Chen YL
L-Editor: A
P-Editor: Yuan YY

REFERENCES

1 **Malamateniou C**, Knapp KM, Pergola M, Woznitza N, Hardy M. Artificial intelligence in radiography: Where are we now and what does the future hold? *Radiography (Lond)* 2021; **27** Suppl 1: S58-S62 [PMID: 34380589 DOI: 10.1016/j.radi.2021.07.015]
2 **Patel BN**, Rosenberg L, Willcox G, Baltaxe D, Lyons M, Irvin J, Rajpurkar P, Amrhein T, Gupta R, Halabi S, Langlotz C, Lo E, Mammarappallil J, Mariano AJ, Riley G, Seekins J, Shen L, Zucker E, Lungren M. Human-machine partnership with artificial intelligence for chest radiograph diagnosis. *NPJ Digit Med* 2019; **2**: 111 [PMID: 31754637 DOI: 10.1038/s41746-019-0189-7]
3 **Currie G**, Hawk KE, Rohren E, Vial A, Klein R. Machine Learning and Deep Learning in Medical Imaging: Intelligent Imaging. *J Med Imaging Radiat Sci* 2019; **50**: 477-487 [PMID: 31601480 DOI: 10.1016/j.jmir.2019.09.005]
4 **Kwolek K**, Gądek A, Kwolek K, Kolecki R, Liszka H. Automated decision support for Hallux Valgus treatment options using anteroposterior foot radiographs. *World J Orthop* 2023; **14**: 800-812 [PMID: 38075473 DOI: 10.5312/wjo.v14.i11.800]
5 **Koski E**, Murphy J. AI in Healthcare. *Stud Health Technol Inform* 2021; **284**: 295-299 [PMID: 34920529 DOI: 10.3233/SHTI210726]
6 **Sauerbrei A**, Kerasidou A, Lucivero F, Hallowell N. The impact of artificial intelligence on the person-centred, doctor-patient relationship: some problems and solutions. *BMC Med Inform Decis Mak* 2023; **23**: 73 [PMID: 37081503 DOI: 10.1186/s12911-023-02162-y]
7 **Gonzalez TA**, Smith JT, Bluman EM, Ready LV, Ciurylo W, Chiodo CP. Republication of "Treatment of Hallux Valgus Deformity Using a Suture Button Device: A Preliminary Report". *Foot Ankle Orthop* 2023; **8**: 24730114231195342 [PMID: 37655934 DOI: 10.1177/24730114231195342]
8 **Nguyen US**, Hillstrom HJ, Li W, Dufour AB, Kiel DP, Procter-Gray E, Gagnon MM, Hannan MT. Factors associated with hallux valgus in a population-based study of older women and men: the MOBILIZE Boston Study. *Osteoarthritis Cartilage* 2010; **18**: 41-46 [PMID: 19747997 DOI: 10.1016/j.joca.2009.07.008]
9 **Ray JJ**, Friedmann AJ, Hanselman AE, Vaida J, Dayton PD, Hatch DJ, Smith B, Santrock RD. Hallux Valgus. *Foot Ankle Orthop* 2019; **4**: 2473011419838500 [PMID: 35097321 DOI: 10.1177/2473011419838500]
10 **Perera AM**, Mason L, Stephens MM. The pathogenesis of hallux valgus. *J Bone Joint Surg Am* 2011; **93**: 1650-1661 [PMID: 21915581 DOI: 10.2106/JBJS.H.01630]
11 **Meng HZ**, Zhang WL, Li XC, Yang MW. Radiographic angles in hallux valgus: Comparison between protractor and iPhone measurements. *J Orthop Res* 2015; **33**: 1250-1254 [PMID: 25763918 DOI: 10.1002/jor.22872]
12 **Lee JG**, Jun S, Cho YW, Lee H, Kim GB, Seo JB, Kim N. Deep Learning in Medical Imaging: General Overview. *Korean J Radiol* 2017; **18**: 570-584 [PMID: 28670152 DOI: 10.3348/kjr.2017.18.4.570]
13 **Eltawil FA**, Atalla M, Boulos E, Amirabadi A, Tyrrell PN. Analyzing Barriers and Enablers for the Acceptance of Artificial Intelligence Innovations into Radiology Practice: A Scoping Review. *Tomography* 2023; **9**: 1443-1455 [PMID: 37624108 DOI: 10.3390/tomography9040115]
14 **Chodaba Y**, Andrews NA, Halstrom J, Sankey T, Sanchez T, Harrelson WM, Agarwal A, Shah A. First Metatarsophalangeal Arthrodesis for Hallux Rigidus and Hallux Valgus: A Comparison of Patient Reported and Clinical Outcomes. *J Foot Ankle Surg* 2023; **62**: 683-688 [PMID: 36964117 DOI: 10.1053/j.jfas.2023.02.008]
15 **Seo JH**, Ahn JY, Boedijono D. Point-Connecting Measurements of the Hallux Valgus Deformity: A New Measurement and Its Clinical Application. *Yonsei Med J* 2016; **57**: 741-747 [PMID: 26996576 DOI: 10.3349/ymj.2016.57.3.741]

16 **Gianfrancesco MA**, Tamang S, Yazdany J, Schmajuk G. Potential Biases in Machine Learning Algorithms Using Electronic Health Record Data. *JAMA Intern Med* 2018; **178**: 1544-1547 [PMID: 30128552 DOI: 10.1001/jamainternmed.2018.3763]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 110-117

DOI: 10.5312/wjo.v15.i2.110

ISSN 2218-5836 (online)

MINIREVIEWS

Review and update on the management of triangular fibrocartilage complex injuries in professional athletes

Valerio Pace, Francesco Bronzini, Giovanni Novello, Giuseppe Mosillo, Luca Braghiroli

Specialty type: Orthopedics

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

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

P-Reviewer: Farì G, Italy; Widmer KH, Switzerland

Received: October 20, 2023
Peer-review started: October 20, 2023
First decision: October 24, 2023
Revised: October 30, 2023
Accepted: December 14, 2023
Article in press: December 14, 2023
Published online: February 18, 2024

Valerio Pace, Department of Trauma and Orthopaedics, AOSP Terni, Terni 05100, Italy

Francesco Bronzini, Giovanni Novello, Department of Trauma and Orthopaedics, University of Perugia, Perugia 06100, Italy

Giuseppe Mosillo, Luca Braghiroli, Department of Trauma and Orthopaedics, Hand Unit, AOSP Terni, Terni 05100, Italy

Corresponding author: Valerio Pace, MBBS, MSc, Researcher, Senior Research Fellow, Surgeon, Department of Trauma and Orthopaedics, AOSP Terni, London HA7 4LP, Terni 05100, Italy. valeriopace@doctors.org.uk

Abstract

Triangular fibrocartilage complex injuries are common in amateur and professional sports. These injuries are mainly caused by acute or chronic repetitive axial loads on the wrist, particularly on the ulnar side and in association with rotations or radial/ulnar deviations. In order to treat professional athletes, a detailed specific knowledge of the pathology is needed. Moreover, the clinician should fully understand the specific and unique environment and needs of the athletes, their priorities and goals, the type of sport, the time of the season, and the position played. An early diagnosis and appropriate management with the quickest possible recovery time are the uppermost goals for both the athlete and the surgeon. A compromise between conservative *vs* surgical indications, athletes' needs and expectations, and financial implications should be achieved. Arthroscopic procedures should be timely planned when indicated as they could allow early diagnosis and treatment at the same time. Conservative measures are often used as first line treatment when possible. Peripheral lesions are treated by arthroscopic repair, whilst central lesions are treated by arthroscopic debridement. Further procedures (such as the Wafer procedure, ulnar osteotomies, *etc.*) have specific indications and great implications with regard to rehabilitation.

Key Words: Triangular fibrocartilage complex injuries; Professional athletes; Ulnar sided wrist pain; Wrist arthroscopy; Wrist debridement

Core Tip: Triangular fibrocartilage complex injuries are common in amateur and professional sports. These injuries are mainly caused by acute or chronic repetitive axial loads on the wrist, particularly on the ulnar side and in association with rotations or radial/ulnar deviations. In order to treat professional athletes, a detailed specific knowledge of the pathology is needed. Moreover, the clinician should fully understand the specific and unique environment and needs of the athletes, their priorities and goals, the type of sport, the time of the season, and the position played. Conservative and surgical management are based on the latter aspects.

Citation: Pace V, Bronzini F, Novello G, Mosillo G, Braghiroli L. Review and update on the management of triangular fibrocartilage complex injuries in professional athletes. *World J Orthop* 2024; 15(2): 110-117
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/110.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.110

INTRODUCTION

The triangular fibrocartilage is a small load-bearing disc-shaped anatomical structure located at the level of the distal part of the ulna and distal radio-ulnar joint, in close relation to the ulnar styloid and the ulnar margin of the distal radius. It is called the "triangular fibrocartilage complex" (TFCC) together with the dorsal and volar distal radio-ulnar ligaments, meniscal homolog, ulno-carpal ligaments and extensor carpi ulnaris tendon sheath. Vascularization is provided by dorsal and palmar branches of the ulnar artery, and palmar branches of the anterior interosseous artery[1-3]. The central portion has reduced regenerative capacities, whilst the peripheral portion is more prone to reparative processes, being provided with a better blood supply compared to the central portion.

The function of the TFCC is to act as a stabilizer for the ulnar aspect of the wrist. It can resist both loading and tensive forces. The TFCC is at risk for either acute traumatic or chronic degenerative injury[1-3]. One can intuitively understand that athletes are at greater risk of acute traumatic injuries to the TFCC rather than degenerative problems.

The diagnostic and therapeutic process can vary between the general population and professional athletes. Several factors must be taken into account in order to choose the most appropriate course of action[1,2].

LITERATURE SEARCH

A narrative review of published papers on the diagnosis and management of TFCC injuries in professional athletes was performed. PubMed, MEDLINE, Cochrane and EMBASE databases were searched. The search keywords were: TFCC injury; triangular fibrocartilage complex injury; TFCC athletes; triangular fibrocartilage complex athletes; TFCC sport; triangular fibrocartilage complex sport; TFCC professional athletes; triangular fibrocartilage complex professional athletes; TFCC treatments; triangular fibrocartilage complex treatments.

All Authors independently performed the review and all included articles were scrutinized. The included articles and results were merged after common agreement among the Authors. Only articles specifically based on the diagnosis and management of TFCC injuries in professional athletes published in the last 20 years were included. In addition, only articles with level of evidence I-II-III-IV were included. Informed consents and ethical approval were not necessary (narrative review).

EPIDEMIOLOGY

Whilst epidemiologic data in the general population have been reported, there is still uncertainty and a lack of high level scientific evidence with regard to the epidemiology of TFCC lesions related to sports. It is reported that these lesions represent between 3% and 9% of the hand-wrist injuries in athletes. It is also reported that the prevalence increases with age[1,2,4,5].

TFCC injuries are common in both amateur and professional sports. These injuries are mainly caused by acute or chronic repetitive axial loads on the wrist, particularly on the ulnar side and in association with rotations or radial/ulnar deviations[1,2,4-9].

Sports that more commonly result in such injuries have been reported to be: Tennis, padel, table tennis, golf, and baseball. Sports that less commonly result in these injuries (but still with a significant number of reported cases) are: Volleyball, basketball, water board sports, and gymnastics[1,2,6-9].

CLASSIFICATIONS

Classifications of TFCC injuries are based on anatomy (central *vs* peripheral) or more commonly on the etiology. In fact

the classification most frequently used is Palmer's classification, which divides TFCC lesions into 2 groups: Type 1 (acute traumatic injuries) and type 2 (degenerative lesions)[10-12].

Type 1 lesions are further divided into subgroups on the basis of the anatomical location of the lesion: Type 1A (isolated central TFCC articular disc perforation); type 1B (peripheral ulnar sided TFCC tear (with or without ulnar styloid fracture); type 1C (distal TFCC disruption (from the distal ulno-carpal ligament); type 1D (radial TFCC disruption with or without sigmoid notch fracture)[10-12].

Type 2 lesions are also further divided into subgroups: Type 2A (TFCC wear); type 2B (TFCC wear with lunate and/or ulnar chondromalacia); type 2C (TFCC perforation with lunate and/or ulnar chondromalacia); type 2D (TFCC perforation with lunate and/or ulnar chondromalacia and with lunotriquetral ligament perforation); type 2E (TFCC perforation with lunate and/or ulnar chondromalacia, lunotriquetral ligament perforation and ulno-carpal arthritis)[10-12] (Table 1).

DIAGNOSIS

The most common symptoms of a TFCC injury are: Ulnar-sided wrist pain with tenderness mainly found at the level of the fovea; ulnar-sided minimal oedema; pain against resistance; reduced range of motion (ROM) of the wrist; joint sagging during rotations or load-bearing activities; audible and palpable "click" from the ulnar side of the wrist during forearm rotations (prono-supination) and sometimes radial and/or ulnar deviation. Pain and reduced function on radio-ulnar deviation can be characteristic of an ulnar impaction syndrome. Injuries can be asymptomatic or pauci-symptomatic [13-17].

Athletes often report sudden occurrence of pain during forearm rotations and axial-loading of the wrist. Different combinations of axial-loading, rotation and radial or ulnar deviations have been reported. Direct trauma on the ulnar side of the wrist is a rare but existing occurrence, especially with the wrist in radial deviation. Another possible finding is a chronic lesion caused by repetitive movements of the wrist and mechanical stress in general of the distal radio-ulnar joint [13,14,18].

These symptoms related to a TFCC injury are often reported by athletes playing sports involving significant axial-load and mechanical stress on the wrist, particularly if the axial-load is associated with rotations and radial/ulnar deviations (such as tennis, padel, golf, ping-pong, baseball, javelin *etc.*)[13-18].

An association between TFCC injuries and other major musculoskeletal lesions (such as Colles' fractures, Galeazzi's injury, Essex-Lopresti injury, *etc.*) in athletes competing in sports involving strong body contact such as football, rugby, *etc.* has rarely been reported [1,2,4,5].

If the TFCC injury is significant, the athlete is rarely able to continue to the end of the training sessions or games/competitions given the significant pain and wrist motion impairment.

Specific tests introduced in order to evaluate wrist stability are as follows: Ulnar fovea sign, piano key test, ulnar grinding test, compression test, and the ballottement test[1,2,19,20] (Table 2).

The next step is radiology. A plain radiograph is a must (at least the common antero-posterior (AP) and lateral view) and is the simplest and quickest radiological exam performed. It is of absolute relevance to identify any fractures (especially affecting the ulnar styloid), measure the standard radiological parameters of the wrist (ulnar variance in particular on the AP view), exclude a subluxation of the distal radio-ulnar joint (by examining the lateral view) and evaluate the potential presence of an ulnar impaction syndrome (especially in degenerative lesions)[1,2,16,19,20] (Table 2).

A computed tomography scan is rarely recommended, and is indicated only in cases of intra-articular fractures of the wrist. A wrist magnetic resonance imaging (MRI) scan is often indicated for TFCC injuries. Its sensitivity and specificity vary depending on the level of resolution of the scanning machine. High resolution MRI scans provide a level of accuracy up to 97%[1,2,16,19,20] (Table 2).

A wrist arthrogram is an option very commonly used in some units as this exam allows visualization of the lesion location and defines the characteristics of the TFCC lesion[1,2,16] (Table 2).

However, the literature indicates that wrist arthroscopy is the gold standard for TFCC injury diagnosis and to potentially allow appropriate treatment simultaneously. It is considered the test with the highest sensitivity and specificity, provides the opportunity to directly visualize the anatomical structures and make a specific diagnosis, and allows arthroscopic treatment at the same time (debridement or repair). Several arthroscopy portals and repair techniques have been reported in the literature, which are chosen specifically depending on the type of patient and lesion[1,2,21,22]. Specific aspects related to the choice and timing of radiological examinations will be discussed in the following sections.

TREATMENTS

Conservative treatments

Athletes with a TFCC injury, after the appropriate diagnostic process, are very often prone to attempt conservative measures first, before more invasive options. However, this will be further developed in this article as many specific factors must be considered when making such decisions[1,2,20,21].

The following conservative measures are applied in different combinations: No sport activity for 3-6 wk (depending on the severity of the injury); immobilization with a splint for 2-4 wk; utilization of non-steroidal anti-inflammatory agents (oral and/or topical); one or more steroid injections and/or hyaluronic acid injections; physical therapy; occupational

Table 1 Palmer's classification

Type 1 acute traumatic injury	Type 2 degenerative injury
Isolated central TFCC articular disk perforation	TFCC wear
Peripheral ulnar-sided TFCC tear with or without ulnar styloid fracture	TFCC wear with lunate and/or ulnar chondromalacia
Distal TFCC disruption (disruption of the distal ulno-carpal ligaments)	TFCC perforation with lunate and/or ulnar chondromalacia
Radial TFCC disruption with or without sigmoid notch fracture	TFCC perforation with lunate and/or ulnar chondromalacia and with lunotriquetral ligament perforation
	TFCC perforation with lunate and/or ulnar chondromalacia, lunotriquetral ligament perforation and ulno-carpal arthritis

TFCC: Triangular fibrocartilage complex.

Table 2 Diagnosis of TFCC injuries

Clinical tests	Radiological tests
Areas of tenderness	X-ray (AP and lateral view)
Ulnar fovea sign	CT (rarely)
Piano key test	MRI
Ulnar grinding test	Wrist arthrogram
Compression test	Wrist arthroscopy (gold standard)
Ballottement test	
ROM evaluation	

AP: Antero-posterior; ROM: Range of motion; CT: computed tomography; MRI: Magnetic resonance imaging.

therapy[1,2,21-24].

If it is necessary for the athlete to carry on to the end of the competitive season or a specific game/competition (weeks or months), the clinician should postpone the surgical treatment until the annual break and carry out the above-mentioned conservative strategies, if the severity of the injury allows and bearing in mind that the athlete must perform at a certain high level. However, if the TFCC injury is very severe and strong surgical indications are defined, especially in the absence of imminent relevant competitions, the orthopaedic surgeon could recommend surgical repair straight away, with the aim of achieving the quickest possible recovery and return to sport activity avoiding long-term degenerative complications[1,2,22-24].

It is suggested that an experienced multidisciplinary team centered on an orthopaedic surgeon with strong experience in hand and wrist surgery should be involved in the treatment of elite athletes with TFCC injuries. In fact, injury management errors would be particularly evident when dealing with professional athletes and significant consequences could be caused by little mistakes. We stress again the importance of the initial decision on the timing of surgical repair: The athlete's entire career is at stake and this "crossroad" is the key management decision that could positively or negatively affect the outcome of treatment[1,2].

Surgical treatments

Type 1A lesions: Isolated central TFCC articular disk perforation. These lesions are avascularized and cannot be arthroscopically repaired. Therefore arthroscopic debridement is the surgical treatment of choice. It is reported in biomechanics studies that up to 80% of the disc could be debrided/removed without causing any significant wrist instability. A standard arthroscopic set up is usually required with the use of 2 portals (rarely 3 portals)[1,2,18-24].

Surgery is followed by 1 or 2 wk of wrist immobilization. This is followed by a rehabilitation program based on passive and active wrist movements. Athletes playing sports requiring strong wrist stress forces (tennis, golf, javelin, padel, *etc.*) are allowed light ball contact after 3 wk. Full return to sport is expected between 4 to 6 wk[1,2,18-24].

If a type 1A lesion is associated with neutral or positive ulnar variance, it may be necessary to perform a shortening ulnar osteotomy or a Wafer-procedure after debridement. The osteotomy could be postponed to the end of the season with the aim of allowing the injured athlete to return to high level performance in a few weeks and manage the remaining problem at the end of the season. The rehabilitation program after an osteotomy could last up to 3-4 mo (it requires immobilization for 6-8 wk) and the entire season could be at risk[1,2,18-24].

Type 1B lesions: Peripheral ulnar-sided TFCC tear with or without ulnar styloid fracture. These lesions are vascularized and can potentially be repaired. Using an inside-out, outside-in or all-inside technique, the lesion is arthroscopically repaired[1,2].

The rehabilitation program includes immobilization (splint or cast) for 4-6 wk, and then a further 6 wk of passive and active wrist exercises to regain an adequate ROM and muscle strength. The program may take up to 3 mo[2,18-24].

Type 1C lesions: Distal TFCC disruption (disruption of the distal ulno-carpal ligaments). These lesions are often diagnosed without arthroscopy and mainly require an open surgery repair. An incision on the ulnar side of the wrist just volar to the extensor carpi ulnaris should be made and the neurovascular structures carefully protected throughout the entire procedure. Following appropriate exposure, the lesion can be directly repaired; several techniques have been described[1,2,18-24].

Type 1D lesions: Radial TFCC disruption with or without sigmoid notch fracture. An arthroscopic repair is suggested for these lesions, together with thorough debridement of the sigmoid notch, particularly at the level of the triangular fibrocartilage insertion[1,2,18-24].

Type 2A lesions: TFCC wear. Symptoms related to these lesions may be insidious. Radiographs are necessary in order to rule out and diagnose degenerative changes in the distal radio-ulnar joint and evaluate the ulnar variance. Elite athletes are often offered surgical management including a shortening ulnar osteotomy for those with neutral or positive ulnar variance. However, the latter is contraindicated in the presence of radio-ulnar joint arthritis. In this case a distal ulnar resection is proposed[1,2,18-24].

Type 2B lesions: TFCC wear with lunate and/or ulnar chondromalacia. The treatment options do not differ from those related to type 2A lesions[1,2,18-24].

Type 2C lesions: TFCC perforation with lunate and/or ulnar chondromalacia. These lesions are treated by arthroscopic debridement and a Wafer resection procedure for those with neutral or positive ulnar variance. If the latter is bigger than 2 mm, a shortening ulnar osteotomy is recommended instead[1,2,18-24].

Type 2D lesions: TFCC perforation with lunate and/or ulnar chondromalacia and with lunotriquetral ligament perforation. This type of lesion rarely affects elite athletes as significant degenerative processes do not generally occur before 30-40 years of age. The treatment does not differ from that of 2C lesions, apart from the necessity to evaluate the stability of the lunotriquetrel ligament. Consequently a Wafer procedure is contraindicated in the case of instability, and accurate debridement of the ligament is also necessary. If instability persists even after the osteotomy procedure, a lunotriquetral arthrodesis should be considered as a second stage treatment option in those whose symptoms do not improve after osteotomy[1,2,18-24].

Type 2E lesions: TFCC perforation with lunate and/or ulnar chondromalacia, lunotriquetral ligament perforation and ulno-carpal arthritis. In the presence of degenerative changes, Wafer procedures and osteotomies are not indicated in these patients. The well studied salvage procedure called Sauve-Kapandji (or hemiresection arthroplasty) is a suitable option for these cases. A Sauve-Kapandji procedure is the treatment of choice for elite athletes as it offers the lowest risk of radio-ulnar impingement during sport activities[1,2,18-24]. The rehabilitation protocol of type 2 lesions does not differ from those described above.

Sport-specific treatments

The treatment of choice may depend and vary on several factors. The clinician should take into account the level of pain and movement limitations, the type of lesion, the severity of the injury, the level of competition, the timing of the injury in relation to the stage of the agonistic season, sport, and position played by the athlete[1,2,22-27].

Very early diagnosis is the key step for elite athletes as this allows early identification of the problem and subsequent early treatment planning. If temporary immobilization is advocated, professional athletes are often very reluctant to be compliant with this treatment strategy. Moreover, athletes participating in sports involving repetitive pronation/supination and radial/ulnar deviation do not significantly benefit from this type of conservative measure and very often immobilization is avoided[5,16,17].

On the other hand, steroid injections (with or without the use of hyaluronic acid) seem to be a quite common temporary or definitive option for professional athletes. These injections are indicated for injuries that do not have surgical indications or for injuries with surgical indications in athletes who are willing to end the season before undergoing surgery. However, there are exceptions: In the presence of radio-ulnar instability, central lesions (an early arthroscopic procedure for central lesions allows both an early and accurate diagnosis and appropriate surgical management at the same time, assuring the shortest rehabilitation time), and lesions associated with neutral or positive ulnar variance (debridement is initially needed, after which further surgical treatments are considered and evaluated in the following months), a prompt surgical plan is warranted[1,2,18-24].

Different to the surgical timing for central lesions, peripheral lesions with surgical indication do not need immediate surgical planning. Careful discussion (with pros and cons evaluation) between the athlete and the surgeon should take place with a shared final decision on whether to decide on a conservative or surgical option. As mentioned previously, several factors should be taken into account and the decision should be athlete-centred and specific. If the type of injury allows, many opt for temporary measures (steroid injections prevalently) in order to complete at least the season. In fact a surgical option implies the need for at least 3 mo rehabilitation. More invasive treatments such as Wafer procedures are very commonly delayed until the end of the season, whilst ulnar osteotomies are widely postponed at least until the end of the season, if not to the end of the professional career[1,2,18-24].

The major issue for all athletes whose injuries have a surgical indication but are treated temporarily with conservative measures until the end of the season, is the possibility of compromising the final surgical results and increasing the risk of medium- and long-term consequences (such as degenerative changes)[1,2,18-24].

SPORT-SPECIFIC REHABILITATION INSIGHT

It is known that central lesions can be treated arthroscopically. Patients are required to use a splint for 1 to 2 wk after the surgical procedure and then start passive and active ROM exercises. Athletes playing sports such as golf are usually able to start their routine training (including ball-contact) after about 3 wk. Full return to competitive sport activities can be achieved in 4-6 wk in these patients. On the contrary, for sports involving significant axial loading forces onto the wrist (such as boxing and gymnastics) full return to competition level may take up to 8-12 wk. Athletes playing sports involving frequent and intense radial-ulnar deviation and rotations of the wrist (such as tennis and padel) may return to competitions in approximately 6-8 wk[1,2,22-27].

The rehabilitation protocol after arthroscopic debridement for peripheral lesions is longer than that described above. In fact, patients require a period of immobilization with a splint or cast for 2-6 wk. This should be followed by a further 6-8 wk of passive and active wrist ROM exercises and strengthening exercises. The return to competitive sport activity may be achieved after 2-3 mo, independent of the type of sport[1,2,22-27].

The return to sport might take longer following surgical treatment of type 2 lesions. A Wafer procedure requires 1-2 wk of immobilization in a splint or cast which should be followed by early active exercises first and strengthening exercises in the second stage. Full return to competition is authorized after 6-8 wk minimum depending on symptoms: The athlete can compete at the end of the rehabilitation protocol when pain free. No differences among the types of sport have been reported[1,2,18-27].

A shortening osteotomy requires 5-6 wk of immobilization, preferably with a cast. This is followed initially by passive and active ROM exercises of the wrist and then by strengthening exercises. Full return to competitive sport may be achieved after 10-12 wk at the earliest. Full bone healing (with radiological evidence from plain radiographs) is necessary in order to allow the athlete to compete again[1,2,18-27].

Elite athletes playing certain sports can be aided by the use of taping, splinting or padded casts, especially after Wafer or osteotomy procedures in order to reduce stress. However, not all sports allow the use of these aids. In fact, athletes playing ball contact sports (such as rugby, football, baseball and tennis) cannot fully compete if they require these aids and their rehabilitation protocol might take longer than expected as a consequence. Therefore, protective equipment varies between non-contact and contact sports, and its use may vary even among different roles played by the athletes within the same sport activity[1,2,18-27].

In general, a professional athlete with key roles within the team or with very high potential and expectations can wait until the end of the season to undergo a surgical procedure after sustaining a TFCC injury (and utilize temporary measures such as steroid injections); moreover, the rehabilitation protocols tend to be more intense as the quickest possible return to sport is attempted. On the other hand, professional athletes with lower expectations decide on surgical treatment at an earlier stage and a slightly more prudent rehabilitation protocol is adopted[1,2,18-27].

With regard to throwing sports, if the lesion affects the non-throwing arm, the return to competitive sport may be achieved quicker at 2 to 4 wk compared to standard rehabilitation protocols for all types of TFCC injuries and surgical treatments[1,2,18-27].

Patient education is absolutely essential in order to allow the best possible rehabilitation, avoid further injuries and disease progression in those conservatively treated (or whilst waiting until the end of the season for definitive surgical management). Activities reproducing the mechanism of injury and pain should be avoided[1,2,18-29].

CONCLUSION

TFCC injuries are common in amateur and professional sports. These are mainly caused by acute or chronic repetitive loads on the wrist, particularly on the ulnar side. This is even worse if axial loads are associated with rotations or radial/ulnar deviations.

In order to treat professional athletes who sustain TFCC injuries, a detailed specific knowledge of the pathology is needed. Moreover, the clinician should fully understand the specific and unique environment and the needs of the athletes, their priorities and goals, the type of sport, the time of the season, and the position played.

An early diagnosis and appropriate management with the quickest possible recovery time are the uppermost goals for both the athlete and the surgeon. A compromise between conservative *vs* surgical indications, athletes' needs and expectations, and financial implications should be achieved. Arthroscopic procedures should be timely planned when indicated as they may allow early diagnosis and treatment at the same time.

Conservative measures are often used as first line treatment when possible. Peripheral lesions are treated by arthroscopic repair, whilst central lesions are treated by arthroscopic debridement. Further procedures (such as the Wafer procedure, ulnar osteotomies, *etc.*) have specific indications and great implications with regard to the rehabilitation time and long-term consequences for the athletes.

Competitive levels are very often achieved by athletes with TFCC injuries surgically. Only a small percentage do not reach satisfactory levels, and this is more common in those undergoing repair procedures or procedures related to radial/ulnar instability and neutral or positive ulnar variance.

FOOTNOTES

Author contributions: Pace V designed the article; Pace V, Bronzini F, Novello G, Mosillo G and Braghiroli L performed research and literature review, analyzed data, wrote and finalized the review.

Conflict-of-interest statement: No conflicts of interest.

Country/Territory of origin: Italy

ORCID number: Valerio Pace 0000-0002-4499-9157.

Corresponding Author's Membership in Professional Societies: General Medical Council (United Kingdom), No. 7192447.

S-Editor: Fan JR
L-Editor: Webster JR
P-Editor: Zhao S

REFERENCES

1 **Ko JH**, Wiedrich TA. Triangular fibrocartilage complex injuries in the elite athlete. *Hand Clin* 2012; **28**: 307-321, viii [PMID: 22883871 DOI: 10.1016/j.hcl.2012.05.014]
2 **Robertson G**, Ang KK, Maffulli N, Simpson CK, Rust PA. Return to sport following surgical management of triangular fibrocartilage tears: a systematic review. *Br Med Bull* 2019; **130**: 89-103 [PMID: 30943287 DOI: 10.1093/bmb/ldz013]
3 **Jarrett CD**, Baratz ME. The management of ulnocarpal abutment and degenerative triangular fibrocartilage complex tears in the competitive athlete. *Hand Clin* 2012; **28**: 329-337, ix [PMID: 22883875 DOI: 10.1016/j.hcl.2012.05.018]
4 **Rettig AC**. Epidemiology of hand and wrist injuries in sports. *Clin Sports Med* 1998; **17**: 401-406 [PMID: 9700410 DOI: 10.1016/s0278-5919(05)70092-2]
5 **Dailey SW**, Palmer AK. The role of arthroscopy in the evaluation and treatment of triangular fibrocartilage complex injuries in athletes. *Hand Clin* 2000; **16**: 461-476 [PMID: 10955219]
6 **Farì G**, Notarnicola A, DI Paolo S, Covelli I, Moretti B. Epidemiology of injuries in water board sports: trauma versus overuse injury. *J Sports Med Phys Fitness* 2021; **61**: 707-711 [PMID: 33975428 DOI: 10.23736/S0022-4707.20.11379-3]
7 **Farì G**, Fischetti F, Zonno A, Marra F, Maglie A, Bianchi FP, Messina G, Ranieri M, Megna M. Musculoskeletal Pain in Gymnasts: A Retrospective Analysis on a Cohort of Professional Athletes. *Int J Environ Res Public Health* 2021; **18** [PMID: 34065250 DOI: 10.3390/ijerph18105460]
8 **Farì G**, Santagati D, Macchiarola D, Ricci V, Di Paolo S, Caforio L, Invernizzi M, Notarnicola A, Megna M, Ranieri M. Musculoskeletal pain related to surfing practice: Which role for sports rehabilitation strategies? A cross-sectional study. *J Back Musculoskelet Rehabil* 2022; **35**: 911-917 [PMID: 35068441 DOI: 10.3233/BMR-210191]
9 **Farì G**, Macchiarola D, Quarta F, Bianchi FP, Caforio L, Cutti AG, Ranieri M. Epidemiology of injuries in wheelchair basketball: Trauma versus overuse mechanism and prevention rehabilitative strategies. *J Prosthet Orthot***35**: 32-37 [DOI: 10.1097/JPO.0000000000000458]
10 **Palmer AK**, Werner FW. The triangular fibrocartilage complex of the wrist--anatomy and function. *J Hand Surg Am* 1981; **6**: 153-162 [PMID: 7229292 DOI: 10.1016/s0363-5023(81)80170-0]
11 **Kovachevich R**, Elhassan BT. Arthroscopic and open repair of the TFCC. *Hand Clin* 2010; **26**: 485-494 [PMID: 20951898 DOI: 10.1016/j.hcl.2010.07.003]
12 **Palmer AK**. Triangular fibrocartilage complex lesions: a classification. *J Hand Surg Am* 1989; **14**: 594-606 [PMID: 2666492 DOI: 10.1016/0363-5023(89)90174-3]
13 **Palmer AK**, Glisson RR, Werner FW. Relationship between ulnar variance and triangular fibrocartilage complex thickness. *J Hand Surg Am* 1984; **9**: 681-682 [PMID: 6491211 DOI: 10.1016/s0363-5023(84)80013-1]
14 **Hagert CG**. Distal radius fracture and the distal radioulnar joint--anatomical considerations. *Handchir Mikrochir Plast Chir* 1994; **26**: 22-26 [PMID: 8150382]
15 **Palmer AK**, Werner FW. Biomechanics of the distal radioulnar joint. *Clin Orthop Relat Res* 1984; 26-35 [PMID: 6744728]
16 **Blazar PE**, Chan PS, Kneeland JB, Leatherwood D, Bozentka DJ, Kowalchick R. The effect of observer experience on magnetic resonance imaging interpretation and localization of triangular fibrocartilage complex lesions. *J Hand Surg Am* 2001; **26**: 742-748 [PMID: 11466652 DOI: 10.1053/jhsu.2001.24966]
17 **Kleinman WB**. Stability of the distal radioulna joint: biomechanics, pathophysiology, physical diagnosis, and restoration of function what we have learned in 25 years. *J Hand Surg Am* 2007; **32**: 1086-1106 [PMID: 17826566 DOI: 10.1016/j.jhsa.2007.06.014]
18 **Farr S**. Editorial Commentary: The Hook Test Is More Accurate for Detecting Foveal Triangular Fibrocartilage Complex Tears but Not More Important Than the Trampoline Test. *Arthroscopy* 2021; **37**: 1808-1810 [PMID: 34090566 DOI: 10.1016/j.arthro.2021.04.011]
19 **Kuru CA**, Uysal O, Karaca NB, Akar Z, Ayhan E, Kuru I. Responsiveness and Validity of Weight-Bearing Test for Measuring Loading Capacity in Patients With Triangular Fibrocartilage Complex Injury. *J Sport Rehabil* 2022; **31**: 876-884 [PMID: 35461186 DOI: 10.1123/jsr.2021-0386]
20 **McAdams TR**, Swan J, Yao J. Arthroscopic treatment of triangular fibrocartilage wrist injuries in the athlete. *Am J Sports Med* 2009; **37**: 291-297 [PMID: 19059892 DOI: 10.1177/0363546508325921]

21 **Papapetropoulos PA**, Ruch DS. Repair of arthroscopic triangular fibrocartilage complex tears in athletes. *Hand Clin* 2009; **25**: 389-394 [PMID: 19643338 DOI: 10.1016/j.hcl.2009.05.011]

22 **Rios-Russo JL**, Lozada-Bado LS, de Mel S, Frontera W, Micheo W. Ulnar-Sided Wrist Pain in the Athlete: Sport-Specific Demands, Clinical Presentation, and Management Options. *Curr Sports Med Rep* 2021; **20**: 312-318 [PMID: 34099609 DOI: 10.1249/JSR.0000000000000853]

23 **Tosti R**, Shin E. Wrist Arthroscopy for Athletic Injuries. *Hand Clin* 2017; **33**: 107-117 [PMID: 27886828 DOI: 10.1016/j.hcl.2016.08.005]

24 **Robba VI**, Karantana A, Fowler APG, Diver C. Perceptions and experiences of wrist surgeons on the management of triangular fibrocartilage complex tears: a qualitative study. *J Hand Surg Eur Vol* 2019; **44**: 572-581 [PMID: 30741080 DOI: 10.1177/1753193419826459]

25 **Henderson CJ**, Kobayashi KM. Ulnar-Sided Wrist Pain in the Athlete. *Orthop Clin North Am* 2016; **47**: 789-798 [PMID: 27637665 DOI: 10.1016/j.ocl.2016.05.017]

26 **Pang EQ**, Yao J. Ulnar-sided wrist pain in the athlete (TFCC/DRUJ/ECU). *Curr Rev Musculoskelet Med* 2017; **10**: 53-61 [PMID: 28185125 DOI: 10.1007/s12178-017-9384-9]

27 **Yamabe E**, Nakamura T, Pham P, Yoshioka H. The athlete's wrist: ulnar-sided pain. *Semin Musculoskelet Radiol* 2012; **16**: 331-337 [PMID: 23047280 DOI: 10.1055/s-0032-1327006]

28 **Rollo G**, Bisaccia M, Irimia JC, Rinonapoli G, Pasquino A, Tomarchio A, Roca L, Pace V, Pichierri P, Giaracuni M, Meccariello L. The Advantages of Type III Scaphoid Nonunion Advanced Collapse (SNAC) Treatment With Partial Carpal Arthrodesis in the Dominant Hand: Results of 5-year Follow-up. *Med Arch* 2018; **72**: 253-256 [PMID: 30514989 DOI: 10.5455/medarh.2018.72.253-256]

29 **Pace V**, Sessa P, Guzzini M, Spoliti M, Carcangiu A, Criseo N, Giai Via A, Meccariello L, Caraffa A, Lanzetti RM. Clinical, functional and radiological outcomes of the use of fixed angle volar locking plates in corrective distal radius osteotomy for fracture malunion. *Acta Biomed* 2021; **92**: e2021180 [PMID: 34212911 DOI: 10.23750/abm.v92i3.11265]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 118-128

DOI: 10.5312/wjo.v15.i2.118

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Retrospective Study

Mid-term outcomes of a kinematically designed cruciate retaining total knee arthroplasty

Jonathan L Katzman, Akram A Habibi, Muhammad A Haider, Casey Cardillo, Ivan Fernandez-Madrid, Morteza Meftah, Ran Schwarzkopf

Specialty type: Orthopedics

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Torres RM, Portugal

Received: October 13, 2023
Peer-review started: October 13, 2023
First decision: December 7, 2023
Revised: December 15, 2023
Accepted: January 9, 2024
Article in press: January 9, 2024
Published online: February 18, 2024

Jonathan L Katzman, Akram A Habibi, Muhammad A Haider, Casey Cardillo, Ivan Fernandez-Madrid, Morteza Meftah, Ran Schwarzkopf, Department of Orthopedic Surgery, Division of Adult Reconstructive Surgery, NYU Langone Orthopedic Hospital, NYU Langone Health, New York, NY 10010, United States

Corresponding author: Ran Schwarzkopf, MD, MSc, Professor, Department of Orthopedic Surgery, Division of Adult Reconstructive Surgery, NYU Langone Orthopedic Hospital, NYU Langone Health, 301 East 17th Street, Suite 1402, New York, NY 10010, United States.
ran.schwarzkopf@nyulangone.org

Abstract

BACKGROUND

Advances in implant material and design have allowed for improvements in total knee arthroplasty (TKA) outcomes. A cruciate retaining (CR) TKA provides the least constraint of TKA designs by preserving the native posterior cruciate ligament. Limited research exists that has examined clinical outcomes or patient reported outcome measures (PROMs) of a large cohort of patients undergoing a CR TKA utilizing a kinematically designed implant. It was hypothesized that the studied CR Knee System would demonstrate favorable outcomes and a clinically significant improvement in pain and functional scores.

AIM

To assess both short-term and mid-term clinical outcomes and PROMs of a novel CR TKA design.

METHODS

A retrospective, multi-surgeon study identified 255 knees undergoing a TKA utilizing a kinematically designed CR Knee System (JOURNEY™ II CR; Smith and Nephew, Inc., Memphis, TN) at an urban, academic medical institution between March 2015 and July 2021 with a minimum of two-years of clinical follow-up with an orthopedic surgeon. Patient demographics, surgical information, clinical outcomes, and PROMs data were collected *via* query of electronic medical records. The PROMs collected in the present study included the Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS JR) and Patient-Reported Outcomes Measurement Information System (PROMIS®) scores. The significance of improvements in mean PROM scores from preoperative scores to

scores collected at six months and two-years postoperatively was analyzed using Independent Samples *t*-tests.

RESULTS

Of the 255 patients, 65.5% were female, 43.8% were White, and patients had an average age of 60.6 years. Primary osteoarthritis (96.9%) was the most common primary diagnosis. The mean surgical time was 105.3 minutes and mean length of stay was 2.1 d with most patients discharged home (92.5%). There were 18 emergency department (ED) visits within 90 d of surgery resulting in a 90 d ED visit rate of 7.1%, including a 2.4% orthopedic-related ED visit rate and a 4.7% non-orthopedic-related ED visit rate. There were three (1.2%) hospital readmissions within 90 d postoperatively. With a mean time to latest follow-up of 3.3 years, four patients (1.6%) required revision, two for arthrofibrosis, one for aseptic femoral loosening, and one for peri-prosthetic joint infection. There were significant improvements in KOOS JR, PROMIS Pain Intensity, PROMIS Pain Interference, PROMIS Mobility, and PROMIS Physical Health from preoperative scores to six month and two-year postoperative scores.

CONCLUSION

The evaluated implant is an effective, novel design offering excellent outcomes and low complication rates. At a mean follow up of 3.3 years, four patients required revisions, three aseptic and one septic, resulting in an overall implant survival rate of 98.4% and an aseptic survival rate of 98.8%. The results of our study demonstrate the utility of this kinematically designed implant in the setting of primary TKA.

Key Words: Total knee arthroplasty; Cruciate retaining; Kinematic design; Survivorship; Bearing material; Prosthetic design; Clinical outcomes; Patient-reported outcome measures

Core Tip: This study aimed to assess mid-term clinical and patient-reported outcomes of 255 total knee arthroplasties (TKAs) using a novel, kinematically-designed cruciate retaining total knee arthroplasty implant. With a mean time to follow-up of 3.3 years, there was a high implant survival rate of 98.4%. Four patients (1.6%) required a revision TKA surgery, including three (1.2%) revised for aseptic indications. Patients who received the kinematically-designed cruciate retaining TKA showed significant improvements in Knee Injury and Osteoarthritis Outcome Score for Joint Replacement, Patient-Reported Outcomes Measurement Information System (PROMIS®) Pain Intensity, PROMIS Pain Interference, PROMIS Mobility, and PROMIS Physical Health.

Citation: Katzman JL, Habibi AA, Haider MA, Cardillo C, Fernandez-Madrid I, Meftah M, Schwarzkopf R. Mid-term outcomes of a kinematically designed cruciate retaining total knee arthroplasty. *World J Orthop* 2024; 15(2): 118-128
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/118.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.118

INTRODUCTION

A cruciate retaining (CR) total knee arthroplasty (TKA) provides the least constraint of TKA designs by preserving the native posterior cruciate ligament[1]. One of the first CR TKA implants was designed in 1968 and has continued to evolve over the last few decades[2]. Improvements in polyethylene material, component surface metal alloy composition, and overall implant designs have attempted to improve patient satisfaction and TKA implant survival[3]. Despite the overall success, up to 25% of patients can be dissatisfied after undergoing a TKA[4-6]. Patients who are dissatisfied may require revision TKA, which is expected to increase in volume over the next several decades[7].

Bearing surface materials and implant designs have continued to evolve to improve implant survival and patient satisfaction. The development of highly cross-linked polyethylene liners has led to decreased wear and improved TKA survival[8,9]. Moreover, a variety of component surfaces have been developed in an attempt to improve implant wear[10-12]. Cobalt-chrome alloys (CoCr) have traditionally been utilized for TKA femoral components, but different material options have emerged. Titanium nitride is a coating applied to implants by physical vapor deposition aimed at improving the properties of traditional CoCr[13]. Oxidized zirconium (OXINIUM™; Smith and Nephew, Inc., Memphis, TN) is a surface-modified metal that was introduced in 2004 with the goal of improving implant survival and longevity by decreasing adhesive and abrasive wear[12,14].

Implant design has progressively evolved with an emphasis on improving kinematics to better mimic the native knee. Some of the first TKA designs included hinged designs that fell out of favor due to their high rates of mechanical failure [15]. TKA designs were refined to minimize knee constraint in an attempt to decrease the rates of failure[15]. The CR TKA prosthesis that was assessed in this study was designed to replicate the shape and position of a native knee, especially coronal alignment and joint line obliquity, to aim for improved function of the knee. Smith *et al*[16] demonstrated that this prosthesis achieved increased posterior femoral rollback and axial rotation when compared to other CR TKA designs[16,

17]. Similarly, the prosthesis also demonstrated better rotation flexion and muscle activation during free walking[18].

To our knowledge, sparse research exists that has examined clinical outcomes of a large cohort of patients undergoing a CR TKA utilizing a kinematically designed implant. Moreover, there is no large-scale study to our knowledge assessing patient reported outcome measures (PROMs) in patients with this implant design. Our study aimed to assess mid-term clinical outcomes and PROMs of this kinematically designed CR TKA implant.

MATERIALS AND METHODS

Study design

A retrospective, multi-surgeon study was designed to assess this kinematically designed CR Knee System (JOURNEY™ II CR; Smith and Nephew, Inc., Memphis, TN) (Figure 1) at an urban, academic medical institution. Institutional Review Board (IRB) approval was received prior to the initiation of the study. All procedures in this study were performed by fellowship-trained arthroplasty surgeons between 2015 and 2021. Only patients with a minimum of two-years of clinical follow-up with an orthopedic surgeon were included in this study. During the study period, multiple implant systems and designs were utilized for TKA in the authors' institution. Only patients who received the study CR TKA system were included.

Generally, a standard medial parapatellar approach was utilized when performing a primary TKA on a native knee. After adequate exposure, the tibial and femoral bone cuts were made according to the preoperative planning. Component sizing, femoral bearing surface material (cobalt-chrome or oxidized zirconium), and liner constraint design (standard CR or deep dish) were based on surgeon preference at the time of the procedure.

Data collection and outcome measures

Patient demographics, surgical information, and outcome data were queried from the institution's electronic medical record (EPIC Systems, Verona, Wisconsin). Patient demographics included age, sex, race, smoking status, insurance, American Society of Anesthesiologists (ASA) score, body mass index (BMI), Charlson Comorbidity Index (CCI), and primary diagnosis at time of TKA. Surgical information included operative time from skin incision to skin closure, liner and femoral bearing surface type, anesthesia type, and use of technology. Clinical outcome data was collected during routine follow-up visits scheduled at the surgeon's discretion. Outcome data included length of stay (LOS), discharge disposition, 90-d emergency department (ED) visits, 90-d readmissions, revisions, and PROMs. Revision surgery included any case in which a procedure was performed on the knee of the index procedure due to a complication.

PROMs

The PROMs collected in the present study included Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS JR) and Patient-Reported Outcomes Measurement Information System (PROMIS®) scores which are widely used and validated metrics for assessing preoperative and postoperative joint function. The KOOS JR is a 6-item questionnaire which has largely replaced the original 40-item KOOS. The 6-items feature answer choices on a 5-point Likert scale ranging from "None" to "Extreme" and cover domains of pain, function and activities of daily living. The survey asks patients to rate their degree of difficulty with activities such as going up and down stairs, bending to the floor and rising from a sitting position, among others. The summed raw score scales to an interval score between 0 and 100, where a score of 0 represents complete knee disability and a score of 100 indicates perfect knee function.

In addition to KOOS JR scores, PROMIS scores were collected in the present study as the PROMIS item banks can offer a more comprehensive assessment of patient perceptions compared to the joint-specific KOOS JR. PROMIS scores analyzed in the this study were pain intensity, pain interference, mobility, and physical health. PROMIS surveys ask patients on a scale of 1 to 5 to rate how much a particular statement applies to them. For example, on the PROMIS mobility survey, patients are asked to rate how often they experience difficulty when going up or down stairs on a scale of 1 ("Never") to 5 ("Always"). These individual items are summed up to calculate a raw sum score which is then standardized to a T-score with a mean of 50 and standard deviation of 10. Higher PROMIS functional scores indicate higher levels of ability and higher PROMIS pain scores indicate greater levels of pain. All PROMs scores were collected preoperatively, at six months postoperatively, and at two-years postoperatively.

Data analysis

Averages and ranges or standard deviations were computed for all interval and ratio values including age, BMI, CCI, LOS, operative time, and PROMs. Percentages were computed for all nominal and ordinal variables including sex, race, smoking status, ASA score, insurance status, discharge disposition, ED visit rate, readmission rate, and revision rate. The significance of improvements in mean PROMs scores from preoperative scores to scores collected at six months and two-years postoperatively was analyzed using Independent Samples *t*-tests. Statistical analysis was done using Microsoft Excel software (Microsoft Corporation, Richmond, WA) and IBM SPSS Statistics (Version 28; IBM Corporation, Armonk, NY). *P* values less than 0.05 were considered statistically significant.

RESULTS

Of the 255 patients who received the study implant, 65.5% were female, 43.8% were White, and patients had an average

Table 1 Patient demographics

	Knees (*n* = 255)
Sex, *n* (%)	
Male	88 (34.5)
Female	167 (65.5)
Age (yr) [range]	60.6 [32-83]
Race, *n* (%)	
White	112 (43.9)
African American	63 (24.7)
Asian	10 (3.9)
Other	70 (27.5)
Smoking status, *n* (%)	
Current	14 (5.5)
Former	92 (36.1)
Never	149 (58.4)
Insurance status, *n* (%)	
Medicare	79 (31.0)
Medicaid	32 (12.5)
Commercial	144 (56.5)
ASA score, *n* (%)	
1	4 (1.6)
2	148 (58.0)
3	102 (40.0)
4	1 (0.4)
BMI (kg/m^2) [range]	33.5 [16.8-57.8]
CCI	3.0 ± 2.2
Primary diagnosis, *n* (%)	
Primary OA	247 (96.9)
Post-Traumatic OA	7 (2.7)
AVN	1 (0.4)

ASA: American Society of Anesthesiologists; BMI: Body mass index; CCI: Charlson Comorbidity Index; OA: Osteoarthritis; AVN: Avascular necrosis.

age of 60.6 (range, 32 to 83) years. Most patients were never smokers (58.4%), had an ASA score of 2 (58.0%) or 3 (40.0%), and had an average BMI of 33.5 (range, 16.8 to 57.8) kg/m^2. Primary osteoarthritis (96.9%) was the most common primary diagnosis (Table 1). The mean surgical time was 105.3 (range, 65 to 237) minutes with 83.5% of patients receiving a standard CR liner and 16.5% receiving a deep-dish CR liner. Most patients received a cobalt-chrome femoral bearing (77.6%) and the rest (22.4%) received an Oxinium™ femoral bearing. Computer-Assisted Navigation was utilized in 34.5% of cases and Robotic-Assisted Surgery was utilized in 3.1% of cases.

Mean LOS postoperatively was 2.1 (range, 0.3 to 19.5) d, and most patients were discharged home (92.5%) (Table 2). Within 90 d, 18 patients (7.1%) presented to the ED with 12 of these patients (4.7%) presenting for orthopedic-related complications. Three patients (1.2%) were readmitted within 90 d due to postoperative complications. One patient was readmitted for a gastric bleed due to non-steroidal anti-inflammatory drug (NSAID) use, one patient was readmitted for an acute kidney injury (AKI), and one patient was readmitted for a periprosthetic joint infection (PJI) (Table 3).

With mean time to latest follow-up of 3.3 (range, 2.1 to 6.6) years, the cohort exhibited a revision-free survivorship of 98.4%. Four patients (1.6%) required revision TKA surgery, all of which occurred within two-years of the primary TKA. The patient readmitted in the setting of PJI ultimately required multiple revision surgeries to treat the PJI; a debridement, antibiotics, and implant retention (DAIR) procedure was performed during the first readmission followed by a later two-stage revision arthroplasty followed by another DAIR. Additionally, two patients required revision surgery due to

Table 2 Intraoperative and implant variables

	Knees (*n* = 255)
Operative time (min) [range]	105.3 [65-237]
Liner, *n* (%)	
Standard	213 (83.5)
Deep dish	42 (16.5)
Anesthesia, *n* (%)	
General	21 (8.2)
Spinal/Regional/Block	234 (91.8)
Bearing surface, *n* (%)	
Oxidized Zirconium-on-Polyethylene	57 (22.4)
Cobalt Chrome-on-Polyethylene	198 (77.6)
Technology, *n* (%)	
Manual	158 (62.0)
Computer navigation	88 (34.5)
Robotic assistance	9 (3.5)

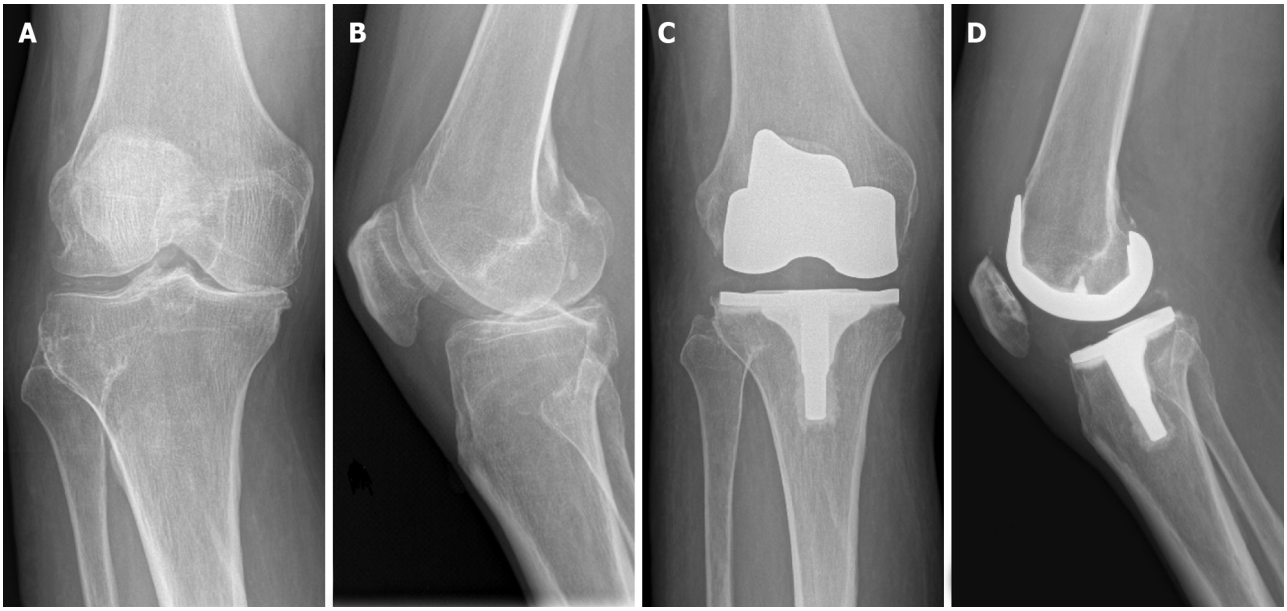


Figure 1 Preoperative anterior-posterior, postoperative anterior-posterior and lateral radiographs. A and B: Preoperative anterior-posterior (AP) and lateral radiographs demonstrating severe primary osteoarthritis; C and D: Postoperative AP and lateral radiographs demonstrating cruciate retaining total knee arthroplasty.

arthrofibrosis and one patient required revision surgery due to aseptic femoral loosening. One of the patients with arthrofibrosis received a manipulation under anesthesia four months after TKA and then, two months later, underwent scar resection and a liner exchange maintaining a CR design. The other patient who experienced arthrofibrosis had a revision surgery twelve months postoperatively that exchanged the polyethylene liner and the femoral component. The patient with aseptic femoral loosening underwent a replacement of the polyethylene liner and the femoral component thirteen months postoperatively (Table 4). Four patients (2.0%) out of the 198 patients who received cobalt chrome bearing surface femoral components required revision surgery, whereas none of the 57 patients who received oxidized zirconium bearing surface femoral components required revision (Table 5). Three patients (1.4%) out of the 213 patients who received standard CR polyethylene liners required revision surgery, and one patient (2.4%) of the 42 patients who received deep dish CR polyethylene liners required revision (Table 6).

Compared to preoperative scores, at six months postoperatively there were significant improvements in KOOS JR (43.3 *vs* 56.5, $P < 0.0001$), PROMIS Pain Intensity (55.6 *vs* 50.1, $P < 0.0001$), PROMIS Pain Interference (65.3 *vs* 61.4, $P < 0.0001$), PROMIS Mobility (35.5 *vs* 38.1, $P < 0.0001$), and PROMIS Physical Health (39.5 *vs* 41.8, $P = 0.029$). At 2 years postoper-

Table 3 Short-term clinical outcomes

	Knees (*n* = 255)
LOS (days) [range]	2.1 [0.3-19.5]
Time to follow-up (years) [range]	3.3 [2.1-6.6]
Discharge disposition, *n* (%)	
Home	236 (92.5)
SNF	16 (6.3)
ARF	3 (1.2)
90-d ED visits, *n* (%)	18 (7.1)
Non-orthopedic related	6 (2.4)
Orthopedic related	12 (4.7)
Knee pain and swelling	6
Knee pain and erythema	1
Calf pain and lightheadedness	1
Groin pain	1
VTE	1
NSAID poisoning	1
Opioid poisoning	1
90-d readmissions, *n* (%)	3 (1.2)
PJI	1
AKI	1
Gastric bleed due to NSAID poisoning	1

LOS: Length of stay; SNF: Skilled nursing facility; ARF: Acute rehabilitation facility; ED: Emergency department; AKI: Acute kidney injury; NSAID: Non-steroidal anti-inflammatory drug; VTE: Venous thromboembolism; PJI: Peri-prosthetic joint infection.

Table 4 Long-term clinical outcomes

	Knees (*n* = 255)	Mean time to revision (years) [range]
Revisions, *n* (%)	4 (1.6)	1.1 [0.7-1.5]
Arthrofibrosis	2	1.3 [1.1-1.5]
Aseptic femoral loosening	1	1.1
PJI	1	0.7

PJI: Peri-prosthetic joint infection.

atively, patients reported further improvements in KOOS JR and all PROMIS measures (Table 7).

DISCUSSION

Some of the earliest TKA implants were restrictive, hinged designs that progressively evolved to less restrictive CR TKA designs over the last few decades[15]. The kinematically designed TKA implant, offers a unique asymmetric design intended to replicate the shape and biomechanics of a native knee and reproduces the joint line obliquity. This design allows for improved femoral rollback and knee kinematics compared to other implants[16,18]. Di Benedetto *et al*[18] performed a pilot study comparing the study implant to a symmetric TKA implant design and demonstrated that the study implant offered better pain resolution, rotational flexion, and muscle activation during free walking[18]. Improved pain control and overall knee strength have been shown to improve the likelihood of home discharges[19]. These factors likely lead to the exceptional rate of home discharges seen in our patient cohort (92.5%) compared to a rate of 85.3% seen

Table 5 Subanalysis: Survivorship by bearing surface material

	Cobalt chrome (*n* = 198)	Oxidized zirconium (*n* = 57)
Revisions, *n* (%)	4 (2.0)	0 (0)
Arthrofibrosis	2	0
Aseptic femoral loosening	1	0
PJI	1	0

PJI: Peri-prosthetic joint infection.

Table 6 Subanalysis: Survivorship by liner type

	Standard (*n* = 213)	Deep dish (*n* = 42)
Revisions, *n* (%)	3 (1.4)	1 (2.4)
Arthrofibrosis	1	1
Aseptic femoral loosening	1	0
PJI	1	0

PJI: Peri-prosthetic joint infection.

in national databases[20].

The implant design and materials utilized in TKA can have a significant influence on complication and revision rates postoperatively. D'Apuzzo *et al*[21] examined a state-wide database of primary TKA patients and found that there was a 1.8% rate of TKA-specific readmissions within 30 d of surgery[21]. Patients in our study had a 1.2% rate of readmission within 90 d of surgery. Koh *et al*[22] examined 11134 patients undergoing primary TKA and found that patients had a 1.9% cumulative incidence of revision within two-years. Moreover, their study demonstrated 1.03% of patients required septic revision surgery and 0.86% of patients required aseptic revision surgery[22]. With a mean time to latest follow-up of 3.3 years, our patient cohort had a lower all-cause revision rate of 1.6%, including a 0.4% septic revision rate and a 1.2% aseptic revision rate. Of the three aseptic revisions in the cohort, one was solely a liner exchange while the other two replaced the femoral component in addition to the liner. No tibial or patellar components were replaced in aseptic cases.

Although TKA remains a relatively successful orthopedic procedure, some patients can be dissatisfied after their procedure. Improving patient outcomes may result in decreased revision rates with Robertsson *et al*[4] demonstrating that patients with unrevised TKAs were comprised of a higher portion of satisfied patients compared to those that required a revision[4]. Our study demonstrated significant improvements in KOOS JR and PROMIS measures at 6 months postoperatively and further improvement at 2 years postoperatively. Similarly, Lutes and Fitch[23] performed a retrospective analysis comparing the studied CR TKA design with a conventional CR TKA design and demonstrated that patients with the kinematically designed TKA implant had significant improvement in short-term functional outcomes [23].

There are several limitations that should be acknowledged in our current study. The use of retrospective data for analysis imparts inherent limitations including data inaccuracies and missing information. Moreover, this study may not be able to appropriately control for confounding factors since it lacks a control group. The generalizability of our results may not be applicable to all patient populations outside of high-volume urban centers. Moreover, if patients received follow-up care such as revisions at other institutions, the data available may not capture these outside encounters. Finally, multiple surgeons were involved in this study, which may introduce heterogeneity into surgical technique and postoperative protocol, possibly influencing patient outcomes. However, most procedures were performed by a single surgeon who utilized computer navigation for mechanical alignment. Tibial cuts were performed in approximately neutral coronal alignment and a posterior femoral referencing guide in approximately 3° of external rotation was used to appropriately size and position the cutting block for the femoral cuts.

CONCLUSION

Our study demonstrated that the studied kinematically designed cruciate-retaining TKA is an effective implant design offering excellent clinical and patient-reported outcomes with low complication rates. Only four patients required revision surgery resulting in a revision-free survival rate of 98.4% with a mean follow-up time of 3.3 years. The results of our study demonstrate the utility of this kinematically designed implant in the setting of primary TKA.

Table 7 Patient reported outcome measures (mean ± SD)

	Knees (*n* = 255)	*P* value
KOOS JR		
Preoperative	43.3 (13.0)	
6 mo	56.5 (16.1)	
2 yr	62.2 (13.9)	
Δ Preop to 6 mo	13.2 (16.4)	< 0.0001
Δ Preop to 2 yr	18.9 (16.9)	< 0.0001
PROMIS pain intensity		
Preoperative	55.6 (6.9)	
6 mo	50.1 (8.1)	
2 yr	48.6 (7.6)	
Δ Preop to 6 mo	-5.5 (8.2)	< 0.0001
Δ Preop to 2 yr	-7.0 (6.7)	< 0.0001
PROMIS pain interference		
Preoperative	65.3 (5.7)	
6 mo	61.4 (8.0)	
2 yr	59.5 (8.0)	
Δ Preop to 6 mo	-3.9 (7.5)	< 0.0001
Δ Preop to 2 yr	-5.8 (6.3)	< 0.0001
PROMIS mobility		
Preoperative	35.5 (4.1)	
6 mo	38.1 (4.3)	
2 yr	40.3 (5.6)	
Δ Preop to 6 mo	2.6 (4.8)	< 0.0001
Δ Preop to 2 yr	4.8 (3.5)	< 0.0001
PROMIS physical health		
Preoperative	39.5 (7.3)	
6 mo	41.8 (6.9)	
2 yr	42.0 (6.1)	
Δ Preop to 6 mo	2.3 (6.6)	0.029
Δ Preop to 2 yr	2.5 (5.4)	0.045

KOOS JR: Knee Injury and Osteoarthritis Outcome Score for Joint Replacement; PROMIS: Patient-Reported Outcomes Measurement Information System.

ARTICLE HIGHLIGHTS

Research background

This study investigates the effectiveness of a specialized knee implant in improving patient outcomes. Focusing on a kinematically designed cruciate retaining (CR) total knee replacement, the research explores its mid-term clinical performance and patient-reported outcomes. It addresses a gap in the existing literature by assessing the implant's impact on patient satisfaction, functional improvement, and complications, emphasizing the need for comprehensive evaluation of specific implant designs to enhance total knee arthroplasty (TKA) procedures. Every novel implant should be evaluated and early and mid-term reports should be published in order to single out low performing implants and limit the effect on the public.

Research motivation

The research motivation lies in the need to address existing challenges in knee arthroplasty, particularly regarding implant design and patient outcomes. We think it is important to have early and midterm reports of novel implants in order to catch early failures and limit usage of failing implants. Key issues, such as achieving optimal knee functionality, improving patient satisfaction, and minimizing postoperative complications, serve as the primary focus. Solving these problems is critical for advancing the field of orthopedics, guiding future research in enhancing implant technologies, refining surgical techniques, and ultimately enhancing the quality of life for individuals undergoing knee replacement surgeries.

Research objectives

The primary aim was to evaluate the short-term and mid-term clinical outcomes as well as patient-reported outcome measures associated with a kinematically designed CR TKA. Through comprehensive clinical assessments and patient reported outcome measures (PROMs), the study aimed to ascertain the efficacy, functional improvements, and patient satisfaction levels achieved with this specific TKA design. This study is significant in the field of orthopedics because it provides empirical evidence regarding the performance and patient-reported experiences related to this particular kinematic design, thereby informing future TKA approaches and enhancing patient care in the orthopedic field.

Research methods

In the conducted retrospective study, we analyzed a cohort of patients who had previously undergone CR TKA by collecting clinical and PROMs data from medical records to assess the short-term and mid-term outcomes. While the design of the study is well-established, the CR TKA implant analyzed is a novel, new device that has been introduced within the past decade and with little available published data on outcomes. Thus, this study will greatly assist surgeons who wish to make better-informed risk assessment when selecting this novel implant for their patients. As a result, this study is truly clinically relevant and innovative in the field of total joint arthroplasty.

Research results

Postoperative hospital stay averaged 2.1 d and most patients were discharged to home (92.5%). The 90 d emergency department visit rate was 7.1% and 90 d readmission rate was 1.2%. The overall revision-free survivorship rate was 98.4% with an average follow-up of 3.3 years. Significant improvements in patient-reported outcome measures [Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS JR) and Patient-Reported Outcomes Measurement Information System (PROMIS®) scores] were observed at six months and further improvements at two-years postoperatively, indicating favorable surgical outcomes and patient satisfaction. This study contributes vital real-world data to the field of knee prosthetic design, showcasing a notably high revision-free survivorship rate of 98.4% over a 3.3-year average follow-up. However, challenges persist, notably in reducing the occurrences of complications like periprosthetic joint infections and addressing issues such as arthrofibrosis and aseptic loosening, which demand further investigation and targeted intervention strategies for improved patient care and long-term surgical success.

Research conclusions

New theories proposed: The study doesn't explicitly mention proposing new theories, but it does contribute to the growing body of evidence supporting the effectiveness of kinematically designed CR TKA implants. The findings suggest that this implant design offers favorable clinical outcomes, low complication rates, and notable improvements in PROMs for patients undergoing primary TKA. New methods used: The study employed a retrospective, multi-surgeon design that gathered data from 255 knees over a period from March 2015 to July 2021. The research collected patient demographics, surgical details, clinical outcomes, and PROMs data through electronic medical records. It specifically utilized the KOOS JR and PROMIS® scores to assess patient-reported outcomes. Statistical analysis, including Independent Samples *t*-tests, was used to determine the significance of improvements in PROMs scores.

Research perspectives

Future research in this field should concentrate on extending long-term follow-up beyond the current mean of 3.3 years to evaluate sustained implant performance. A prospective study, tracking patients undergoing CR TKA from preoperative stages through long-term postoperative follow-up, could offer comprehensive insights into its performance, complications, and patient-reported outcomes, further solidifying its efficacy and addressing any evolving concerns in real-time. Comparative studies against existing TKA designs, assessment across diverse patient populations, and investigations into health economics and cost-effectiveness are essential for validating this implant design's superiority, understanding its efficacy in varied demographics, and informing healthcare decisions. Additionally, biomechanical analyses to comprehend how the implant's design influences joint mechanics could aid in further optimizing its performance and durability.

FOOTNOTES

Author contributions: All authors contributed to the study conception and design; Material preparation, data collection and analysis were performed by Katzman JL, Habibi AA, Haider MA, Cardillo C, Fernandez-Madrid I, Meftah M, Schwarzkopf R; The first draft of the manuscript was written by Katzman JL and Habibi AA; Haider MA, Cardillo C, Fernandez-Madrid I, Meftah M, and Schwarzkopf R

wrote, reviewed, and revised parts of the manuscript; All authors read and approved the final manuscript.

Institutional review board statement: The study was reviewed and approved by the NYU Langone Institutional Review Board, No. i17-01223.

Informed consent statement: Waiver of informed consent.

Conflict-of-interest statement: Morteza Meftah reports financial relationships with multiple companies including CAIRA Surgical (Stock or stock Options), Conformis (Paid consultant), Constance (Stock or stock Options), Innomed (IP royalties), Intellijoint (Paid consultant) and involvement with the following organizations ISTA (Board or committee member) and Orthopedics (Editorial or governing board). Ran Schwarzkopf discloses financial relationships with Gauss Surgical (Stock or stock Options), Intellijoint (Paid consultant; Stock or stock Options), PSI (Stock or stock Options), Smith & Nephew (IP royalties; Paid consultant; Research support), and Zimmer (Paid consultant) and oganizational associations with AAOS (Board or committee member), American Association of Hip and Knee Surgeons (Board or committee member), Arthroplasty Today (Editorial or governing board), and Journal of Arthroplasty (Editorial or governing board). The remaining authors, Jonathan L. Katzman, Akram A. Habibi, Muhammad A. Haider, Casey Cardillo, and Ivan Fernandez-Madrid, have nothing to disclose.

Data sharing statement: The data presented in this retrospective study were obtained following approval from the Institutional Review Board (IRB) (i17-01223) which granted permission for the use of anonymized patient information without individual consent. The retrospective nature of this study involved the analysis of de-identified retrospective data, ensuring anonymity and minimizing the risk of identification. As such, no explicit consent from each patient was obtained due to the retrospective design and the anonymization process. The IRB approval ensures compliance with ethical guidelines and regulations regarding data use and protection. For data sharing purposes, the presented data, while anonymized, are available upon request to qualified researchers, subject to appropriate ethical approvals and data sharing agreements.

Country/Territory of origin: United States

ORCID number: Jonathan L Katzman 0000-0002-3973-0735; Ivan Fernandez-Madrid 0000-0002-3191-7204; Ran Schwarzkopf 0000-0003-0681-7014.

S-Editor: Fan JR
L-Editor: A
P-Editor: Yuan YY

REFERENCES

1 **Marya SKS**, Singh C. Options and limitations of implant constraint. *J Orthop* 2021; **23**: 18-24 [PMID: 33424186 DOI: 10.1016/j.jor.2020.12.013]
2 **Richard S**, Volatile T. Twelve Years' Experience with Posterior Cruciate-retaining Total Knee Arthroplasty. *Clin Orthop Relat Res* 1986; **4**
3 **Wong JM**, Khan WS, Chimutengwende-Gordon M, Dowd GS. Recent advances in designs, approaches and materials in total knee replacement: literature review and evidence today. *J Perioper Pract* 2011; **21**: 165-171 [PMID: 21834287 DOI: 10.1177/175045891102100503]
4 **Robertsson O**, Dunbar M, Pehrsson T, Knutson K, Lidgren L. Patient satisfaction after knee arthroplasty: a report on 27,372 knees operated on between 1981 and 1995 in Sweden. *Acta Orthop Scand* 2000; **71**: 262-267 [PMID: 10919297 DOI: 10.1080/000164700317411852]
5 **Noble PC**, Conditt MA, Cook KF, Mathis KB. The John Insall Award: Patient expectations affect satisfaction with total knee arthroplasty. *Clin Orthop Relat Res* 2006; **452**: 35-43 [PMID: 16967035 DOI: 10.1097/01.BLO.0000238825.63648.1E]
6 **Lau RL**, Gandhi R, Mahomed S, Mahomed N. Patient satisfaction after total knee and hip arthroplasty. *Clin Geriatr Med* 2012; **28**: 349-365 [PMID: 22840303 DOI: 10.1016/j.cger.2012.05.001]
7 **Shichman I**, Askew N, Habibi A, Nherera L, Macaulay W, Seyler T, Schwarzkopf R. Projections and Epidemiology of Revision Hip and Knee Arthroplasty in the United States to 2040-2060. *Arthroplast Today* 2023; **21**: 101152
8 **Greenwald AS**, Bauer TW, Ries MD; Committee on Biomedical Engineering, Committee on Hip and Knee Arthritis. New polys for old: contribution or caveat? *J Bone Joint Surg Am* 2001; **83-A** Suppl 2: 27-31 [PMID: 11685841 DOI: 10.2106/00004623-200100021-00007]
9 **Brown TS**, Van Citters DW, Berry DJ, Abdel MP. The use of highly crosslinked polyethylene in total knee arthroplasty. *Bone Joint J* 2017; **99-B**: 996-1002 [PMID: 28768774 DOI: 10.1302/0301-620X.99B8.BJJ-2017-0028.R1]
10 **Breugem SJM**, Linnartz J, Sierevelt I, Bruijn JD, Driessen MJM. Evaluation of 1031 primary titanium nitride coated mobile bearing total knee arthroplasties in an orthopedic clinic. *World J Orthop* 2017; **8**: 922-928 [PMID: 29312851 DOI: 10.5312/wjo.v8.i12.922]
11 **Kennard E**, Scholes SC, Sidaginamale R, Gangadharan R, Weir DJ, Holland J, Deehan D, Joyce TJ. A comparative surface topographical analysis of explanted total knee replacement prostheses: Oxidised zirconium vs cobalt chromium femoral components. *Med Eng Phys* 2017; **50**: 59-64 [PMID: 29042144 DOI: 10.1016/j.medengphy.2017.10.003]
12 **Laskin RS**. An oxidized Zr ceramic surfaced femoral component for total knee arthroplasty. *Clin Orthop Relat Res* 2003; 191-196 [PMID:

14646761 DOI: 10.1097/01.blo.0000093003.90435.1f]

13 **Wisbey A**, Gregson PJ, Tuke M. Application of PVD TiN coating to Co-Cr-Mo based surgical implants. *Biomaterials* 1987; **8**: 477-480 [PMID: 3427147 DOI: 10.1016/0142-9612(87)90085-8]

14 **Ries MD**, Salehi A, Widding K, Hunter G. Polyethylene wear performance of oxidized zirconium and cobalt-chromium knee components under abrasive conditions. *J Bone Joint Surg Am* 2002; **84-A** Suppl 2: 129-135 [PMID: 12479351 DOI: 10.2106/00004623-200200002-00018]

15 **Ranawat AS**, Ranawat CS. The history of total knee arthroplasty. The Knee Joint: Surgical Techniques and Strategies. New York: Springer, 2012: 699-707

16 **Smith LA**, Nachtrab J, LaCour M, Cates H, Freeman MG, Komistek RD. In Vivo Knee Kinematics: How Important Are the Roles of Femoral Geometry and the Cruciate Ligaments? *J Arthroplasty* 2021; **36**: 1445-1454 [PMID: 33214016 DOI: 10.1016/j.arth.2020.10.020]

17 **Dennis DA**, Komistek RD, Mahfouz MR, Walker SA, Tucker A. A multicenter analysis of axial femorotibial rotation after total knee arthroplasty. *Clin Orthop Relat Res* 2004; 180-189 [PMID: 15534541 DOI: 10.1097/01.BLO.0000148777.98244.84]

18 **Di Benedetto P**, Vidi D, Colombo A, Buttironi MM, Cainero V, Causero A. Pre-operative and post-operative kinematic analysis in total knee arthroplasty. A pilot study. *Acta Biomed* 2019; **90**: 91-97 [PMID: 31821291 DOI: 10.23750/abm.v90i12-S.8984]

19 **Causey-Upton R**, Howell DM, Kitzman PH, Custer MG, Dressler EV. Factors Influencing Discharge Readiness After Total Knee Replacement. *Orthop Nurs* 2019; **38**: 6-14 [PMID: 30676569 DOI: 10.1097/NOR.0000000000000513]

20 **DeMik DE**, Carender CN, Glass NA, Callaghan JJ, Bedard NA. More Patients Are Being Discharged Home After Total Knee Arthroplasty, However Rates Vary Between Large Databases. *J Arthroplasty* 2021; **36**: 173-179 [PMID: 32843255 DOI: 10.1016/j.arth.2020.07.059]

21 **D'Apuzzo M**, Westrich G, Hidaka C, Jung Pan T, Lyman S. All-Cause Versus Complication-Specific Readmission Following Total Knee Arthroplasty. *J Bone Joint Surg Am* 2017; **99**: 1093-1103 [PMID: 28678122 DOI: 10.2106/JBJS.16.00874]

22 **Koh CK**, Zeng I, Ravi S, Zhu M, Vince KG, Young SW. Periprosthetic Joint Infection Is the Main Cause of Failure for Modern Knee Arthroplasty: An Analysis of 11,134 Knees. *Clin Orthop Relat Res* 2017; **475**: 2194-2201 [PMID: 28573549 DOI: 10.1007/s11999-017-5396-4]

23 **Lutes W**, Fitch D. Comparison of functional outcomes following total knee arthroplasty with a conventional implant design or one designed to mimic natural knee kinematics. Presented at: 39th SICOT Orthopaedic World Congress; 2018 Oct 10-13; Montreal, Canada. Available from: https://www.sicot.org/montreal

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 129-138

DOI: 10.5312/wjo.v15.i2.129

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Retrospective Study

Academic productivity correlates with industry earnings in foot and ankle fellowship programs in the United States: A retrospective analysis

Albert T Anastasio, Anthony N Baumann, Kempland C Walley, Kyle J Hitchman, Conor O'Neill, Jonathan Kaplan, Samuel B Adams

Specialty type: Orthopedics

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Papazafiropoulou A, Greece

Received: October 19, 2023
Peer-review started: October 19, 2023
First decision: November 29, 2023
Revised: December 8, 2023
Accepted: January 3, 2024
Article in press: January 3, 2024
Published online: February 18, 2024

Albert T Anastasio, Conor O'Neill, Jonathan Kaplan, Samuel B Adams, Department of Orthopedic Surgery, Duke University Hospital, Durham, NC 27710, United States

Anthony N Baumann, College of Medicine, Northeast Ohio Medical University, Rootstown, OH 44272, United States

Kempland C Walley, Department of Orthopedic Surgery, University of Michigan, Ann Arbor, MI 48109, United States

Kyle J Hitchman, School of Osteopathic Medicine, Campbell University, Lillington, NC 27546, United States

Corresponding author: Albert T Anastasio, MD, Doctor, Surgeon, Department of Orthopedic Surgery, Duke University Hospital, 200 Trent Dr, Durham, NC 27710, United States.
albert.anastasio@gmail.com

Abstract

BACKGROUND

The study investigates the connection between academic productivity and industry earnings in foot and ankle orthopedic surgery fellowships. Utilizing metrics like the H-index and Open Payments Database (OPD) data, it addresses a gap in understanding the relationship between scholarly achievements and financial outcomes, providing a basis for further exploration in this specialized medical field.

AIM

To elucidate the trends between academic productivity and industry earnings across foot and ankle orthopedic surgery fellowship programs in the United States.

METHODS

This study is a retrospective analysis of the relationship between academic productivity and industry earnings of foot and ankle orthopedic surgery fellowships at an individual faculty and fellowship level. Academic productivity was defined *via* H-index and recorded from the Scopus website. Industry earnings

were recorded from the OPD.

RESULTS

Forty-eight foot and ankle orthopedic surgery fellowships (100% of fellowships) in the United States with a combined total of 165 physicians (95.9% of physicians) were included. Mean individual physician (n = 165) total life-time earnings reported on the OPD website was United States Dollar (USD) 451430.30 ± 1851084.89 (range: USD 25.16-21269249.85; median: USD 27839.80). Mean physician (n = 165) H-index as reported on Scopus is 14.24 ± 12.39 (range: 0-63; median: 11). There was a significant but weak correlation between individual physician H-index and individual physician total life-time earnings (P < 0.001; Spearman's rho = 0.334) and a significant and moderate positive correlation between combined fellowship H-index and total life-time earnings per fellowship (P = 0.004, Spearman's rho = 0.409).

CONCLUSION

There is a significant and positive correlation between academic productivity and industry earnings at foot and ankle orthopedic surgery fellowships in the United States. This observation is true on an individual physician level as well as on a fellowship level.

Key Words: Sunshine act; Foot and ankle; Orthopedic surgery; Orthopedic fellowship; Industry earnings

Core Tip: We determined there to be a statistically significant correlation between individual physician H-index and individual physician total life-time, non-research-related earnings reported on Centers for Medicare and Medicaid Services. This finding remained true when collective H index of the faculty at a given orthopedic foot and ankle fellowship was correlated to collective industry payments to the faculty at that fellowship. Further efforts should seek to characterize any potential disadvantages to the high degree of industry involvement of the most academically productive foot and ankle surgeons.

Citation: Anastasio AT, Baumann AN, Walley KC, Hitchman KJ, O'Neill C, Kaplan J, Adams SB. Academic productivity correlates with industry earnings in foot and ankle fellowship programs in the United States: A retrospective analysis. *World J Orthop* 2024; 15(2): 129-138

URL: https://www.wjgnet.com/2218-5836/full/v15/i2/129.htm

DOI: https://dx.doi.org/10.5312/wjo.v15.i2.129

INTRODUCTION

The Physician Payments Sunshine Act was established in 2010 as part of the Affordable Care Act[1]. The Sunshine Act served to authorize the establishment of a publicly accessible electronic record of physician financial relationships with industry termed the "Open Payments" public database[1]. The database, geared towards improved physician accountability for potential industry biases, requires the recording of all payments greater than USD 10 made to physicians from drug and device manufacturers. Payments are categorized as either general payments, ownership interests, or research payments[2]. The vast majority of payments to orthopedic surgeons are characterized as royalties and license fees (69%, USD 74.4 million) with consulting fees (13%, USD 13.9 million) and non-consulting services (5%, USD 5.8 million) also awarded as sizeable yearly payments[3].

The Open Payments Database (OPD) reveals substantial industry involvement within foot and ankle surgery, with 802 orthopedic foot and ankle surgeons receiving nearly USD 39 million from industry through 29442 transactions during a 3-year period[4]. Relationships with industry can be complex; some studies have revealed no association between industry involvement and positive research findings[5], whereas others have demonstrated a potential source of bias, with industry funding leading to a higher likelihood of positive outcome reporting regarding a specific implant or pharmaceutical[6,7]. Orthopedic foot and ankle surgeons are heavily influenced by the mentors they have worked with throughout their training processes, including residency and fellowship periods[8]. Thus, choice in foot and ankle fellowship will likely influence the practice patterns, academic interests, and level of future involvement with industry of surgeons-in-training.

A substantial body of work has explored the OPD across physician subspecialities, attempting to understand demographic trends in industry payments and delineate sources of potential bias in practice patterns[9-13]. However, no study to date has tabulated the total industry payments to the faculty at a particular foot and ankle fellowship program and explored the correlation with academic productivity of that fellowship. Thus, the purpose of this study was to elucidate the trends between research output and involvement in industry across foot and ankle fellowship programs. Our primary goal was to explore whether academic productivity at a particular fellowship correlates with industry compensation. Our hypothesis was that higher industry payments would be associated with increased total research

productivity, defined *via* the H-index, at a given fellowship.

MATERIALS AND METHODS

Study set-up

This study is a retrospective analysis of the relationship between academic productivity and industry earnings of foot and ankle orthopedic surgery fellowships at an individual faculty level as well as a fellowship level. The current study used the Centers for Medicare and Medicaid Services (CMS) website (https://openpaymentsdata.cms.gov/search) for physician earnings and payments, the Scopus website for physician H-index (https://openpaymentsdata.cms.gov/search), and the American Orthopedic Foot and Ankle Society website for fellowship data (https://www.aofas.org/education/fellowship-match-program/orthopedic-foot-and-ankle-fellowship-programs) while visiting each individual fellowship site for information about the fellowship and faculty. All information found on these databases is public access, therefore IRB approval for this study was not necessary.

Data extraction

Data extraction was performed by one author. Data collected included H-index per individual physician, total life-time earnings per individual physician, total payments made to individual physician, combined H-index per fellowship, combined total life-time earnings per fellowship, average total life-time earnings per physician per fellowship, and average total life-time earnings per fellowship per H-index. For subgroup analysis, individual physicians were placed one of four groups depending on the quartile of their H-index.

Statistical analysis

Statistical analysis was completed using SPSS version 29.0 (IBM Corp., Armonk, NY, United States). The Kolmogorov-Smirnov test or the Shapiro-Wilk test was used to determine the normality of the data based on sample size. Means between three or more groups were compared using the independent-samples median test with Bonferroni correction due to the non-parametric nature of the data and extreme outliers. Significance values were set at 0.05. Correlation was performed for continuous data using Spearman's rho due to the non-parametric nature of the data. Frequency counts, summative data, and descriptive data were used for demographics.

RESULTS

Search results

There are a total of 48 foot and ankle orthopedic surgery fellowships in the United States with a combined total of 172 physicians as fellowship faculty. Seven physicians were missing data on CMS and four physicians were missing an H-index on Scopus. Only physicians with compete CMS money data and H-index on Scopus (n = 165 physicians, 95.9%) were included in data analysis.

Individual physician demographics

Mean individual physician (n = 165 physicians) total life-time earnings reported on the CMS website was USD 451430.30 ± USD 1851084.89 (range: USD 25.16-21269249.85; median: USD 27839.80). Mean individual physician (n = 165 physicians) H-index as reported on H-index is 14.24 ± 12.39 (range: 0-63; median: 11). See Table 1 below for more information on individual physicians who are faculty at foot and ankle orthopedic surgery fellowships in the United States with the top five total-life time earnings.

Fellowship demographics

Mean combined physician H-index reported on Scopus per fellowship (n = 48 fellowships) was 48.94 ± 38.92 (range: 9-187; median: 35.50). Mean combined physician life-time earnings reported on CMS per fellowship was USD 1551791.66 ± USD 4136091.64 (range: USD 8668.93-21274853.70; median: USD 359425.24). See Table 2 below for more information on fellowship programs for foot and ankle orthopedic surgery in the United States.

Total life-time earnings and h-index correlations for individual physicians

There was a significant but weak correlation between individual physician H-index and individual physician total life-time earnings reported on CMS (P < 0.001; Spearman's rho = 0.334). See Figure 1A below for scatter plot with best fit line showing correlation between individual physician H-index who are fellowship faculty and total life-time earnings reported on CMS. There was a significant association between total life-time earnings and level of H-Index per individual physician by H-index quartile (P = 0.005). For subgroup post hoc analysis based on individual physician H-index, the four quartile group (n = 41 physicians) had significantly more total life-time earnings than the first quartile group (n = 42 physicians) (P = 0.004) and the second quartile group (n = 41 physicians) (P = 0.025). However, there was no significant difference between the total life-time earnings in the third quartile group and the fourth quartile group (P = 0.281). The first quartile group (n = 42 physicians) had a mean total life-time earnings of USD 184342.91 ± 1024600.21 (range: USD 214.21-6660954.43; median: USD 14005.88). The second quartile group (n = 41 physicians) had a mean total life-time

Table 1 Information on individual physicians who are faculty at foot and ankle orthopedic surgery fellowships in the United States with the top five total life-time earnings

Physician ranking	H-index	Total life-time earnings in USD	Overall payments
1	58	21269249.85	694
2	3	6660954.43	2028
3	21	5215497.93	1293
4	24	4409146.87	591
5	22	3420158.94	903

Information includes H-Index, total life-time earnings, and total-life time payments paid to the individual physician. USD: United States Dollar.

earnings of USD 179626.75 ± 443691.76 (range: USD 437.84-1960346.56; median: USD 17894.85). The third quartile group (n = 41 patients) had a mean total life-time earnings of USD 140744.38 ± 241444.40 (range: USD 25.16-1290811.98; median: USD 31056.22). The fourth quartile group (n = 41 patients) had a mean total life-time earnings of USD 1307521.49 ± 3422970.09 (range: USD 242.61-21269249.85; median: USD 252327.86).

Total life-time earnings and h-index correlations for fellowship programs

There was also a significant and moderate positive correlation between combined fellowship H-index and total life-time earnings per fellowship (P = 0.004, Spearman's rho = 0.409). See Figure 1B below for scatter plot with best fit line showing correlation between combined fellowship H-index and total life-time earnings per fellowship.

DISCUSSION

Orthopedic surgeons are heavily influenced by their fellowship training programs with regards to practice patterns[14]. Thus, choice of fellowship may predict future academic engagement[15], subspeciality society participation, and involvement with industry as a consultant, design-team member, or paid educator. Therefore, this study aimed to build upon our understanding of the degree of industry involvement within foot and ankle fellowship programs. We sought to assess whether academic productivity at a particular fellowship correlated with industry compensation as recorded in the OPD. As a secondary outcome, we assessed whether higher H index of an individual surgeon is correlated with larger net industry earnings.

We determined there to be a statistically significant and moderate positive correlation between combined fellowship H-index and total life-time earnings per fellowship, further indicating that academic productivity of an orthopedic foot and ankle fellowship group correlates to overall industry involvement. In addition, we found a statistically significant correlation between individual physician H-index and individual physician total life-time earnings reported on CMS. While this result achieved only a weak correlation based on Spearman's rho (0.334) given substantial heterogeneity within the data, examination of the actual numbers reveals a clearer trend. The first quartile group (n = 42 physicians) had a mean total life-time earnings of USD 184342.91 ± 1024600.21 (range: USD 214.21-6660954.43; median: USD 14005.88). The second quartile group (n = 41 physicians) had a mean total life-time earnings of USD 179626.75 ± 443691.76 (range: USD 437.84-1960346.56; median: USD 17894.85). The third quartile group (n = 41 patients) had a mean total life-time earnings of USD 140744.38 ± 241444.40 (range: USD 25.16-1290811.98; median: USD 31056.22). The fourth quartile group (n = 41 patients) had a mean total life-time earnings of USD 1307521.49 ± 3422970.09 (range: USD 242.61-21269249.85; median: USD 252327.86). These data provides strong support to the notion that surgeons who are extensively involved with industry have a substantial academic background.

The relationship between academic involvement and industry support for research activity is straightforward: academicians are more likely to receive monetary backing to carry out investigation of a specific pharmaceutical or surgical implant. Industry-funded research is the topic of substantial debate with concerns for conflict of interest and bias factoring in to the legitimacy of the findings[16-20]. The most obvious case example is the tobacco industry funding faulty research regarding smoking and use of tobacco products[21-25]. Several authors have raised concern regarding bias related to industry funding of research within orthopedics as well[26,27]. For example, Shah *et al*[26] demonstrated a higher likelihood for industry-funded studies to report positive results than studies funded from other sources. While cash or cash-equivalent payments represent the majority of the payment types to foot and ankle surgeons, there is substantial contribution from industry to support research efforts within foot and ankle[28].

Several studies have sought to investigate the impact of industry funding on reporting of positive (or favorable) results within foot and ankle surgery. Cole *et al*[29] revealed a large percentage of undisclosed conflicts of interest within systematic reviews related to Achilles tendon rupture. Despite this finding, these authors note that the lack of conflict of interest disclosure did not increase the likelihood of a positive finding in the results of the intervention being investigated. Donoughe at al. evaluated the association between positive outcome reporting in total ankle arthroplasty research, and determined that payments were not significantly correlated with favorable outcomes for a specific implant[30]. While these studies generally indicate a lack of substantial industry influence in the reporting of positive results within foot and

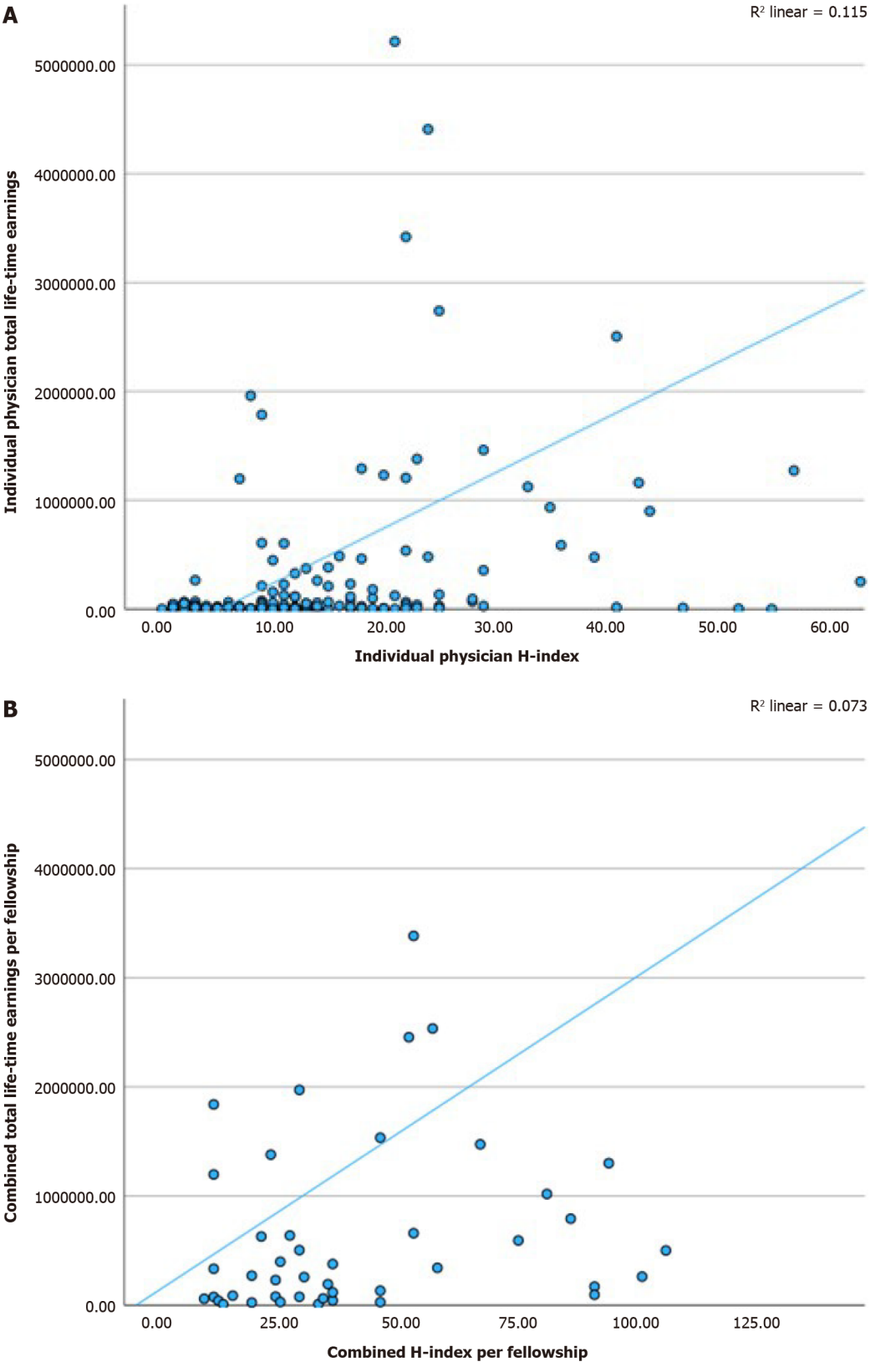


Figure 1 Correlation between individual physician H-index and individual physician total life-time earnings made as recorded on Centers for Medicare and Medicaid Services website and correlation between the combined H-index per foot and ankle orthopedic surgery fellowship and the combined money made on Centers for Medicare and Medicaid Services website from all faculty of the fellowship program. A: Correlation between individual physician H-index and individual physician total life-time earnings made as recorded on Centers for Medicare and Medicaid Services website. Y-axis was shortened to United States Dollar (USD) 5000000 to allow for better visualization of relationship. Line represents best-fit line for correlation; B: Correlation between the combined H-index per foot and ankle orthopedic surgery fellowship and the combined money made on Centers for Medicare and Medicaid Services website from all faculty of the fellowship program. X-axis set at H-index of 140 and y-axis set at USD 5000000 to allow a better visualization of the relationship. Line represents best-fit line for correlation.

Table 2 Information on foot and ankle orthopedic surgery fellowships in the United States

Fellowship ranking	Total life-time earnings per fellowship	Mean total life-time earnings per physician per fellowship	Total H-index per fellowship	Total life-time earnings per fellowship per h index
1	21274853.70	10637426.85	60	354580.90
2	20016633.67	2859519.10	107	187071.34
3	4553357.43	650479.63	187	24349.50
4	3383361.89	676672.38	53	63837.02
5	2534816.19	1267408.10	57	44470.46
6	2454950.69	818316.90	52	47210.59
7	1971933.15	657311.05	29	67997.69
8	1839321.97	919660.99	11	167211.09
9	1534450.54	306890.11	46	33357.62
10	1473486.49	245581.08	67	21992.34
11	1379087.01	1379087.01	23	59960.30
12	1300744.31	260148.86	94	13837.71
13	1197536.88	598768.44	11	108866.99
14	1018902.47	254725.62	81	12579.04
15	792190.87	132031.81	86	9211.52
16	659032.20	164758.05	53	12434.57
17	637897.63	159474.41	27	23625.84
18	629068.07	314534.04	21	29955.62
19	592739.33	118547.87	75	7903.19
20	504161.78	252080.89	29	17384.89
21	501127.63	100225.53	106	4727.62
22	437773.15	87554.63	165	2653.17
23	397822.34	132607.45	25	15912.89
24	376893.59	125631.20	36	10469.27
25	341956.88	68391.38	58	5895.81
26	333624.90	111208.30	11	30329.54
27	270203.44	90067.81	19	14221.23
28	261673.77	87224.59	101	2590.83
29	257580.01	85860.00	30	8586.00
30	230313.03	57578.26	24	9596.38
31	192293.20	48073.30	35	5494.09
32	170156.75	42539.19	91	1869.85
33	132455.07	66227.54	46	2879.46
34	117478.39	39159.46	36	3263.29
35	95286.89	15881.15	91	1047.11
36	87086.03	21771.51	15	5805.74
37	78504.91	39252.46	24	3271.04
38	76441.36	38220.68	29	2635.91
39	75612.14	25204.05	11	6873.83
40	61503.60	15375.90	34	1808.93

41	58786.54	58786.54	9	6531.84
42	42676.26	10669.07	36	1185.45
43	40725.72	20362.86	12	3393.81
44	28846.60	28846.60	25	1153.86
45	27864.96	13932.48	46	605.76
46	24067.73	8022.58	19	1266.72
47	10049.69	3349.90	33	304.54
48	8668.93	8668.93	13	666.84

Data are United States Dollar, unless otherwise indicated. Information includes total life-time money made for all physician faculty combined, mean total life-time money made per faculty physician, combined H-index, and mean total life-time money made per combined H-index. Fellowships were ordered by highest total life-time earnings per fellowship.

ankle, these results are inconclusive and non-generalizable. Further work should seek to identify other potential sources of bias within foot and ankle surgery research.

While industry funding of research is a topic of much debate, our study sought to characterize payments which were made for reasons specifically not related to research, including for food and drink, travel, cash payments, and cash-equivalent payments. We determined that payments unrelated to research are correlated with H index – a less intuitive finding than the observation that research payment correlates with H index. This finding was true both at the individual surgeon level and at the fellowship-grouped level. Surgeons with more academic influence may be able to command higher consulting fees and may be more likely to be approached with implant design-team opportunities. Benefits of this relationship include more incentive for foot and ankle practitioners to participate in research, which often comes at a significant time and opportunity cost for surgeons with busy surgical practices. Potential disadvantages of a system where heavy academic involvement is rewarded by larger industry payouts are poorly investigated in the literature. Surgeons may be encouraged to publish a higher total number of manuscripts rather than focusing on areas of highest impact. Additionally, surgeon-leaders with considerable academic influence who are heavily involved with foot and ankle fellowship education may be the most problematically impacted by loyalty to a specific implant manufacturer. Further research should seek to expand upon these findings and quantify the repercussions of heavy industry involvement within academically-active foot and ankle surgeons.

Limitations of this analysis include lack of granularity regarding specific fellowship or individual identifiers. Despite the public availability of the information contained within the OPD, we attempted to avoid personally-identifying information contained within this manuscript, as small fellowship programs with only several faculty members may preclude full anonymity. Moreover, we utilized H index as a surrogate for academic involvement. While the H index does correlate with number of publications and citation count of a given author's combined research works, this metric has come under criticism as overly simplistic and failing to capture actual impact of scientific investigation[31]. As a final limitation, we did not control for the age of a given surgeon or the average age of the surgeons at a given fellowship, as this information was not readily available online. Furthermore, high fellowship total life-time earnings may be a result of a single surgeon's high earnings or multiple surgeons' high earnings, and our statistical analysis did not account for this factor. As H index is associated with age[32], industry involvement may more closely be associated with more years of experience within foot and ankle surgery than with academic involvement. However, older surgeons who are employed in private practice may have very low H indices, and are unlikely to accrue the number of publications and citations necessary to be a part of the "Greater than 25 H-index" cohort in this investigation. Additionally, different institutions may have differing rules or attitudes towards these payments, which could not be accounted for and could skew data.

CONCLUSION

In conclusion, we determined there to be a statistically significant correlation between individual physician H-index and individual physician total life-time, non-research-related earnings reported on CMS. This finding remained true when collective H index of the faculty at a given orthopedic foot and ankle fellowship was correlated to collective industry payments to the faculty at that fellowship. Further efforts should seek to characterize any potential disadvantages to the high degree of industry involvement of the most academically productive foot and ankle surgeons.

ARTICLE HIGHLIGHTS

Research background

The study opens the door for future research by revealing a significant positive correlation between academic productivity and industry earnings in foot and ankle orthopedic surgery fellowships. Subsequent research could explore

the underlying factors influencing this correlation, identifying causal mechanisms and potential interventions to enhance both academic productivity and financial outcomes in this specialized medical field. Additionally, future studies may look into the broader implications of these findings for the education and practice of foot and ankle orthopedic surgeons.

Research motivation

The study does not explicitly propose new theories. Instead, it focuses on investigating and establishing a correlation between academic productivity (measured by the H-index) and industry earnings in foot and ankle orthopedic surgery fellowships. The primary contribution lies in highlighting the relationship between scholarly achievements and financial outcomes in this specific medical field, without introducing novel theoretical frameworks.

Research objectives

The findings indicate a significant correlation between academic productivity (H-index) and industry earnings in foot and ankle orthopedic surgery fellowships. This contributes to our understanding of the relationship between scholarly achievements and financial outcomes. However, the study does not investigate specific factors influencing these correlations, leaving room for future research to explore the nuances further.

Research methods

The study is a retrospective analysis. We utilized data from two primary sources: Scopus for academic productivity metrics, specifically the H-index, and the Open Payments Database (OPD) for industry earnings data. The research involved the examination of 48 foot and ankle orthopedic surgery fellowships in the United States, covering 100% of such programs and 95.9% of physicians. Academic productivity was assessed through the H-index recorded from the Scopus website, while industry earnings were obtained from the OPD, encompassing total life-time earnings from 2015 to 2021. The novelty of the research lies in the comprehensive analysis of the correlation between academic productivity and industry earnings at both individual physician and fellowship levels within the context of foot and ankle orthopedic surgery, providing a unique perspective on the intersection of scholarly achievements and financial outcomes in this specialized medical field.

Research results

The main objectives of this study were to investigate the correlation between academic productivity and industry earnings in foot and ankle orthopedic surgery fellowships in the United States. The study aimed to quantify academic productivity using the H-index and measure industry earnings through the OPD. The objectives that were realized include identifying a significant positive correlation between academic productivity and industry earnings at both individual physician and fellowship levels. The significance of realizing these objectives lies in shedding light on the intricate relationship between scholarly achievements and financial outcomes in this specialized medical field, providing a foundation for future research to delve deeper into the factors influencing this correlation and its implications for the field of foot and ankle orthopedic surgery.

Research conclusions

This study investigates the relationship between academic productivity and industry earnings in foot and ankle orthopedic surgery fellowships in the United States. Key topics include individual physician and fellowship-level metrics, such as the H-index for academic productivity and total life-time earnings from the OPD. The study identifies a significant positive correlation between academic productivity and industry earnings, addressing the crucial link between scholarly achievements and financial outcomes in the field, providing valuable insights for future research in understanding these dynamics.

Research perspectives

This retrospective analysis explores the correlation between academic productivity and industry earnings in foot and ankle orthopedic surgery fellowships across the United States. Examining individual physician and fellowship-level data from 48 programs, the study reveals a significant positive association between academic productivity (measured by the H-index) and industry earnings. The findings highlight the interconnections of scholarly achievements and financial outcomes in this specialized medical field, both at the individual physician and fellowship levels.

ACKNOWLEDGEMENTS

We would like to thank Dr. Keith Baldwin, MD, MSPT, MPH for his statistical consultation.

FOOTNOTES

Author contributions: Anastasio AT created the idea for the study, performed data collection, contributed to the manuscript and revisions; Baumann AN contributed to the manuscript, performed statistical analysis, and assisted with revisions; Walley KC performed data collection, contributed to the manuscript and editing process; Hitchman KJ uploaded the submission and was responsible for revisions of the manuscript; O'Neill C wrote portions of the manuscript, performed data collection and was involved in the editing

process; Kaplan J was involved with the editing process and served as a mentor for the project; Adams SB served as the Principal Investigator for this study and was involved with the editing process; all authors have read and approve of the final manuscript.

Institutional review board statement: All the data included in the manuscript are available publicly online. Additionally, no human or animal research was carried out at any point during the study. For these reasons, we do not believe IRB approval or exemption is necessary.

Informed consent statement: No human subjects were involved in this research project. Additionally, there were no experimental groups. The data in this study were obtained from readily available online resources.

Conflict-of-interest statement: Albert Anastasio: Consulting fees from QPIX Solutions. Anthony Baumann: Declarations of interest: None. Kempland Walley: Declarations of interest: None. Kyle Hitchman: Declarations of interest: None. Conor O'Neill: Relationships with Medtronic, Stryker, and Fortis Surgical. Jonathan Kaplan: Relationships with Novastep, Exactech, Encore Medical, Stryker, Vilex, Bioventus, and Micromed. Samuel B. Adams: Consulting fees/relationships with Conventus, Enovis, in2bones, Restor3d, and Stryker. See COI form for more relationships.

Data sharing statement: Technical appendix, statistical code, and dataset are available from the corresponding author at albert.anastasio@gmail.com.

Country/Territory of origin: United States

ORCID number: Albert T Anastasio 0000-0001-5817-3826; Anthony N Baumann 0000-0002-4175-3135; Kempland C Walley 0000-0003-4488-0663; Kyle J Hitchman 0009-0000-6652-0891.

S-Editor: Lin C
L-Editor: Filipodia
P-Editor: Yuan YY

REFERENCES

1 **Kirschner NM**, Sulmasy LS, Kesselheim AS. Health policy basics: the Physician Payment Sunshine Act and the Open Payments program. *Ann Intern Med* 2014; **161**: 519-521 [PMID: 25069795 DOI: 10.7326/M14-1303]
2 **Parisi TJ**, Ferre IM, Rubash HE. The Basics of the Sunshine Act: How It Pertains to the Practicing Orthopaedic Surgeon. *J Am Acad Orthop Surg* 2015; **23**: 455-467 [PMID: 26209143 DOI: 10.5435/JAAOS-D-14-00426]
3 **Samuel AM**, Webb ML, Lukasiewicz AM, Bohl DD, Basques BA, Russo GS, Rathi VK, Grauer JN. Orthopaedic Surgeons Receive the Most Industry Payments to Physicians but Large Disparities are Seen in Sunshine Act Data. *Clin Orthop Relat Res* 2015; **473**: 3297-3306 [PMID: 26088767 DOI: 10.1007/s11999-015-4413-8]
4 **Pathak N**, Galivanche AR, Lukasiewicz AM, Mets EJ, Mercier MR, Bovonratwet P, Walls RJ, Grauer JN. Orthopaedic Foot and Ankle Surgeon Industry Compensation Reported by the Open Payments Database. *Foot Ankle Spec* 2021; **14**: 126-132 [PMID: 32059613 DOI: 10.1177/1938640020903145]
5 **Somerson JS**, Comley MC, Mansi A, Neradilek MB, Matsen FA 3rd. Industry payments to authors of Journal of Shoulder and Elbow Surgery shoulder arthroplasty manuscripts are accurately disclosed by most authors and are not significantly associated with better reported treatment outcomes. *J Shoulder Elbow Surg* 2020; **29**: 667-673 [PMID: 31899091 DOI: 10.1016/j.jse.2019.09.045]
6 **Matsen FA 3rd**, Jette JL, Neradilek MB. Demographics of disclosure of conflicts of interest at the 2011 annual meeting of the American Academy of Orthopaedic Surgeons. *J Bone Joint Surg Am* 2013; **95**: e29 [PMID: 23467877 DOI: 10.2106/JBJS.K.01514]
7 **Narain AS**, Hijji FY, Yom KH, Kudaravalli KT, Singh K. Cervical disc arthroplasty: do conflicts of interest influence the outcome of clinical studies? *Spine J* 2017; **17**: 1026-1032 [PMID: 28343045 DOI: 10.1016/j.spinee.2017.03.018]
8 **Schiller JR**, DiGiovanni CW. Foot and ankle fellowship training: a national survey of past, present, and prospective fellows. *Foot Ankle Int* 2008; **29**: 34-41 [PMID: 18275734 DOI: 10.3113/FAI.2008.0034]
9 Financial relationships between neurologists and Industry: The 2015 Open Payments database. *Neurology* 2019; **92**: 1026 [PMID: 31110151 DOI: 10.1212/WNL.0000000000007639]
10 **Boas SR**, Niforatos JD, Summerville L, Isbester K, Chaturvedi A, Wee C, Kumar AR. The Open Payments Database and Top Industry Sponsors of Plastic Surgeons: Companies and Related Devices. *Plast Reconstr Surg* 2019; **144**: 530e-532e [PMID: 31461072 DOI: 10.1097/PRS.0000000000005927]
11 **Brauer PR**, Morse E, Mehra S. Industry Payments for Otolaryngology Research: A Four-Year Analysis of the Open Payments Database. *Laryngoscope* 2020; **130**: 314-320 [PMID: 31059584 DOI: 10.1002/lary.27896]
12 **Haque W**, Haque E, Hsiehchen D. Female dermatology journal editors accepting pharmaceutical payments: An analysis of the Open Payments database, 2013 to 2018. *Int J Womens Dermatol* 2021; **7**: 451-453 [PMID: 34632038 DOI: 10.1016/j.ijwd.2021.02.008]
13 **Heckmann ND**, Mayfield CK, Chung BC, Christ AB, Lieberman JR. Industry Payment Trends to Orthopaedic Surgeons From 2014 to 2018: An Analysis of the First 5 Years of the Open Payments Database. *J Am Acad Orthop Surg* 2022; **30**: e191-e198 [PMID: 34967798 DOI: 10.5435/JAAOS-D-21-00412]

14 **DePasse JM**, Daniels AH, Durand W, Kingrey B, Prodromo J, Mulcahey MK. Completion of Multiple Fellowships by Orthopedic Surgeons: Analysis of the American Board of Orthopaedic Surgery Certification Database. *Orthopedics* 2018; **41**: e33-e37 [PMID: 29136254 DOI: 10.3928/01477447-20171106-05]

15 **Haimowitz S**, Veliky J, Forrester LA, Ippolito J, Beebe K, Chu A. Subspecialty Selection Impacts Research Productivity and Faculty Rank of Academic Orthopaedic Surgeons. *J Bone Joint Surg Am* 2022; **104**: e31 [PMID: 34793371 DOI: 10.2106/JBJS.21.00443]

16 **Elliott DB**. Industry-funded research bias and conflicts of interest. *Ophthalmic Physiol Opt* 2013; **33**: 1-2 [PMID: 23252850 DOI: 10.1111/opo.12016]

17 **Chapman S**, Bhangu A. Ban on publishing industry funded research could harm surgical innovation. *BMJ* 2014; **348**: g1291 [PMID: 24500350 DOI: 10.1136/bmj.g1291]

18 **Smith R**, Gøtzsche PC, Groves T. Should journals stop publishing research funded by the drug industry? *BMJ* 2014; **348**: g171 [PMID: 24423895 DOI: 10.1136/bmj.g171]

19 **Breault JL**, Knafl E. Pitfalls and Safeguards in Industry-Funded Research. *Ochsner J* 2020; **20**: 104-110 [PMID: 32284691 DOI: 10.31486/toj.19.0093]

20 **Plottel GS**, Adler R, Jenter C, Block JP. Managing Conflicts and Maximizing Transparency in Industry-Funded Research. *AJOB Empir Bioeth* 2020; **11**: 223-232 [PMID: 32808880 DOI: 10.1080/23294515.2020.1798562]

21 **Godlee F**, Malone R, Timmis A, Otto C, Bush A, Pavord I, Groves T. Journal policy on research funded by the tobacco industry. *BMJ* 2013; **347**: f5193 [PMID: 24129479 DOI: 10.1136/bmj.f5193]

22 **Malone RE**. Changing Tobacco Control's policy on tobacco industry-funded research. *Tob Control* 2013; **22**: 1-2 [PMID: 23239401 DOI: 10.1136/tobaccocontrol-2012-050874]

23 **Polito JR**. Non-publication of tobacco funded research should extend to replacement nicotine studies funded by the drug industry. *BMJ* 2013; **347**: f6740 [PMID: 24255926 DOI: 10.1136/bmj.f6740]

24 **Smith R**. Arguments against publishing tobacco funded research also apply to drug industry funded research. *BMJ* 2013; **347**: f6732 [PMID: 24252687 DOI: 10.1136/bmj.f6732]

25 **Dunn AG**, Coiera E. Should comparative effectiveness research ignore industry-funded data? *J Comp Eff Res* 2014; **3**: 317-320 [PMID: 25275226 DOI: 10.2217/cer.14.31]

26 **Shah RV**, Albert TJ, Bruegel-Sanchez V, Vaccaro AR, Hilibrand AS, Grauer JN. Industry support and correlation to study outcome for papers published in Spine. *Spine (Phila Pa 1976)* 2005; **30**: 1099-104; discussion 1105 [PMID: 15864166 DOI: 10.1097/01.brs.0000161004.15308.b4]

27 **McDonnell JM**, Dalton DM, Ahern DP, Welch-Phillips A, Butler JS. Methods to Mitigate Industry Influence in Industry Sponsored Research. *Clin Spine Surg* 2021; **34**: 143-145 [PMID: 33086256 DOI: 10.1097/BSD.0000000000001098]

28 **Casciato DJ**, Mendicino RW. CMS Open Payments Database Analysis of Industry Payments for Foot and Ankle Surgery Research. *J Foot Ankle Surg* 2022; **61**: 1013-1016 [PMID: 35172954 DOI: 10.1053/j.jfas.2022.01.005]

29 **Cole WT**, Hillman C, Corcoran A, Anderson JM, Weaver M, Torgerson T, Hartwell M, Vassar M. Financial Conflicts of Interest Among Systematic Review Authors Investigating Interventions for Achilles Tendon Ruptures. *Foot Ankle Orthop* 2021; **6**: 24730114211019725 [PMID: 35097455 DOI: 10.1177/24730114211019725]

30 **Donoughe JS**, Safavi KS, Rezvani A, Healy N, Jupiter DC, Panchbhavi VK, Janney CC. Industry Payments to Foot and Ankle Surgeons and Their Effect on Total Ankle Arthroplasty Outcomes. *Foot Ankle Orthop* 2021; **6**: 24730114211034519 [PMID: 35097468 DOI: 10.1177/24730114211034519]

31 **Koltun V**, Hafner D. The h-index is no longer an effective correlate of scientific reputation. *PLoS One* 2021; **16**: e0253397 [PMID: 34181681 DOI: 10.1371/journal.pone.0253397]

32 **Kelly CD**, Jennions MD. H-index: age and sex make it unreliable. *Nature* 2007; **449**: 403 [PMID: 17898745 DOI: 10.1038/449403c]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 139-146

DOI: 10.5312/wjo.v15.i2.139

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Retrospective Study

Burden of routine orthopedic implant removal a single center retrospective study

Ammar K AlOmran, Nader Alosaimi, Ahmed A Alshaikhi, Omar M Bakhurji, Khalid J Alzahrani, Basil Ziyad Salloot, Tamim Omar Alabduladhem, Ahmed I AlMulhim, Arwa Alumran

Specialty type: Orthopedics

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: He Z, China; Zhang H, China

Received: November 17, 2023
Peer-review started: November 17, 2023
First decision: December 7, 2023
Revised: December 18, 2023
Accepted: January 9, 2024
Article in press: January 9, 2024
Published online: February 18, 2024

Ammar K AlOmran, Nader Alosaimi, Ahmed A Alshaikhi, Omar M Bakhurji, Khalid J Alzahrani, Basil Ziyad Salloot, Tamim Omar Alabduladhem, Ahmed I AlMulhim, Department of Orthopedic, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam 31441, Saudi Arabia

Arwa Alumran, Health Information Management and Technology Department, Imam Abdulrahman Bin Faisal University, Dammam 31441, Saudi Arabia

Corresponding author: Ahmed I AlMulhim, MBBS, MD, Surgeon, Department of Orthopedic, College of Medicine, Imam Abdulrahman Bin Faisal University, King Faisal Ibn Abdulaziz Road, Dammam 31441, Saudi Arabia. ahlmulhim@iau.edu.sa

Abstract

BACKGROUND

Open reduction and internal fixation represent prevalent orthopedic procedures, sparking ongoing discourse over whether to retain or remove asymptomatic implants. Achieving consensus on this matter is paramount for orthopedic surgeons. This study aims to quantify the impact of routine implant removal on patients and healthcare facilities. A retrospective analysis of implant removal cases from 2016 to 2022 at King Fahad Hospital of the University (KFHU) was conducted and subjected to statistical scrutiny. Among these cases, 44% necessitated hospitalization exceeding one day, while 56% required only a single day. Adults exhibited a 55% need for extended hospital stays, contrasting with 22.8% among the pediatric cohort. The complication rate was 6%, with all patients experiencing at least one complication. Notably, 34.1% required sick leave and 4.8% exceeded 14 d. General anesthesia was predominant (88%). Routine implant removal introduces unwarranted complications, particularly in adults, potentially prolonging hospitalization. This procedure strains hospital resources, tying up the operating room that could otherwise accommodate critical surgeries. Clearly defined institutional guidelines are imperative to regulate this practice.

AIM

To measure the burden of routine implant removal on the patients and hospital.

METHODS

This is a retrospective analysis study of 167 routine implant removal cases treated

at KFHU, a tertiary hospital in Saudi Arabia. Data were collected in the orthopedic department at KFHU from February 2016 to August 2022, which includes routine asymptomatic implant removal cases across all age categories. Nonroutine indications such as infection, pain, implant failure, malunion, nonunion, restricted range of motion, and prominent hardware were excluded. Patients who had external fixators removed or joints replaced were also excluded.

RESULTS

Between February 2016 and August 2022, 360 implants were retrieved; however, only 167 of those who met the inclusion criteria were included in this study. The remaining implants were rejected due to exclusion criteria. Among the cases, 44% required more than one day in the hospital, whereas 56% required only one day. 55% of adults required more than one day of hospitalization, while 22.8% of pediatric patients required more than one day of inpatient care. The complication rate was 6%, with each patient experiencing at least one complication. Sick leave was required in 34.1% of cases, with 4.8% requiring more than 14 d. The most common type of anesthesia used in the surgeries was general anesthesia (88%), and the mean (SD) surgery duration was 77.1 (54.7) min.

CONCLUSION

Routine implant removal causes unnecessary complications, prolongs hospital stays, depletes resources and monopolizing operating rooms that could serve more critical procedures.

Key Words: Implant removal; Healed fracture; Orthopedic implant; Complications; Healthcare system

Core Tip: This retrospective study examines the implications of routine asymptomatic implant removal on both patients and healthcare institutions. The study reveals that such practices impose substantial financial and health-related challenges for both individuals and hospitals.

Citation: AlOmran AK, Alosaimi N, Alshaikhi AA, Bakhurji OM, Alzahrani KJ, Salloot BZ, Alabduladhem TO, AlMulhim AI, Alumran A. Burden of routine orthopedic implant removal a single center retrospective study. *World J Orthop* 2024; 15(2): 139-146
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/139.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.139

INTRODUCTION

Elective removal of implants post-fracture union is a prevalent procedure in global orthopedic practice. However, extant literature lacks consensus on the merits and hazards of routine removal in asymptomatic individuals. This procedure demands judicious consideration due to potential operative challenges, encompassing persistent pain, soft tissue infections, and prolonged hospitalization[1]. Moreover, implant removal entails substantial resource utilization, imposing an economic strain on healthcare systems[2,3].

A Finnish retrospective study revealed that routine implant removal constituted nearly 30% of elective surgeries, necessitating further investigation into the efficacy of this orthopedic practice[4]. Notably, studies highlight the impact on productivity, with 11-16 d of missed work or school post-removal, accompanied by a 2.6-d hospital stay[3,5,6]. The mean operating room time for implant removal surgeries was reported as 37 min[7]. While some studies affirm significant functional enhancements and positive outcomes following elective implant removal[8-10], the literature remains contentious.

Despite this, orthopedic surgeons universally concur on the necessity of removing symptomatic implants (*e.g.*, infected, painful, or prominent)[1]. Pediatric patients routinely undergo implant removal due to potential long-term complications, including growth restriction, allergy, implant migration, and carcinosis[11,12]. This study aims to quantify the impact of routine implant removal on patient health, hospital resources, and sick leave duration in both adult and pediatric populations.

MATERIALS AND METHODS

This retrospective analysis examines cases of implant removal treated at King Fahad Hospital of the University (KFHU) in the Eastern Province, Saudi Arabia. Data were gathered from February 2016 to August 2022, encompassing routine asymptomatic implant removal cases across all age groups in the orthopedic department at KFHU. Excluded were cases involving nonroutine indications such as infection, pain, implant failure, malunion, nonunion, limited range of motion, and prominent hardware. Patients who underwent removal of external fixators or replaced joints were also excluded.

Ethical approval was secured from the Institutional Review Board of Imam Abdulrahman bin Faisal University, adhering to the Declaration of Helsinki (IRB number: IRB-UGS-2022-01-396). Informed consent from participants was waived for this retrospective study, as per the Institutional Review Board at Imam Abdulrahman bin Faisal University.

A total of 360 cases were retrieved from the Quadramed electronic record system at KFHU. Following the application of inclusion and exclusion criteria, the sample size was refined to 167. The gathered data encompassed demographic details (age, sex, and nationality) and clinical characteristics such as length of hospital stay, complication rate, days of sick leave, type of anesthesia, surgery duration in minutes, and the interval in months between implant insertion and removal.

Categorical variables (*e.g.*, anesthetic type and gender) were analyzed descriptively using frequencies and percentages, while continuous variables (*e.g.*, surgery duration and insertion-to-removal period) were characterized by mean and standard deviation. The Student's t-test compared continuous variables, and the chi-square test assessed categorical variables. Data analysis employed Statistical Package for the Social Sciences (SPSS) version 25. A significance level of 0.05 was applied to *P* values.

RESULTS

Between February 2016 and August 2022, 360 implants were extracted; however, only 167 meeting inclusion criteria were included in this study. Exclusion criteria led to the dismissal of the remaining implants. Predominantly, patients were male (68%) and Saudi nationals (90%). Hospital stays varied, with 44% extending beyond a day, and 56% requiring only a single day. Complications affected 6% of cases, with all patients experiencing at least one. Among these, 34.1% necessitated sick leave, 4.8% exceeding 14 d. General anesthesia prevailed (88%). Mean (SD) surgery duration was 77.1 (54.7) min, and implant removal occurred on average 18.6 (17.9) months post-insertion. Patients' mean (SD) age was 25 (18) years (Table 1).

Table 2 presents associations between variables and implant areas in 167 participants. Of these, 32.9% had upper limb or spine implants, while 67.1% had lower limb implants. No significant correlation was found between sex and implant area. Both upper and lower limb implant prevalence was higher in Saudis, though statistically insignificant. Age, adults, pediatrics (≤ 14 years), length of stay, and complication rate showed no significant association with implant area. However, the implant area correlated significantly with anesthesia type and insertion-to-removal period. General anesthesia prevailed, yet lower limb implants notably favored regional anesthesia (P = 0.02). Upper limb/spine implants had a significantly shorter insertion-to-removal period [14.5 (13.5) mo] than lower limb implants [20.6 (19.5) mo], P = 0.037.

Table 3 illustrates associations between variables and age groups (pediatrics, age ≤ 14). Among 167 participants, 57 (34.1%) were children. Males predominated in adults (75.5%) versus pediatric patients (54.4%, P = 0.006), signifying a significant sex-age group correlation. Nationality, complication rates, and sick leave showed no age-related significance. However, age influenced hospital stay duration, anesthesia type, and insertion-removal intervals. Adults exceeded pediatric patients in hospitalization beyond one day (55.5% *vs* 22.8%, P = 0.001) and regional anesthesia use (16.4% *vs* 3.5%, P = 0.015). Pediatrics demonstrated notably shorter mean insertion-removal duration [12.3 (8.3) mo] compared to adults [21.9 (20.6) mo, P = 0.001].

DISCUSSION

Our investigation assessed routine implant removal in 167 patients, predominantly Saudi males, revealing a 6% complication rate. Surgical duration averaged 77.1 (SD 54.7) min, and the period between implant insertion and removal averaged 18.6 (SD 17.9) months, with patients averaging 25 (SD 18) years in age. The 6% complication rate imposes a burden on patients without prior complaints. Studies indicate that non-medically indicated removal carries a 28% complication rate, while medically indicated removals had a complication rate of approximately 12%[13]. Another study reported a 10% complication rate[10], and ankle implant removal exhibited a 14% perioperative complication rate[14]. This variability highlights a gray area among centers, influenced by factors like medical necessity, surgeon experience, and anatomical location. Notably, most cases in our study avoided sick leave, whereas 29.3% and 4.8% took ≤ 14 and > 14 d, respectively. In contrast, a different prospective study reported an average of 16 d away from work or school[2]. This underscores the economic ramifications of missed work or school days as a risk factor for implant removal.

General anesthesia predominated in upper limb, spine, and lower limb procedures. Notably, regional anesthesia exhibited a higher prevalence in the lower limb cohort, indicating a statistically significant discrepancy (P = 0.02). The predominant modality of regional anesthesia was spinal, administered *via* a needle insertion at L4-L5 to mitigate spinal cord injury and prevent intrathecal drug injection. Consequently, its utilization in upper limb procedures was less frequent, necessitating advanced training and ultrasonography for nerve blocks (*e.g.*, supraclavicular and interscalene). Unilateral targeting may be insufficient, and patient preferences could influence the adoption of novel anesthesia methods[15,16].

The mean (SD) interval between insertion and removal in the lower limb [20.6 (19.5) mo] surpassed that in the upper limb or spine group [14.5 (13.5) mo], exhibiting statistical significance (P = 0.037). Notably, implant removal timing in uncomplicated fracture healing cases tends to be briefer in the upper limbs, aligning with our findings[17]. This variance may be attributed to the distinctive physiological function of the lower limb (*e.g.*, weight-bearing), intricate anatomical structures, and prolonged healing duration, prompting surgeons to defer the removal procedure.

Table 1 Total sample with demographic and clinical characteristics (*n* = 167)

Variable	Frequency (%)
Gender	
Male	114 (68)
Female	53 (32)
Nationality	
Saudi	150 (90)
Non-Saudi[1]	17 (10)
Length of stay	
1 d	93 (56)
> 1 d	74 (44)
Complication rate	
At least 1[2]	10 (6)
No complication	157 (94)
Sick leave	
No sick leave	110 (65.9)
≤ 14 d	49 (29.3)
> 14 d	8 (4.8)
Type of anesthesia	
Regional	20 (12)
General	147 (88)
Duration of surgery (min)	
Mean (SD)	77.1 (54.7)
Period between insertion and removal (mo)	
Mean (SD)	18.6 (17.9)
Age	
Mean (SD)	25 (18)

[1]Non-Saudis include patients from Yemen, Palestine, Nigeria, Nazih (no nationality), Pakistan, Australia, Somalia, Sudan, Sri Lanka, Philippines, and Jordan.
[2]Complications include stiffness, contaminated wound, pain, and limited range of motion.

The adult cohort exhibited a markedly elevated male prevalence in contrast to the pediatric group (P = 0.006). This divergence is attributable to the predominant impact of motor vehicle collision-related fractures on young adult males in Saudi Arabia, as opposed to pediatric patients who demonstrate a comparable incidence across genders[18]. Notably, most orthopedic hardware removal interventions target young adult males[19,20]. This explains why the number of adult women in this study was less than that of adult males, which is consistent with national and global literature.

The hospitalization duration following implant removal exhibited a statistically significant disparity between adults and the pediatric cohort (P = 0.001), with adults experiencing prolonged stays. While our study diverges from the reported average pediatric length of stay (2.9 d), it is crucial to note the non-routine nature of implant removal in the reported patient population[21]. In a retrospective analysis, noninfected implant removal in adults averaged 5 d[1]. Although a comprehensive age-group comparison is absent, our findings align with the prevailing literature, reinforcing the noteworthy impact of non-routine removal on hospitalization duration.

Our data indicates a notably higher utilization of regional anesthesia in adults compared to pediatric patients. Despite its proven safety and efficacy for perioperative pain management, regional blocks are less prevalent in the pediatric demographic[22]. This discrepancy may stem from a potential lack of awareness among families regarding the advantages of regional anesthesia for their children.

Furthermore, our study reveals a significantly longer mean interval between implant insertion and removal in adults compared to pediatric patients. Consistent with similar research, a majority of adults opted for implant removal within 1-2 years post-implantation[23]. Additional investigations support these findings, showing that adults typically remove orthopedic implants within a 4-36 mo interval[24]. In a retrospective case series involving pediatric patients undergoing

Table 2 Upper limb or spine *vs* lower limb with demographic and clinical characteristics of patients

Variable	Upper limb or spine, *n* = 55 (%)	Lower limb, *n* = 112 (%)	Test (*P* value)
Gender			χ^2 = 2.48 (0.115)
Male	42 (76.4)	72 (64.3)	
Female	13 (23.6)	40 (35.7)	
Nationality			χ^2 = 0.106 (0.744)
Saudi	50 (90.9)	100 (89.3)	
Non-Saudi[1]	5 (9.1)	12 (10.7)	
Age			*t* = -0.355 (0.723)
Mean (± SD)	24 (± 16)	25 (± 18)	
Adults or pediatrics			χ^2 = 0.598 (0.439)
Adults	34 (61.8)	76 (67.9)	
Pediatrics	21 (38.2)	36 (32.1)	
Length of stay			χ^2 = 0.618 (0.432)
1 d	33 (60)	60 (53.6)	
> 1 d	22 (40)	52 (46.4)	
Complication rate			χ^2 = 0.041 (0.839)
At least 1[2]	3 (5.5)	7 (6.25)	
No complication	52 (94.5)	105 (93.75)	
Sick leave			χ^2 = 1.606 (0.448)
No sick leave	37 (67.3)	73 (65.2)	
≤ 14 d	17 (30.9)	32 (28.6)	
> 14 d	1 (1.8)	7 (6.2)	
Type of anesthesia			**χ^2 = 5.411 (0.02)**
Regional	2 (3.6)	18 (16.1)	
General	53 (96.4)	94 (83.9)	
Duration of surgery (min) mean (SD)	74.7 (57.1)	78.2 (53.8)	*t* = -0.387 (0.699)
Period between insertion and removal (mo) mean (SD)	14.5 (13.5)	20.6 (19.5)	***t* = -2.104 (0.037)**

[1]Non-Saudis include patients from Yemen, Palestine, Nigeria, Nazih (no nationality), Pakistan, Australia, Somalia, Sudan, Sri Lanka, Philippines, and Jordan.
[2]Complications include stiffness, contaminated wound, pain, and limited range of motion. Bold indicated significant associations.

hardware removal, the mean period between insertion and removal was 16 mo[25]. Surgeons in the pediatric population generally prefer post-fracture healing implant removal due to potential growth issues if left in place for an extended period.

The investigation was conducted within a government-owned healthcare facility, characterized by complimentary healthcare services, rendering precise cost determination challenging. Nevertheless, the burden on the hospital can be approximated through various indicators, such as length of stay, surgical duration, and routine implant removal frequency from orthopedic procedures. The average hospital stay was 4.2 d, with a mean (SD) surgery duration of 77.1 (54.7) min, imposing strain on the operating room schedule. Between January 2016 and August 2022, the Department of Orthopedic Surgery performed 4583 operations, including 167 routine implant removals (3.6% of the total). A prospective economic analysis indicated the cost of single-implant removal as $708.37 (± 22.10) with a range of $366.97-$1100.92[2].

The study was limited by its small sample size and only one center's experience. Therefore, we recommend conducting a large prospective multicenter study to investigate routine implant removal.

CONCLUSION

The contentious nature of routine implant removal in clinical discourse lacks a definitive consensus. Surgeons often

Table 3 Demographic and clinical characteristics of pediatric *vs* adult patient

Variable	Pediatrics, *n* = 57 (%)	Adults, *n* = 110 (%)	Test (*P* value)
Gender			χ^2 = 7.69 (0.006)
Male	31 (54.4)	83 (75.5)	
Female	26 (45.6)	27 (24.5)	
Nationality			χ^2 = 0.188 (0.665)
Saudi	52 (91.2)	98 (89.1)	
Non-Saudi[1]	5 (8.8)	12 (10.9)	
Length of stay			χ^2 = 16.2 (< 0.001)
1 d	44 (77.2)	49 (44.5)	
> 1 d	13 (22.8)	61 (55.5)	
Upper limb and spine or lower limb			χ^2 = 0.598 (0.439)
Upper limb or spine	21 (36.8)	34 (30.9)	
Lower limb	36 (63.2)	76 (69.1)	
Complication rate			χ^2 = 0.081 (0.776)
At least 1[2]	3 (5.3)	7 (6.4)	
No complication	54 (94.7)	103 (93.6)	
Sick leave			χ^2 = 4.13 (0.127)
No sick leave	43 (75.4)	67 (60.9)	
≤ 14 d	13 (22.8)	36 (32.7)	
> 14 d	1 (1.8)	7 (6.4)	
Type of anesthesia			χ^2 = 5.89 (0.015)
Regional	2 (3.5)	18 (16.4)	
General	55 (96.5)	92 (83.6)	
Duration of surgery (min) mean (± SD)	77.07 (37.8)	77.05 (61.9)	*t* = 0.003 (0.997)
Period between insertion and removal (mo) mean (± SD)	12.3 (8.3)	21.9 (20.6)	***t* = -4.27 (< 0.001)**

[1]Non-Saudis include patients from Yemen, Palestine, Nigeria, Nazih (No nationality), Pakistan, Australia, Somalia, Sudan, Sri Lanka, Philippines, and Jordan.
[2]Complications include stiffness, contaminated wound, pain, and limited range of motion. Bold indicated significant associations.

grapple with conflicting data and familial pressures, presenting a dilemma. This study elucidates the repercussions on patient well-being, healthcare resources, and workforce absenteeism, contributing to a comprehensive understanding of its public health and systemic impact. Positioned as a fiscal and health burden, particularly for adult patients and healthcare institutions, routine implant removal engenders avoidable complications and protracts hospital stays. Additionally, it depletes hospital resources, monopolizing operating rooms that could serve critical procedures. Conclusively, establishing explicit institutional directives is imperative to regulate this practice.

ARTICLE HIGHLIGHTS

Research background

Elective removal of asymptomatic implants remains a controversial area, with no defined guidelines to direct this orthopedic practice. Hence, placing a considerable clinical and economic burden on both patients and healthcare systems.

Research motivation

Little data is known regarding routine orthopedic implant removal in the literature, particularly in the Middle East.

Research objectives

The objective of this study is to measure the burden of routine implant removal on both patients' health and hospital

facilities.

Research methods

A retrospective cohort study was conducted at a single tertiary center between February 2016 and August 2022 and included participants across all age groups who underwent asymptomatic implant removal in the orthopedic department. Participant's demographic and clinical data were retrieved from the electronic record system and statistically analyzed *via* Statistical Package for the Social Sciences version 25.

Research results

Complications were observed in 6% of the patients in our study, and sick leave was given in 34.1% of all cases. In 56% of cases, a single day in the hospital was necessary, whereas 44% required more than one day. These findings will shed light on this obscure area of literature, encouraging scholars to do further investigation in this area.

Research conclusions

In conclusion, this study proposes that routine implant removal places a heavy load on patients and healthcare facilities.

Research perspectives

More prospective multi-center studies with larger sample sizes are needed to investigate further the impact of elective implant removal on patients and hospitals.

FOOTNOTES

Author contributions: AlOmran AK, Alosaimi N contributed to the concept; Alshaikhi AA, Bakhurji OM contributed to design; Alzahrani KJ, Salloot BZ, Alabduladhem TO, AlMulhim AI contributed to study execution; AlOmran AK, Alosaimi N, Alshaikhi AA, Bakhurji OM, Alzahrani KJ, Salloot BZ, Alabduladhem TO, AlMulhim A contributed to manuscript writing and review; Alumran A contributed to statistical analysis.

Institutional review board statement: Ethical approval was obtained from the Institutional Review Board of Imam Abdulrahman bin Faisal University following the ethical requirements of the Declaration of Helsinki (IRB number: IRB-UGS-2022-01-396).

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

Conflict-of-interest statement: All authors have no conflict of interests.

Data sharing statement: Raw data and materials are available as needed.

Country/Territory of origin: Saudi Arabia

ORCID number: Ammar K AlOmran 0000-0001-6659-5105; Nader Alosaimi 0000-0002-5973-9550; Ahmed A Alshaikhi 0000-0002-6603-1614; Omar M Bakhurji 0009-0008-4081-1971; Khalid J Alzahrani 0009-0003-8249-5878; Basil Ziyad Salloot 0009-0002-1655-4799; Tamim Omar Alabduladhem 0000-0002-9446-8442; Ahmed I AlMulhim 0009-0005-0668-7039; Arwa Alumran 0000-0001-6454-3678.

S-Editor: Liu JH
L-Editor: A
P-Editor: Yuan YY

REFERENCES

1 **Haseeb M**, Butt MF, Altaf T, Muzaffar K, Gupta A, Jallu A. Indications of implant removal: A study of 83 cases. *Int J Health Sci (Qassim)* 2017; **11**: 1-7 [PMID: 28293156]
2 **Onche II**, Osagie OE, INuhu S. Removal of orthopaedic implants: indications, outcome and economic implications. *J West Afr Coll Surg* 2011; **1**: 101-112 [PMID: 25452945]
3 **Busam ML**, Esther RJ, Obremskey WT. Hardware removal: indications and expectations. *J Am Acad Orthop Surg* 2006; **14**: 113-120 [PMID: 16467186 DOI: 10.5435/00124635-200602000-00006]
4 **Böstman O**, Pihlajamäki H. Routine implant removal after fracture surgery: a potentially reducible consumer of hospital resources in trauma units. *J Trauma* 1996; **41**: 846-849 [PMID: 8913214 DOI: 10.1097/00005373-199611000-00013]
5 **Boerger TO**, Patel G, Murphy JP. Is routine removal of intramedullary nails justified. *Injury* 1999; **30**: 79-81 [PMID: 10476274 DOI:

10.1016/s0020-1383(98)00200-9]

6 **Wang J**, Chidambaram R, Mok D. Is removal of clavicle plate after fracture union necessary? *Int J Shoulder Surg* 2011; **5**: 85-89 [PMID: 22223957 DOI: 10.4103/0973-6042.90998]

7 **Suda AJ**, Heilgeist E, Tinelli M, Bischel OE. High early post-operative complication rate after elective aseptic orthopedic implant removal of upper and lower limb. *J Orthop Res* 2018; **36**: 1035-1039 [PMID: 28862357 DOI: 10.1002/jor.23718]

8 **Ko S**, Lee J, Nam J. Effectiveness of orthopedic implant removal surgery in patients with no implant-related symptoms after fracture union of isolated lower extremity shaft fractures: patient-centered evaluation. *Arch Orthop Trauma Surg* 2023; **143**: 107-114 [PMID: 34180004 DOI: 10.1007/s00402-021-03993-y]

9 **Yuan W**, Chua T, Kwek E. Is Elective Implant Removal after Fracture Healing Beneficial? - A Prospective Cohort Study. *Malays Orthop J* 2022; **16**: 55-60 [PMID: 36589381 DOI: 10.5704/MOJ.2211.010]

10 **Reith G**, Schmitz-Greven V, Hensel KO, Schneider MM, Tinschmann T, Bouillon B, Probst C. Metal implant removal: benefits and drawbacks--a patient survey. *BMC Surg* 2015; **15**: 96 [PMID: 26250649 DOI: 10.1186/s12893-015-0081-6]

11 **Vos DI**, Verhofstad MH. Indications for implant removal after fracture healing: a review of the literature. *Eur J Trauma Emerg Surg* 2013; **39**: 327-337 [PMID: 26815392 DOI: 10.1007/s00068-013-0283-5]

12 **Montgomery BK**, Gamble JG, Kha ST, Hecht GG, Vorhies JS, Lucas JF. Indications for and Risks Associated With Implant Removal After Pediatric Trauma. *J Am Acad Orthop Surg Glob Res Rev* 2022; **6** [PMID: 35427259 DOI: 10.5435/JAAOSGlobal-D-22-00050]

13 **Kovar FM**, Strasser E, Jaindl M, Endler G, Oberleitner G. Complications following implant removal in patients with proximal femur fractures - an observational study over 16 years. *Orthop Traumatol Surg Res* 2015; **101**: 785-789 [PMID: 26456285 DOI: 10.1016/j.otsr.2015.07.021]

14 **Kasai T**, Matsumoto T, Iga T, Tanaka S. Complications of implant removal in ankle fractures. *J Orthop* 2019; **16**: 191-194 [PMID: 30906121 DOI: 10.1016/j.jor.2019.02.017]

15 **Broadbent CR**, Maxwell WB, Ferrie R, Wilson DJ, Gawne-Cain M, Russell R. Ability of anaesthetists to identify a marked lumbar interspace. *Anaesthesia* 2000; **55**: 1122-1126 [PMID: 11069342 DOI: 10.1046/j.1365-2044.2000.01547-4.x]

16 **John RS**, Mckean G, Sarkar RA. Upper Limb Block Anesthesia. 2023 May 27. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [PMID: 30285355]

17 **Wood II GW**. Fracture and dislocation. In: Canale ST, Beaty JH, editors. Campbell's Operative Orthopaedics. 11th ed. Philadelphia, PA: Mosby/Elsevier; 2007; 3055-3059

18 **Alotaibi F**, Alqahtani AH, Alwadei A, Al-Raeh HM, Abusaq I, Mufrrih SA, Alqahtani AA, Alsabaani A, Alsulami MM. Pattern of orthopedic injuries among Victims of Road Traffic Accidents in Aseer region, Saudi Arabia. *Ann Med Surg (Lond)* 2021; **67**: 102509 [PMID: 34234947 DOI: 10.1016/j.amsu.2021.102509]

19 **Bhandari R**, Dawadi P, Thapa Magar M, Sinha R, Kayastha N, Pratap Shah R, Babu Thapa B, Rana Magar S. Orthopedic Implant Removal in the Department of Orthopedics of a Tertiary Care Centre of Nepal: A Descriptive Cross-sectional Study. *JNMA J Nepal Med Assoc* 2021; **59**: 116-119 [PMID: 34506453 DOI: 10.31729/jnma.6171]

20 **Shrestha R**, Shrestha D, Dhoju D, Parajuli N, Bhandari B, Kayastha SR. Epidemiological and outcome analysis of orthopedic implants removal in Kathmandu University Hospital. *Kathmandu Univ Med J (KUMJ)* 2013; **11**: 139-143 [PMID: 24096221 DOI: 10.3126/kumj.v11i2.12489]

21 **Boulos A**, DeFroda SF, Kleiner JE, Thomas N, Gil JA, Cruz AI Jr. Inpatient orthopaedic hardware removal in children: A cross-Sectional study. *J Clin Orthop Trauma* 2017; **8**: 270-275 [PMID: 28951646 DOI: 10.1016/j.jcot.2017.06.020]

22 **Ponde V**. Recent trends in paediatric regional anaesthesia. *Indian J Anaesth* 2019; **63**: 746-753 [PMID: 31571688 DOI: 10.4103/ija.IJA_502_19]

23 **Kuubiere CB**, Mogre V, Alhassan A. Incidence and Indications for Orthopaedic Implant Removal: A Retrospective Analysis. Lifsc [Internet]. September 28; 2015 [cited November 16, 2023]; 2: 76-80. Available from: https://www.asianonlinejournals.com/index.php/Lifsc/article/view/627

24 **Labosky DA**, Cermak MB, Waggy CA. Forearm fracture plates: to remove or not to remove. *J Hand Surg Am* 1990; **15**: 294-301 [PMID: 2324461 DOI: 10.1016/0363-5023(90)90112-5]

25 **Davids JR**, Hydorn C, Dillingham C, Hardin JW, Pugh LI. Removal of deep extremity implants in children. *J Bone Joint Surg Br* 2010; **92**: 1006-1012 [PMID: 20595123 DOI: 10.1302/0301-620X.92B7.24201]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 147-155

DOI: 10.5312/wjo.v15.i2.147

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Observational Study

Limb Lengthening and Reconstruction Society orthopedic surgeons in the United States: An analysis of geographical distribution, academic, leadership, and demographic characteristics

Amir Human Hoveidaei, Reza Niakan, Seyed Hossein Hosseini-Asl, Abijith Annasamudram, Janet D Conway

Specialty type: Orthopedics

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Wiratnaya IGE, Indonesia

Received: October 30, 2023
Peer-review started: October 30, 2023
First decision: December 7, 2023
Revised: December 25, 2023
Accepted: January 19, 2024
Article in press: January 19, 2024
Published online: February 18, 2024

Amir Human Hoveidaei, Abijith Annasamudram, Janet D Conway, International Center for Limb Lengthening, Rubin Institute for Advanced Orthopedics, Sinai Hospital of Baltimore, Baltimore, MD 21215, United States

Reza Niakan, Student Research Committee, Shiraz University of Medical Sciences, Shiraz 73, Iran

Seyed Hossein Hosseini-Asl, Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran 1417755331, Iran

Corresponding author: Amir Human Hoveidaei, MD, MSc, Research Fellow, International Center for Limb Lengthening, Rubin Institute for Advanced Orthopedics, Sinai Hospital of Baltimore, 2401 West Belvedere Avenue, Baltimore, MD 21215, United States.
hoveidaei.a.h@gmail.com

Abstract

BACKGROUND

The Limb Lengthening and Reconstruction Society (LLRS) is a premier orthopedic specialty organization that promotes limb reconstruction for all ages. LLRS membership characteristics, however, are poorly reported. This study delineates orthopedic surgeon LLRS members' demographic traits, academic achievement, leadership attainment, and geographical distribution across the United States.

AIM

To inform aspiring orthopedic professionals, as well as to promote growth and diversity in both the LLRS organization and overarching field.

METHODS

This cross-sectional study examined United States LLRS members' academic, leadership, demographic, and geographical attributes. After reviewing the 2023 LLRS member directory, Google search results were matched to the listings and appended to the compiled data. Sex and ethnicity were evaluated visually utilizing retrieved images. The Hirsch index (H-index) of academic activity, residency and fellowship training, other graduate degrees, leadership positions, practice type (academic or non-academic), and spoken languages were categorized. LLRS members per state and capita determined geographic distribution. The Mann-

Whitney *U* test was applied to compare H-index between males and females, as well as to assess member differences pertaining to affiliation with academic *vs* non-academic practice facilities.

RESULTS

The study included 101 orthopedic surgeons, 78 (77.23%) Caucasian and 23 (22.77%) non-Caucasian, 79 (78.22%) male and 22 (21.78%) female. Surgeons with DO degrees comprised only 3.96% (4) of the cohort, while the vast majority held MDs [96.04% (97)]. Mean H-index was 10.55, with male surgeons having a significantly higher score ($P = 0.002$). Most orthopedic surgeons (88.12%,) practiced in academic centers. Of those professionals who occupied leadership positions, 14% were women, while 86% were men. Additionally, 19 (37.25%) United States regions and the District of Columbia lacked an LLRS-member orthopedic surgeon. Total per capita rate across the United States was 0.30 LLRS orthopedic surgeons per 1 million people.

CONCLUSION

Over 21% of LLRS members are women, surpassing prior benchmarks noted in orthopedic faculty reporting. LLRS members' high research productivity scores imply field dedication that can refine expertise in the limb lengthening and reconstruction space. Gender disparities in leadership remain, however, necessitating greater equity efforts. A low rate of LLRS representation per capita must be addressed geographically as well, to affect improvements in regional care access. This study can serve to support aspiring orthopedic professionals, inform diversity, leadership, and field advancement strategies, and maintain the continued goal of enhanced patient care worldwide.

Key Words: Limb lengthening and reconstruction; Orthopedic surgeon demographics; Orthopedic surgeon societal membership; Orthopedic fellowships

Core Tip: Societal membership characteristics for the Limb Lengthening and Reconstruction Society had previously been poorly reported. These attributes were analyzed comparatively with industry precedents to glean insights for aspiring orthopedic professionals, inform organizational decision-making in support of growth, diversity, and equity, as well as to uphold the foundational goal of patient care optimization.

Citation: Hoveidaei AH, Niakan R, Hosseini-Asl SH, Annasamudram A, Conway JD. Limb Lengthening and Reconstruction Society orthopedic surgeons in the United States: An analysis of geographical distribution, academic, leadership, and demographic characteristics. *World J Orthop* 2024; 15(2): 147-155

URL: https://www.wjgnet.com/2218-5836/full/v15/i2/147.htm

DOI: https://dx.doi.org/10.5312/wjo.v15.i2.147

INTRODUCTION

The Limb Lengthening and Reconstruction Society (LLRS) is a prominent orthopedic specialty society operating within the American Academy of Orthopaedic Surgery (AAOS) volunteer structure. Initially founded in 1989 as the Association for the Study and Application of the Method of Ilizarov-North America, the LLRS is dedicated to advancing techniques to treat complex congenital and developmental deformities, as well as traumatic and post-traumatic limb conditions[1]. The organization has since been recognized as a branch of the AAOS's Board of Specialty Societies (1999), solidifying its stature as an instrumental entity in advancing the field of limb reconstruction for patients of all ages[2,3].

The LLRS encompasses a diverse, international group of orthopedic surgeons, physicians, and allied health professionals dedicated to encouraging research, scientific exchange, and collaboration. Leveraging the principles of distraction osteogenesis, its primary clinical focus is to deliver exceptional patient care for limb lengthening and reconstruction, extremity deformity correction, and complex fracture treatment[3,4].

The LLRS comprises 214 professionals, 49.5% (106) of whom reside in the United States. This membership base positions the LLRS as a pioneering authority within the United States[4,5]. Nevertheless, there remains a dearth of comprehensive reporting on leadership career paths within the field. Similar to other fields, positions of increasing organizational authority within the medical profession tend to be associated with certain distinguishing characteristics, such as innovation and specialization, scientific organization membership, research activity, mentorship, collaboration, and optimization of patient outcomes[6]. Objective criteria differentiating these exceptional individuals, and likewise those in LLRS leadership, remain elusive, however, engendering ambiguity about the specific qualifications needed to navigate such pathways to success[2,5].

On the other hand, sub-specialization and rising patient volumes have been extensively documented in other orthopedic fields[7]. The growing prevalence of motorized intramedullary lengthening nails for limb deformity correction

is one example of how surgical options have expanded in this relatively new subspecialty[8,9]. The treatment of limb deformity, and namely limb lengthening, has recently enjoyed increased recognition and understanding within the field. Nonetheless, the availability of such dedicated clinical services within academic orthopedic and societal institutions is still limited[10].

Considering this, the present study aims to achieve two primary goals. First, we want to identify the objective characteristics shared by LLRS members. Toward this end, we delve into the membership's demographics, institutional training backgrounds, and academic experiences, providing a useful framework for aspiring orthopedic professionals seeking similar career paths. In addition, we hope to shed light on the geographical distribution of LLRS members across the United States, highlighting areas where representation may be lacking, thus indicating opportunities for growth and diversity. We hypothesize that if there is diversity and gender-inclusivity among LLRS members, it may be associated with higher academic achievements within the society, compared to other orthopedic societies documented in the literature.

MATERIALS AND METHODS

Overview

This cross-sectional study utilized data from the LLRS directory to analyze members' academic, leadership, and demographic characteristics, as well as their geographical distribution in the United States. Excluded were 5 LLRS members who were not orthopedic surgeons. The study was deemed exempt by the institutional review board, as all data utilized were publicly available.

Data source

The 2023 LLRS member directory, accessed on May 22, 2023, was thoroughly reviewed to identify all LLRS-member professionals across the United States. Additional demographic data, including educational background, curriculum vitae, institutional biographies, and Scopus records, were collected *via* Google search.

To determine the population of each state in the United States, data from the United States Census Bureau was obtained.

Two evaluators (authors AHH and RN) independently assessed the data in a blinded manner. In cases of disagreement, findings were discussed in a mutual session and resolved by consensus.

Variables

Sex and ethnicity were defined based on the retrieved photographs, which had been matched to the membership listings where practicable. Ethnicity was categorized as Caucasian or non-Caucasian. Based on a previously documented method [11,12], "Caucasian" described visible characteristics consistent with persons of European or Caucasian descent. "Non-Caucasian" individuals displayed visible characteristics associated with diverse racial and ethnic backgrounds. This included those of African, Asian, Hispanic, Middle Eastern, Indigenous, and other non-European descent. We also endeavored to confirm categorization based on the additionally available data in the individuals' profiles.

Other variables included residency and fellowship training, and the member's H-index. H-index was obtained by querying the Scopus database (Elsevier BV, Waltham, MA, United States), which contains an extensive repository of peer-reviewed scientific literature, with a citation-tracking component.

In addition, this paper reports on other graduate degrees, leadership positions held, type of practice center (academic *vs* non-academic), and languages spoken other than English.

To derive the geographical distribution of LLRS members, totals per state were tallied. Calculations of per capita ratios were then performed using Census Bureau population statistics culled from the 9 divisions of the United States census Bureau.

Statistical analysis

Statistical analysis was conducted *via* Microsoft Office Excel 2019. LLRS member per capita values were assessed as the sum of LLRS members in a given area, divided by the total population of the corresponding state or census division, and scaled by a factor of 1000000 people. Tableau 2019.4.4 was utilized for geocoding labels.

To compare H-index between males and females, and between members practicing in academic or non-academic centers, the Mann-Whitney *U* test was applied using the SPSS version 26.0.

RESULTS

This study reviewed LLRS member listings for 101 orthopedic surgeons, 79 (78.22%) of whom were male, and 22 (21.78%) of whom were female. Seventy-eight (77.23%) were Caucasian, with the remainder belonging to non-Caucasian ethnicities. Only 4 (3.96%) held a DO degree, while 97 (96.04%) held an MD degree. Half of the DOs (2 of 4) had another graduate degree, whereas just 13 (13.40%) MDs had an additional graduate degree. Twenty-five individuals (27.75%) were reported to speak a second language, 36% of which was listed as Spanish fluency.

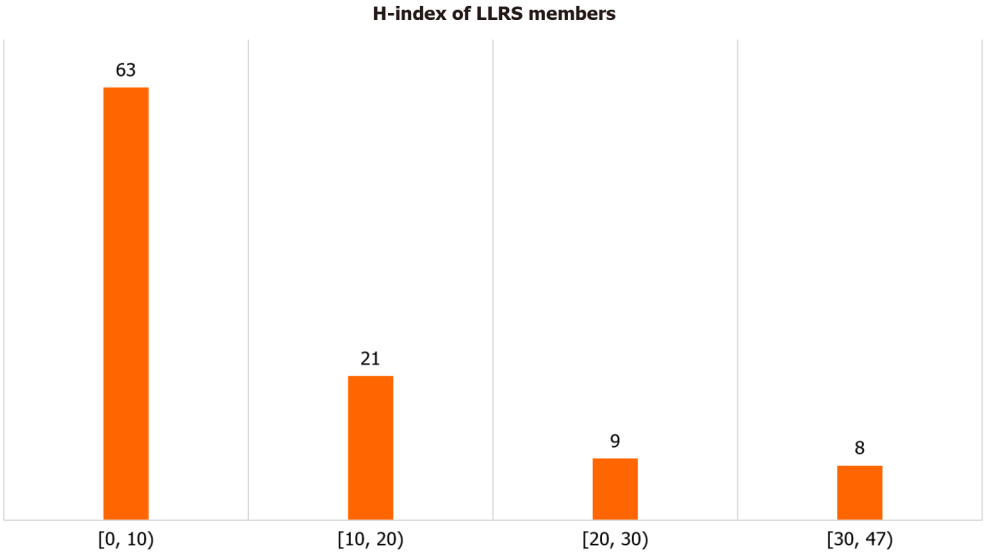


Figure 1 H-index of Limb Lengthening and Reconstruction Society members. LLRS: Limb Lengthening and Reconstruction Society.

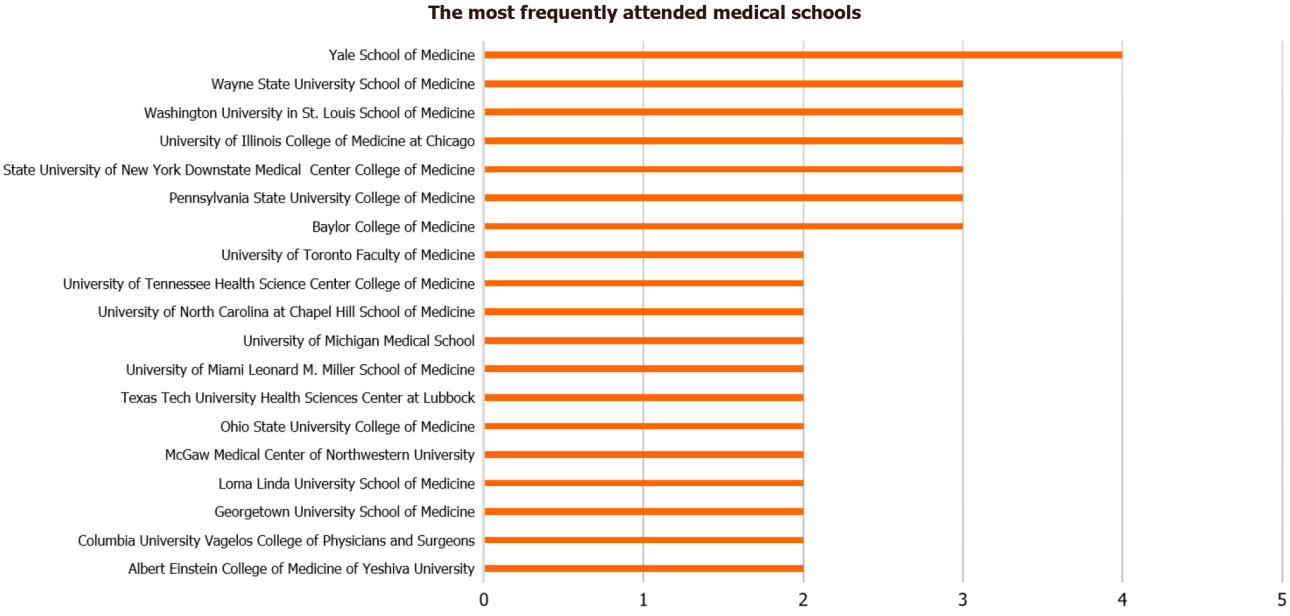


Figure 2 The most frequently attended medical schools.

In addition to the 3 Canadian school graduates, there were 11 surgeons who had graduated from international medical schools. Three of these schools were in India, and the others were situated in various countries. Most orthopedic surgeons worked in academic centers (89, 88.12%), while 12 (11.88%) did not. Average H-index was 10.55. Those who did not work in academic centers had a significantly lower mean H-index (2.00) than the others (11.71), ($P < 0.001$). The mean H-index for male surgeons was 12.03, as compared to 5.27 for females ($P < 0.002$). The Scopus H-indices of all LLRS members are depicted in Figure 1.

Among the members evaluated, 28 held positions of leadership, such as department chair, society president, and clinic or fellowship director. Of these, 24 (85.71%) were men, and 4 (14.29%) were women.

Yale School of Medicine, Baylor College of Medicine, Pennsylvania State University College of Medicine, State University of New York Downstate Medical Center College of Medicine, University of Illinois College of Medicine at Chicago, Washington University in St. Louis School of Medicine, and Wayne State University School of Medicine, each produced at least 3 future LLRS orthopedic surgeons (Figure 2).

Cleveland Clinic Foundation and University of California (San Francisco) were the most frequently listed residency programs among LLRS members, with 4 LLRS members each, followed closely by Case Western Reserve University/ University Hospitals Cleveland Medical Center, Icahn School of Medicine at Mount Sinai, and New York University School of Medicine/NYU Langone Orthopedic Hospital, at 3 per facility (Figure 3).

Table 1 Limb Lengthening and Reconstruction Society distribution of orthopedic surgeons across United States census divisions

	Geographic region	LLRS orthopedic surgeons	LLRS orthopedic surgeons per 1 million people
	Total	101	0.30
Northeast region	New England	2	0.13
	Middle Atlantic	9	0.21
Midwest region	East North Central	12	0.25
	West North Central	5	0.23
South region	South Atlantic	29	0.44
	East South Central	5	0.26
	West South Central	14	0.34
West region	Mountain	6	0.24
	Pacific	19	0.35

LLRS: Limb Lengthening and Reconstruction Society.

Ninety-six (95.05%) of the 101 LLRS members evaluated had participated in at least one clinical fellowship during their professional career. These totaled 133, with 62 (46.62%) pediatric concentrations, 28 (21.05%) trauma-focused, 27 (20.30%) geared toward limb lengthening and reconstruction/deformity correction, 4 (3.01%) in musculoskeletal oncology, 4 (3.01%) for foot and ankle surgery, and 8 (6.01%) which included other types of fellowships. The International Center for Limb Lengthening (ICLL) at Sinai Hospital of Baltimore stood out as the program producing the most LLRS orthopedic surgeons pursuant to limb lengthening and reconstruction/deformity correction fellowships (excluding the LLRS traveling fellowship) (Figure 4).

There were no LLRS member orthopedic surgeons in 19 (37.25%) states. States with the most LLRS member orthopedic surgeons were California, Florida, Ohio, and Texas, with 13, 11, 9, and 9 members, respectively (Figure 5). The District of Columbia, Delaware, Alaska, and Oregon had the highest per capita numbers, with 2.90, 2.02, 1.36, and 1.18 LLRS orthopedic surgeons per 1 million population (Figure 6).

In the United States, the overall per capita rate of LLRS member orthopedic surgeons was 0.3 per 1 million people. Table 1 details the distribution of members across census divisions.

DISCUSSION

Gender equality in the LLRS compares favorably to recently reported findings in the literature. While the percentage of women holding orthopedic faculty positions and/or AAOS memberships has been purported to range from 6.5% to 10.5%, females comprised more than 21% of LLRS membership ranks[13,14].

Demographic distributions culled from orthopedic societies have noted an approximately 20.2% proportion of ethnic minorities among members, with even lower representation for the same groups in leadership positions. Similarly, an estimated 22.77% of LLRS members belong to non-Caucasian ethnicities[15].

The research and scientific productivity of LLRS members, as reflected by their H-index, is notable. While recent studies have reported a median H-index of 5 for academic orthopedic surgery faculty, the LLRS membership, including both academic and non-academic practitioners, had a higher median H-index of 6, and a mean of 10.55[16]. This demonstrates the overall higher research productivity of LLRS members compared to their academic counterparts. Additionally, the pattern of males being more productive in research aligns with the trends observed among the academic orthopedic surgery faculty[16-18].

Despite the encouraging female representation among LLRS members (21%), there remains a significant sex-related disparity in leadership roles, with only 14% of such titles held by women, *vs* an overwhelming majority (86%) which were occupied by men. This highlights the need for increased awareness to drive gender equality initiatives and promote equitable access to leadership opportunities, regardless of sex[19].

Our analysis revealed that LLRS member orthopedic surgeons were more likely to have graduated from certain medical schools and residency programs, such Yale School of Medicine (4), and Cleveland Clinic Foundation and University of California (San Francisco). Many LLRS members pursued pediatric or trauma fellowships, rather than limb lengthening and reconstruction/deformity correction specifically. The authors speculate that this may be due to the non-accredited nature of limb lengthening and reconstruction/deformity correction programs. This emphasizes the potential benefits of establishing accreditation, encouraging and enabling surgeons interested in such specialized fellowship training[20].

A call for accreditation in limb lengthening and reconstruction/deformity correction fellowships could facilitate increased participation of surgeons interested in this specific field[20]. Moreover, involving teaching centers specializing in limb lengthening and reconstruction/deformity correction fellowships in LLRS and AAOS initiatives could further

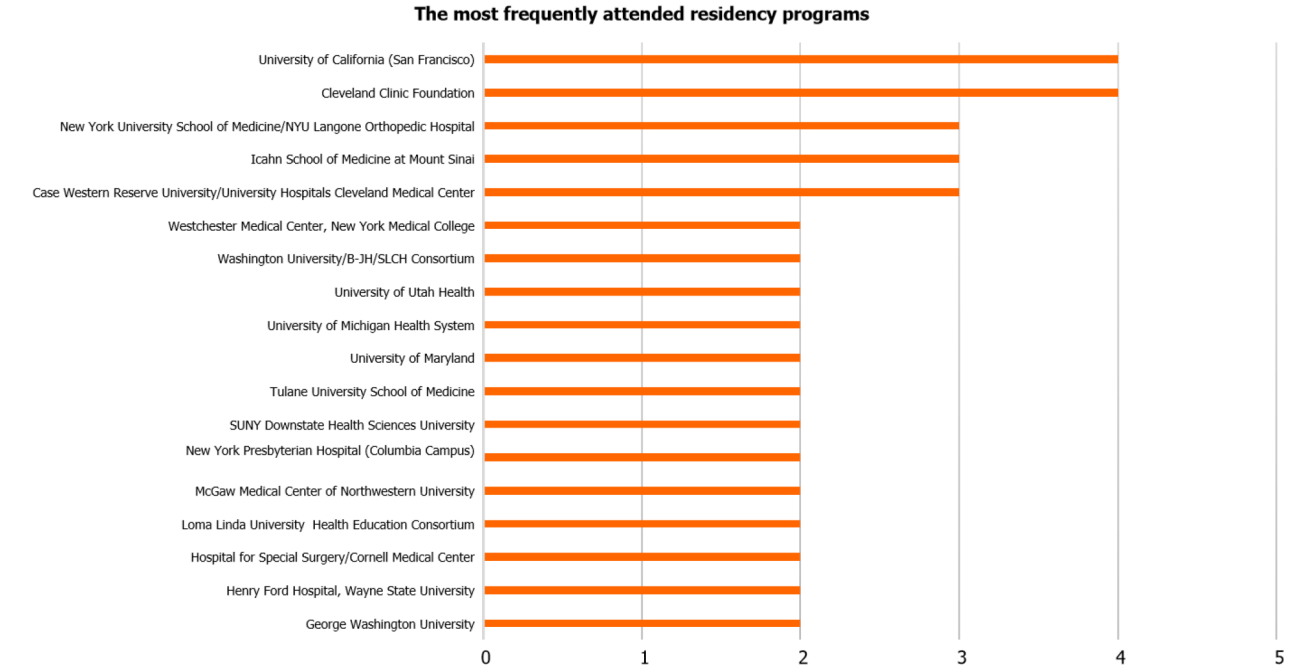


Figure 3 The most frequently attended residency programs.

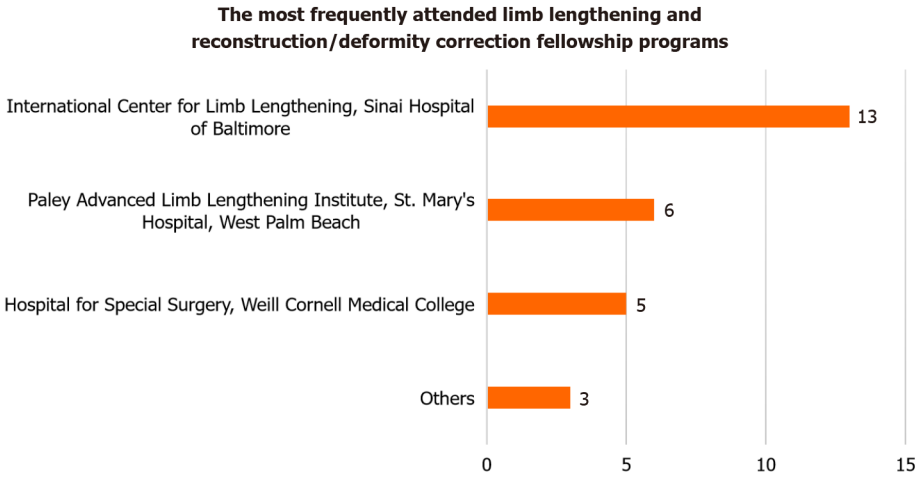


Figure 4 The most frequently attended fellowship programs.

advance the field. For instance, the ICLL at Sinai Hospital of Baltimore emerged as a leading producer of LLRS member orthopedic surgeons across the United States, despite Baltimore having being home to only two LLRS members.

It is important to address the geographical distribution of LLRS members. Our analysis reveals that 19 states in the United States had no LLRS member orthopedic surgeons at all. Ensuring the availability of LLRS member surgeons in areas with the lowest per capita representation, particularly in the New England and Middle Atlantic or Northeast regions, should be a notable consideration for future development.

To the best of our knowledge, this is the largest analysis of the LLRS, expounding upon the existing knowledge base in the field of limb lengthening and reconstruction by providing insights into the academic, leadership, demographic, and geographical distribution of its members. The findings herein can serve as a resource for aspiring orthopedic professionals and inform strategies for increasing diversity and equity, promoting equality and growth in leadership development, and advancing the field toward patient care optimization.

The novel findings of this study include the positive observation of a higher representation of women within LLRS compared to recent studies on orthopedic faculty and AAOS members. Additionally, the research emphasizes the prolific engagement of LLRS members in research, irrespective of their affiliation with academic or non-academic facilities. The identified medical schools and residency programs associated with LLRS surgeons provide new insights into potential pathways for specialized training. In terms of future directions, the study calls for addressing persistent gender disparities in leadership positions within LLRS, advocating for increased equity efforts.

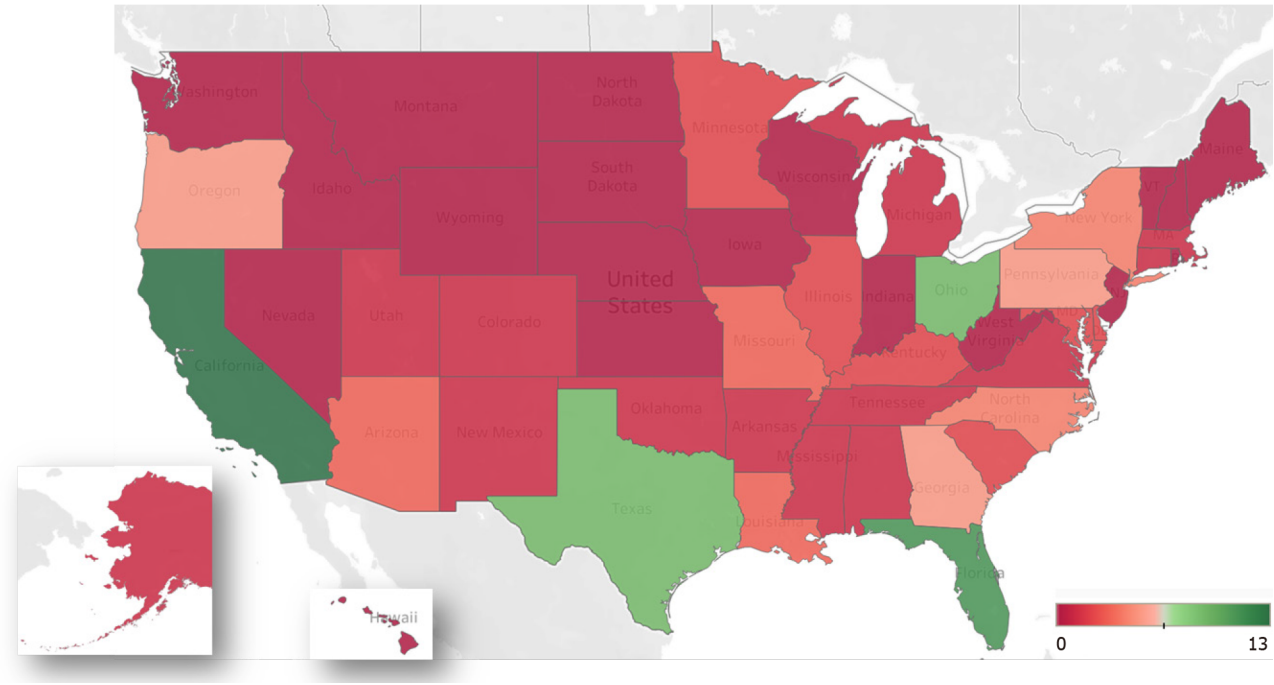


Figure 5 United States total distribution of Limb Lengthening and Reconstruction Society orthopedic surgeons.

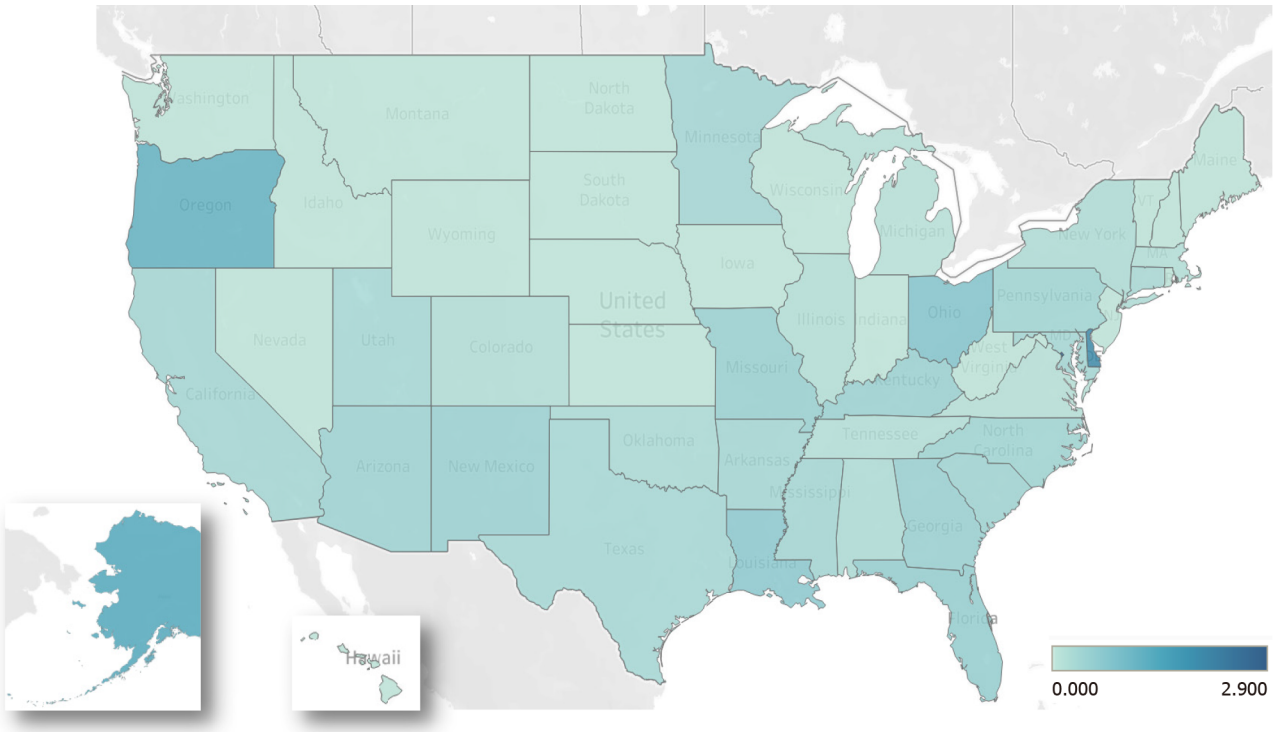


Figure 6 Per capita distribution of Limb Lengthening and Reconstruction Society orthopedic surgeons in the United States.

We do acknowledge certain limitations inherent to our study. Given the cross-sectional nature of the reporting, which represents the characteristics of LLRS members at the current time, we cannot comment retrospectively on the evolution of demographic and geographical diversity which constitutes the society's precedent progress. By design, we also relied on information obtained from websites, institutional biographies, and publicly accessible databases, which carry the innate possibility of containing inaccurate or outdated reporting, particularly in the application of the ethnicity definition method.

CONCLUSION

The LLRS is a specialized organization of orthopedic professionals for the advancement of limb lengthening and reconstruction. Its membership includes a favorably higher representation of women than recently reported in studies on orthopedic faculty and AAOS members. In general, LLRS members are prolifically engaged in research activity, regardless of academic or non-academic facility affiliation. Gender disparities do persist, however, in the attainment of leadership positions. The analysis also identified key medical schools and residency programs associated with LLRS orthopedic surgeons, emphasizing the potential benefits of accreditation and increased involvement of specialized centers. Geographical distribution highlights the need to address the lack of LLRS surgeons in certain regions. This study enhances the existing knowledge base in limb lengthening and reconstruction, providing valuable insights for various stakeholders in the field.

ARTICLE HIGHLIGHTS

Research background

This study delves into the demographic traits of Limb Lengthening and Reconstruction Society (LLRS) orthopedic surgeons in the United States, aiming to fill existing information gaps.

Research motivation

Motivated by the need to guide aspiring orthopedic professionals and promote diversity within LLRS, the research contributes valuable insights for organizational growth and inclusivity.

Research objectives

The study analyzes LLRS members' demographic, academic, and leadership attributes to inform aspiring professionals and support future research in the orthopedic field.

Research methods

Utilizing a cross-sectional approach, the study employs various metrics, including the Hirsch index, and applies the Mann-Whitney *U* test for specific comparisons.

Research results

The study reveals demographic trends among 101 orthopedic surgeons, emphasizing progress in gender diversity. It underscores the dedication of LLRS members and highlights the need to address geographic disparities for improved regional care access.

Research conclusions

Concluding that gender disparities persist in leadership roles; the study calls for increased equity efforts. It also emphasizes the need for strategic improvements in regional care access, aligning with the goal of enhancing global patient care.

Research perspectives

Future research should focus on mitigating gender disparities in LLRS leadership and improving the geographic distribution of members, ensuring equitable access to limb lengthening and reconstruction expertise across diverse regions.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Sharon Finn, MA for her editorial assistance.

FOOTNOTES

Co-corresponding authors: Amir Human Hoveidaei and Janet D Conway.

Author contributions: Hoveidaei AH and Conway JD designed the study; Hoveidaei AH, Niakan R, Hosseini-Asl SH and Annasamudram A reviewed the data; all authors drafted the primary manuscript; Hoveidaei AH and Conway JD revised the primary draft critically; all the authors read and approve the final manuscript.

Institutional review board statement: The study was done in International Center for Limb Lengthening, Rubin Institute for Advanced Orthopedics, Sinai Hospital of Baltimore, Baltimore, Maryland, USA. It was deemed exempt by the institutional review board (IRB), as all data utilized were publicly available.

Conflict-of-interest statement: Hoveidaei AH, Annasamudram A, and Conway JD are members of Sinai Hospital of Baltimore.

Data sharing statement: Data are available on request.

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

Country/Territory of origin: United States

ORCID number: Amir Human Hoveidaei 0000-0003-4607-354X; Reza Niakan 0009-0000-9261-4728; Janet D Conway 0000-0001-5694-3081.

S-Editor: Gong ZM
L-Editor: A
P-Editor: Yuan YY

REFERENCES

1 **Ilizarov AftSaAotMo**. ASAMI's STORY PAGE - Historical Review. 2023. Available from: http://www.asami.org/asami_story/default.asp
2 **Rozbruch SR**, Rozbruch ES, Zonshayn S, Borst EW, Fragomen AT. What is the Utility Of a Limb Lengthening and Reconstruction Service in an Academic Department of Orthopaedic Surgery? *Clin Orthop Relat Res* 2015; **473**: 3124-3132 [PMID: 25828942 DOI: 10.1007/s11999-015-4267-0]
3 **LLRS**. Limb Lengthening and Reconstruction Society. 2021. Available from: http://llrs.org
4 **Nicholas LR**. Seeks to Forge Bright Path for Limb Deformity and Reconstruction Education. LLRS 31st Annual Scientific Meeting. AAOS, 2023. Available from: https://www.aaos.org/aaosnow/2023/jan/commentary/commentary03/
5 **Limb Lengthening and Reconstruction Society**. About Executive Board. 2021. Available from: http://llrs.org/about/
6 **Sutton K**, Retzky J, Bedi A, Provencher CMT, Mulcahey MK. Leadership in Orthopaedic Surgery: Creating a Highly Effective Leader. *Instr Course Lect* 2023; **72**: 29-37 [PMID: 36534844]
7 **Sarmiento A**. Subspecialization in orthopaedics. Has it been all for the better? *J Bone Joint Surg Am* 2003; **85**: 369-373 [PMID: 12571318 DOI: 10.2106/00004623-200302000-00028]
8 **Lorange JP**, Alamiri N, Marwan Y, Alshammari A, Hamdy RC, Bernstein M. Humerus Lengthening with a Motorized Intramedullary Nail: A Systematic Review of Outcomes and Complications. *Strategies Trauma Limb Reconstr* 2022; **17**: 165-171 [PMID: 36756294 DOI: 10.5005/jp-journals-10080-1568]
9 **Powell KP**, Hammouda AI, Hlukha LP, Rivera JC, Patel M, Rozbruch SR, Conway JD, Herzenberg JE. Motorized Intramedullary Nail Lengthening in the Older Population. *J Clin Med* 2022; **11** [PMID: 36079171 DOI: 10.3390/jcm11175242]
10 **Horst PK**, Choo K, Bharucha N, Vail TP. Graduates of Orthopaedic Residency Training Are Increasingly Subspecialized: A Review of the American Board of Orthopaedic Surgery Part II Database. *J Bone Joint Surg Am* 2015; **97**: 869-875 [PMID: 25995502 DOI: 10.2106/JBJS.N.00995]
11 **Driesen AMDS**, Romero Arenas MA, Arora TK, Tang A, Nfonsam VN, O'Grady CL, Riall TS, Morris-Wiseman LF. Do General Surgery Residency Program Websites Feature Diversity? *J Surg Educ* 2020; **77**: e110-e115 [PMID: 32600889 DOI: 10.1016/j.jsurg.2020.06.014]
12 **Cohen SA**, Xiao M, Zhuang T, Michaud J, Wadhwa H, Shapiro L, Kamal RN. How do orthopaedic surgery residency program websites feature diversity? An analysis of 187 orthopaedic surgery programs in the United States. *Curr Orthop Pract* 2022; **33**: 258-263 [PMID: 35685001 DOI: 10.1097/bco.0000000000001101]
13 **Gerull KM**, Kim DJ, Cogsil T, Rhea L, Cipriano C. Are Women Proportionately Represented as Speakers at Orthopaedic Surgery Annual Meetings? A Cross-Sectional Analysis. *Clin Orthop Relat Res* 2020; **478**: 2729-2740 [PMID: 32667757 DOI: 10.1097/CORR.0000000000001359]
14 **Chambers CC**, Ihnow SB, Monroe EJ, Suleiman LI. Women in Orthopaedic Surgery: Population Trends in Trainees and Practicing Surgeons. *J Bone Joint Surg Am* 2018; **100**: e116 [PMID: 30180066 DOI: 10.2106/JBJS.17.01291]
15 **Ramirez RN**, Franklin CC. Racial Diversity in Orthopedic Surgery. *Orthop Clin North Am* 2019; **50**: 337-344 [PMID: 31084836 DOI: 10.1016/j.ocl.2019.03.010]
16 **Ence AK**, Cope SR, Holliday EB, Somerson JS. Publication Productivity and Experience: Factors Associated with Academic Rank Among Orthopaedic Surgery Faculty in the United States. *J Bone Joint Surg Am* 2016; **98**: e41 [PMID: 27194503 DOI: 10.2106/JBJS.15.00757]
17 **Herzog I**, Mendiratta D, Liggio DF, Ahn DB, Vosbikian M, Kaushal NK, Chu A. Use of the Relative Citation Ratio in Conjunction With H-Index to Promote Equity in Academic Orthopaedics. *J Am Acad Orthop Surg Glob Res Rev* 2023; **7** [PMID: 37406178 DOI: 10.5435/JAAOSGlobal-D-23-00080]
18 **Day CS**, Lage DE, Ahn CS. Diversity based on race, ethnicity, and sex between academic orthopaedic surgery and other specialties: a comparative study. *J Bone Joint Surg Am* 2010; **92**: 2328-2335 [PMID: 20926728 DOI: 10.2106/JBJS.I.01482]
19 **Elkadi SH**, Donaldson S, Krisanda E, Kessler MW. Trends in Medical Training and Leadership at Academic Orthopedic Programs. *Cureus* 2022; **14**: e29100 [PMID: 36249616 DOI: 10.7759/cureus.29100]
20 **Makarewich CA**, Herzenberg JE, McClure PK. Latest Advances in Limb Lengthening Using Magnetically Controlled Intramedullary Lengthening Nails. *Surg Technol Int* 2020; **36**: 404-411 [PMID: 32297969]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 156-162

DOI: 10.5312/wjo.v15.i2.156

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Prospective Study

High rate of clinically relevant improvement following anatomical total shoulder arthroplasty for glenohumeral osteoarthritis

Marc Randall Kristensen Nyring, Bo Sanderhoff Olsen, Alexander Amundsen, Jeppe Vejlgaard Rasmussen

Specialty type: Orthopedics

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Oommen AT, India

Received: October 4, 2023
Peer-review started: October 4, 2023
First decision: December 12, 2023
Revised: December 20, 2023
Accepted: January 8, 2024
Article in press: January 8, 2024
Published online: February 18, 2024

Marc Randall Kristensen Nyring, Bo Sanderhoff Olsen, Alexander Amundsen, Jeppe Vejlgaard Rasmussen, Section for Shoulder and Elbow Surgery, Department of Orthopaedic Surgery, Herlev and Gentofte University Hospital, Hellerup 2900, Denmark

Corresponding author: Marc Randall Kristensen Nyring, MD, Doctor, Researcher, Section for Shoulder and Elbow Surgery, Department of Orthopaedic Surgery, Herlev and Gentofte University Hospital, 12 Gentofte Hospitalsvej, Hellerup 2900, Denmark.
marcrandallkristensen@gmail.com

Abstract

BACKGROUND

The minimal clinically important difference (MCID) is defined as the smallest meaningful change in a health domain that a patient would identify as important. Thus, an improvement that exceeds the MCID can be used to define a successful treatment for the individual patient.

AIM

To quantify the rate of clinical improvement following anatomical total shoulder arthroplasty for glenohumeral osteoarthritis.

METHODS

Patients were treated with the Global Unite total shoulder platform arthroplasty between March 2017 and February 2019 at Herlev and Gentofte Hospital, Denmark. The patients were evaluated preoperatively and 3 months, 6 months, 12 months, and 24 months postoperatively using the Western Ontario Osteoarthritis of the Shoulder index (WOOS), Oxford Shoulder Score (OSS) and Constant-Murley Score (CMS). The rate of clinically relevant improvement was defined as the proportion of patients who had an improvement 24 months postoperatively that exceeded the MCID. Based on previous literature, MCID for WOOS, OSS, and CMS were defined as 12.3, 4.3, and 12.8 respectively.

RESULTS

Forty-nine patients with a Global Unite total shoulder platform arthroplasty were included for the final analysis. Mean age at the time of surgery was 66 years (range 49.0-79.0, SD: 8.3) and 65% were women. One patient was revised within the two years follow-up. The mean improvement from the preoperative assessment to the two-year follow-up was 46.1 points [95% confidence interval (95%CI): 39.7-53.3, $P < 0.005$] for WOOS, 18.2 points (95%CI: 15.5-21.0, $P < 0.005$) for OSS

and 37.8 points (95%CI: 31.5-44.0, $P < 0.005$) for CMS. Two years postoperatively, 41 patients (87%) had an improvement in WOOS that exceeded the MCID, 45 patients (94%) had an improvement in OSS that exceeded the MCID, and 42 patients (88%) had an improvement in CMS that exceeded the MCID.

CONCLUSION
Based on three shoulder-specific outcome measures we find that approximately 90% of patients has a clinically relevant improvement. This is a clear message when informing patients about their prognosis.

Key Words: Minimal clinically important difference; Patient reported outcome measures; Glenohumeral osteoarthritis; Anatomical total shoulder arthroplasty; Clinically relevant improvement

Core Tip: In this study, we present a new approach for analyzing and interpreting improvement in patient-reported outcome measures (PROM) scores by linking the improvement in PROM scores to the minimal clinical difference for each patient. We found that approximately 90% of patients treated with an anatomical total shoulder arthroplasty for glenohumeral osteoarthritis had a clinically relevant improvement two years postoperatively.

Citation: Nyring MRK, Olsen BS, Amundsen A, Rasmussen JV. High rate of clinically relevant improvement following anatomical total shoulder arthroplasty for glenohumeral osteoarthritis. *World J Orthop* 2024; 15(2): 156-162
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/156.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.156

INTRODUCTION

The anatomical total shoulder arthroplasty is the most common type of arthroplasty for glenohumeral osteoarthritis in Denmark[1,2] and it has long been known that the anatomical total shoulder arthroplasty yields pain relief and improved shoulder function in the treatment of glenohumeral osteoarthritis[3]. In this study, a platform shoulder arthroplasty system is used. The platform system is characterized by the ability of converting an anatomical arthroplasty to a reverse shoulder arthroplasty with retention of the stem. A systematic review[4] reported statistically significant lower complication rates, iatrogenic fractures, reoperations, blood loos and operative time in revision procedures with stem retention compared to stem removal procedures.

Improvements after shoulder arthroplasty are often reported as mean improvement for the entire population. In large populations, even small mean improvements can lead to a statistically significant improvement. The question is whether these statistically significant improvements are also clinically relevant for the patients. To assess this, the minimal clinically important difference (MCID) can be included in the analyses. MCID is a measurement tool in the interpretation of changes in patient-reported outcome measures (PROM) scores and it is defined as the smallest meaningful change in a health domain that a patient would identify as important[5]. An improvement exceeding MCID is therefore regarded as clinically relevant. The MCID can also provide an important insight into how the patients are doing on an individual level. By focusing on the improvements in PROM scores from preoperatively to postoperatively for each individual patient, we can get a precise estimate of how many patients who achieve a clinically relevant improvement. This gives a better indication of how successful the surgery is at patient level.

The primary aim was to determine the proportion of patients achieving a clinically important improvement after treatment with an anatomical total shoulder platform arthroplasty for osteoarthritis. Our hypothesis was that the anatomical total shoulder arthroplasty with a common platform system would lead to significant improvement for a high proportion of patients.

MATERIALS AND METHODS

Patients

Between March 2017 and February 2019 all patients referred to Herlev and Gentofte University Hospital with glenohumeral osteoarthritis indicating an anatomical total shoulder arthroplasty were evaluated and offered participation. The following inclusion and exclusion criteria were applied before offering participation:

Inclusion criteria

(1) Primary glenohumeral osteoarthritis independent of previous joint preserving surgery; (2) Osteoarthritis on plain radiographs with standard anterior-posterior and lateral projections; (3) Insufficient effect of non-surgical treatment with symptoms severe enough to justify shoulder arthroplasty; and (4) American Society of Anesthesiology (ASA) scores 1-3,

physically fit for surgery and rehabilitation.

Exclusion criteria

(1) Below 18 years of age; (2) Cognitive or linguistic impairment; (3) Rotator cuff insufficiency defined as rotator cuff lesions or grade 2 fat infiltrations on magnetic resonance imaging according to the Goutallier classification[6,7] verified with impaired functional strength and perioperative findings; (4) Insufficient preoperative glenoid bone-stock or large (> 1 cm) humeral bone cysts on computed tomography (CT) verified with perioperative findings; and (5) ASA scores 4-5.

The included patients were treated with the Global Unite Anatomical Shoulder Arthroplasty System (DePuy Synthes, Raynham, Massachusetts, United States of America). Operations were performed or supervised by one of five experienced shoulder surgeons. All procedures were performed with the patient under general anesthesia in beach chair position and with the standard deltopectoral approach and subscapularis tenodesis. The literature on rehabilitation after shoulder arthroplasty surgery is sparse. At our institution, a sling was used for the first two weeks. After two weeks non-weight bearing training was allowed since we want the patients start movements early. However, we focus on protecting the subscapularis, why weight bearing training is not allowed before six weeks. All patients were supervised by a physiotherapist once a week for a minimum of three months. The patients were asked to complete the Western Ontario Osteoarthritis of the Shoulder score (WOOS), the Oxford Shoulder Score (OSS) and the Constant-Murley Score (CMS) preoperatively and subsequently at three months, six months, one year and two years postoperatively. The rate of clinically relevant improvement was defined as the proportion of patients who had an improvement between the preoperative measurement and the final follow-up measurement at two years that exceeded the MCID.

Functional outcome measures

The Western Ontario Osteoarthritis of the Shoulder index is a disease-specific patient-reported outcome score[8]. There are 19 questions divided into four domains: Physical symptoms, sports and work, lifestyle, and emotions. Each question is answered on a visual analogue scale ranging from 0 to 100. The overall score ranges from 0 to 1900, with 1900 being the worst. For ease of interpretation, we converted the total score to a percentage of the maximum score with 100 being the best. We used the Danish version of WOOS which was translated according to international guidelines[9] and validated using classical test theory in a cohort of patients treated with shoulder arthroplasty for osteoarthritis[10]. MCID is reported to be 12.3 points for WOOS[11] in patients with glenohumeral osteoarthritis treated with an anatomical total shoulder arthroplasty.

The Oxford Shoulder Score is a measurement tool for the assessment of pain and function after elective shoulder surgery[12]. There are 12 questions with each item scored from 0 to 4. The overall score ranges from 0 to 48, with 48 being the best. We use a Danish version of OSS which was translated according to international guidelines and validated using classical test theory[13]. MCID is reported to be 4.3 points for OSS[11] in patients with glenohumeral osteoarthritis treated with an anatomical total shoulder arthroplasty.

The Constant-Murley Score is a combined subjective and objective assessment tool. The score has four sub-scale scores: Pain (15 points), activities of daily living (20 points), range of motion (40 points), and strength (25 points). The total score ranges from 0 to 100, with 100 being the best. We used a Danish version[14] of the modified score described by Constant *et al*[15]. MCID is reported to be 12.8 points for CMS in patients with glenohumeral osteoarthritis or rheumatoid arthritis treated with an anatomical total shoulder arthroplasty[16].

Statistical analysis

SPSS (IBM Corp, Armonk, NY, United States) was used for the statistical analysis. The level of statistical significance was set at $P < 0.05$ and P value were 2-tailed. The differences between preoperative and postoperative data are normally distributed (Figure 1). Therefore, we used the paired sample t-test to test for differences within the same groups.

RESULTS

Fifty-five patients with a Global Unite Anatomical Shoulder Arthroplasty were included. Two patients died and four patients did not respond to the invitation for the two-year follow-up, which left 49 patients for the final analysis. Mean age at the time of surgery was 66 years (range: 49-79, SD: 8.3) and 65% were women. One patient was revised within the two years follow-up. This patient was revised 18 months postoperatively because of periprosthetic joint infection with four out of five tissue samples positive for Cutibacteirum Acnes. The follow up results two years after the primary surgery for this patient were 23 for WOOS, 17 for OSS and 25 for CMS and are included in the overall analysis. None of the six patients who were lost to follow-up was revised.

Forty-one patients (87%) had an improvement in WOOS that exceeded the MCID, five patients improved less than the MCID, and one patient had an outcome at two years that was worse than the preoperative score. Forty-five patients (94%) had an improvement in OSS that exceeded the MCID, one patient improved less than the MCID and two patients had an outcome at two years that was worse than the preoperative score. Forty-two patients (88%) had an improvement in CMS that exceeded the MCID, five patients improved less than the MCID, and one patient had an outcome at two years that was worse than the preoperative score. For all three outcome measures, the majority of patients improved much more than the MCID (Figure 1). The patient in need of revision surgery had scores below the MCID in all three outcome measures. However, it was a different patient reporting a two-year outcome worse than the preoperative score.

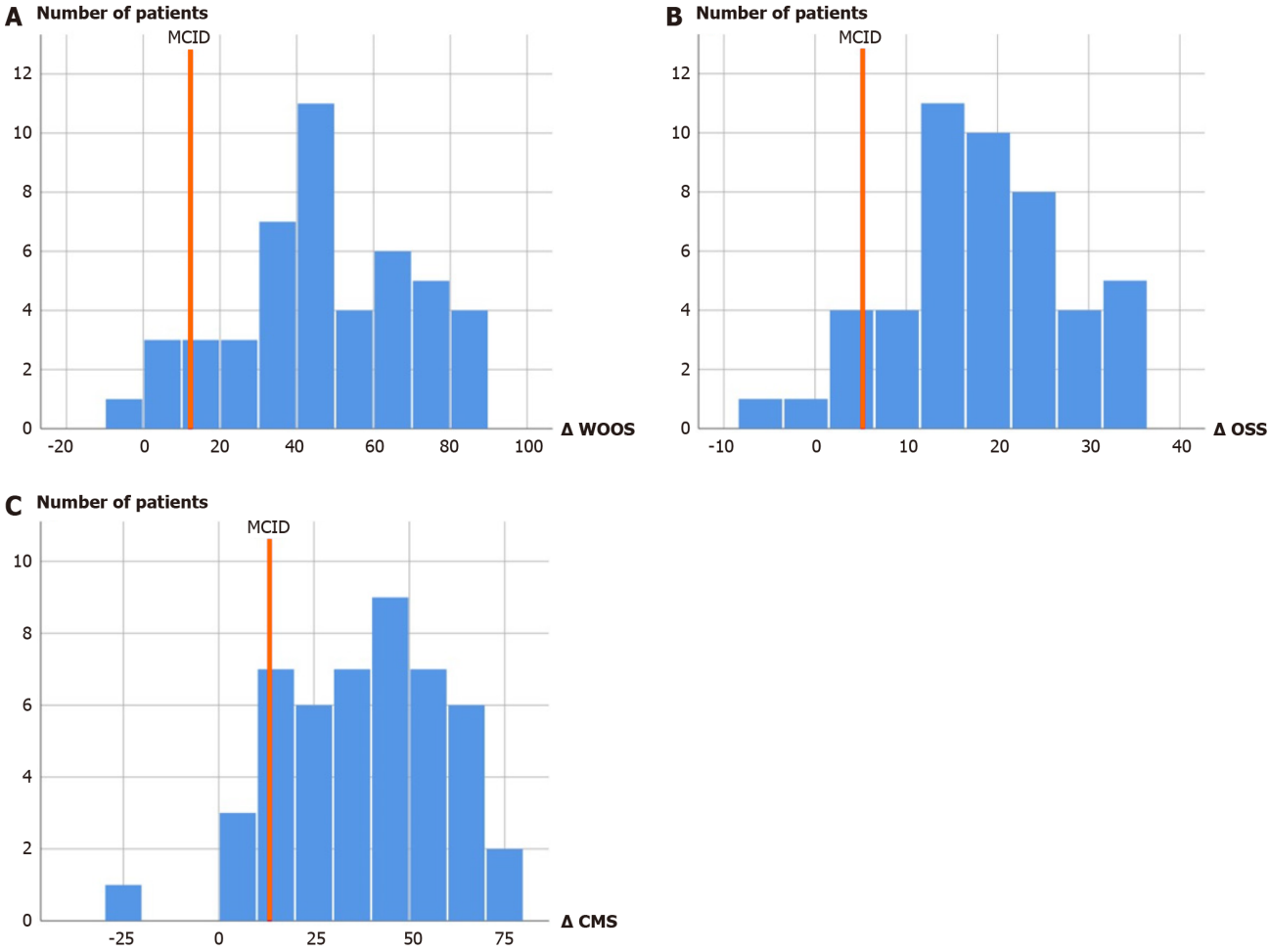


Figure 1 Distributions of improvements. A: Western Ontario Osteoarthritis of the Shoulder index; B: Oxford Shoulder Score; C: Constant-Murley Score. MCID: Minimal clinically important difference; WOOS: Western Ontario Osteoarthritis of the Shoulder index; OSS: Oxford Shoulder Score; CMS: Constant-Murley Score.

The mean WOOS, OSS, and CMS were 82.1 (range 22.2 to 100.0), 40.7 (range 15.0 to 48.0) and 66.4 (range 19.0 to 98.0) at two years. The scores improved continuously during the follow-up period (Table 1). The mean improvement from the preoperative assessment to the two-year follow-up was 46.1 points [95% confidence interval (95%CI): 39.7-53.3, $P < 0.005$] for WOOS, 18.2 points (95%CI: 15.5-21.0, $P < 0.005$) for OSS and 37.8 points (95%CI: 31.5-44.0, $P < 0.005$) for CMS. For all three outcome measures, the mean improvement exceeded the associated MCID.

DISCUSSION

In a prospective cohort of patients with glenohumeral osteoarthritis treated with an anatomical total shoulder arthroplasty, we found the proportion of patients who had a clinically important improvement to be 87% for WOOS, 94% for OSS and 88% for CMS.

It might be problematic to make conclusions on the treatment effect based on mean values from PROM scores. The mean values provide an estimate on group level, but do not give any information on individual level. When reporting mean values, it is unknown whether everyone have an improvement that corresponds to the mean value or if most of the patients have a large improvement, while a few patients have a very poor outcome. We have presented a method to remedy this issue by linking the improvement in PROM scores to the MCID for each patient. The MCID is defined as the smallest meaningful change in the PROM score that a patient would identify as important[5]. To give a better estimate of how the individual patient is doing, it would therefore be interesting to report the proportion of patients who achieve this improvement. For three different outcome measures, we found that approximately 90% of the patients achieved an improvement which exceed the MCID. This is equivalent to saying that 90% of patients who are treated with an anatomical total shoulder arthroplasty for osteoarthritis achieve a significant clinical improvement two years after surgery. In our opinion, this is a clear and tangible message which can be used by the surgeon to inform the patients about their prognosis.

According to our knowledge, no previous studies have reported the proportion of patients who exceed the MCID for WOOS or OSS. In a combined group of patients with either an anatomical or a reverse total shoulder arthroplasty, Simovitch *et al*[16] found that the MCID for CMS was 5.7. Based on this MCID value, the authors concluded that 94.7% of

Table 1 Mean (range) outcome measures at different time-points

	Preoperative	3 months	6 months	1 yr	2 yr
WOOS	35.6 (5.5-74.1)	73.8 (48.6-96.8)	76.8 (22.7-98.6)	81.4 (34.9-99.7)	83.9 (22.2-100.0)
OSS	22.4 (5.0-38.0)	36.6 (19.0-47.0)	38.3 (14.0-48.0)	40.0 (17.0-48.0)	40.7 (15.0-48.0)
CMS	28.5 (7.0-71.0)	48.1 (20.0-87.0)	53.7 (27.0-81.0)	61.0 (25.0-95.0)	66.4 (19.0-98.0)

WOOS: Western Ontario Osteoarthritis of the Shoulder index; OSS: Oxford Shoulder Score; CMS: Constant-Murley Score.

the patients in their cohort achieved a result at two years which exceed the MCID for CMS. In the subgroup of patients who were treated with an anatomical total shoulder arthroplasty, the authors defined the MCID for CMS as 12.8, which is the value we used in this study. Although the authors reported this MCID for CMS, they did not report the proportion of patients with an anatomical total shoulder arthroplasty who exceeded this MCID. Therefore, according to our knowledge, no previous studies have reported the proportion exceeding the MCID for CMS in patients with an anatomical total shoulder arthroplasty. In a study by Ahmed *et al*[17], they analyzed improvements in the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES) based on patients with an anatomical total shoulder arthroplasty used for glenohumeral osteoarthritis. They found 89% of the patients to either have a moderate or substantial clinical benefit, corresponding to an improvement that exceeds the MCID. In addition, a study by Cohn *et al*[18] based on patients treated with either an anatomical or reverse total shoulder arthroplasty, found that the proportion of patients exceeding MCID two years postoperatively was 90% for ASES and 89 % for CMS. These results are very relatable to this study, contributing to an increase of the external validity.

PROM scores can be difficult for patients to understand and some questions might not be relevant to all patients. In addition, they can be very time consuming. In the study by Cohn *et al*[18] they tried to remedy these issues of the PROM scores by also using the Single Assessment Numeric Evaluation (SANE) score, which is based on only one question. They compared the correlation between the SANE score and ASES and CMS, and concluded a moderate correlation between the PROM scores and approximately the same percentage of patients exceeding the MCID. However, it is unknown whether this correlation also exists for WOOS and OSS.

The MCID for CMS is based on patients with glenohumeral osteoarthritis or rheumatoid arthritis treated with an anatomical total shoulder arthroplasty. The MCID for WOOS and OSS are based on patients with glenohumeral osteoarthritis treated with an anatomical total shoulder arthroplasty. Thus, the MCID values are, to a great extent, directly attributable to the population in this study. An important limitation in the use of MCID is the dependency on the diagnoses and treatments from which they are determined[19]. Therefore, it is a clear advantage of this study that the MCID values used are based on almost the same cohort of patients as analyzed in this study.

The mean two years WOOS, OSS, and CMS reported in this study are comparable to previous reported postoperative values based on shoulder arthroplasty registries[2,20,21]. This substantiates an extrapolation of the above results to a general population of patients with glenohumeral osteoarthritis treated with an anatomical total shoulder arthroplasty. However, it would be of great interest to validate the proportion of patients achieving a clinically important improvement in a larger multicenter study or a registry study in order to further increase the external validity.

CONCLUSION

In this study we have presented a new approach for analyzing and interpreting improvement in PROMs after shoulder arthroplasty for osteoarthritis. Previous studies have reported statistically significant and clinically relevant improvement in mean values. However, mean values does necessarily reflect the outcome of a patient, and it can be difficult to use in patient-guidance. We found that approximately 90% of patients who were treated with an anatomical total shoulder arthroplasty with a common platform system for osteoarthritis had a clinically relevant improvement. This is a clear and distinct message that together with information about implant survival can be used to inform patients about their prognosis following surgery.

ARTICLE HIGHLIGHTS

Research background

Anatomical shoulder arthroplasties used for glenohumeral osteoarthritis are often evaluated by mean improvement in patient reported outcome measurements. However, these mean improvements do not talk much about how the individual patient is performing. Therefore, we have aimed to focus on each individual patient's improvement. These improvements are linked to the minimal clinical important difference, allowing us to determine the proportion of patients achieving a clinically relevant improvement.

Research motivation

To determine the proportion of patients with glenohumeral osteoarthritis and treated with an anatomical shoulder arthroplasty that achieve a clinically relevant improvement. This a new way of analyzing the results which is much more relevant to the individual patient.

Research objectives

To determine the proportion of patients having a clinically relevant improvement two years postoperatively after treatment with an anatomical total shoulder arthroplasty. In future research, we believe that this will be a frequently used analysis method.

Research methods

We used data from three different patient reported outcome measurements. The improvements from preoperatively to two years postoperatively were connected to the associated minimal clinically important difference (MCID). The proportion of patients exceeding the MCID was defined as the rate of clinically relevant improvement.

Research results

The rate of clinically relevant improvement was 87%, 94%, and 88% for the three different patient reported outcome measurements.

Research conclusions

Using a new method for analysis of improvements in patient reported outcome measurements, we found that approximately 90% of patients with glenohumeral osteoarthritis and treated with an anatomical shoulder arthroplasty achieved a clinically relevant improvement.

Research perspectives

In future research, this method will probably be a frequently used analysis method. The results of this study should be confirmed in larger cohorts.

FOOTNOTES

Author contributions: Nyring MRK contributed to data collection, design of the study, data analysis, and draft of manuscript; Olsen BS contributed to design of the study and review of manuscript; Amundsen A contributed to data collection, review of manuscript; Rasmussen JV contributed to design of the study and review of manuscript; and all authors have read and approve the final manuscript.

Institutional review board statement: The study is conducted according to the ethics outlined in the Helsinki Declaration. A permission to handle and store data has been obtained from the Danish Data Protection Agency (No. 2012-58-0004). The study was evaluated by the regional Research Ethics Committee and it was decided that the study did not need approval (No. H-17003344). All patients have given informed consent prior to participation. The Ethics Committee/Institutional Review Board is from "Region Hovedstaden". "Region Hovedstaden" is the overall organization that manages all hospitals in the capital region of Denmark, including Herlev and Gentofte Hospital, to which the authors are affiliated.

Clinical trial registration statement: This study is registered at https://clinicaltrials.gov/study/NCT03097406?at=55.7388014&lng=12.5469817&locStr=Gentofte%20Hospital,%20Gentofte%20Hospitalsvej,%20Hellerup,%20Denmark&distance=50&term=Arthroplasty&start=2016-12-01_&page=5&rank=50. The registration identification number is NCT03097406.

Informed consent statement: Due to Danish regulations, written consent was not necessary since the treatment was the standard treatment at the hospital, just with extra follow-up visits. However, all patients have given informed oral consent to participation.

Conflict-of-interest statement: The authors Bo S Olsen, Alexander Amundsen, and Jeppe V Rasmussen received institutional support for conducting the study "Functional outcome and complications after Global Unite prostheses" which provided data for the present study. In addition, Bo S Olsen and Jeppe V Rasmussen are paid speakers for DePuy Synthes (Raynham, Massachusetts, United States of America).

Data sharing statement: Data will be made available on reasonable request.

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

Country/Territory of origin: Denmark

ORCID number: Marc Randall Kristensen Nyring 0000-0001-5964-5602; Jeppe Vejlgaard Rasmussen 0000-0001-5886-1629.

Corresponding Author's Membership in Professional Societies: Danish Orthopedic Society.

S-Editor: Chen YL
L-Editor: A
P-Editor: Yuan YY

REFERENCES

1 **International Committee of Medical Journal Editors**. International Committee of Medical Journal Editors (ICMJE) authorship guidelines. 2023. [cited 1 October 2023]. Available from: https://www.icmje.org/
2 **Rasmussen JV**, Amundsen A, Sørensen AKB, Klausen TW, Jakobsen J, Jensen SL, Olsen BS. Increased use of total shoulder arthroplasty for osteoarthritis and improved patient-reported outcome in Denmark, 2006-2015: a nationwide cohort study from the Danish Shoulder Arthroplasty Registry. *Acta Orthop* 2019; **90**: 489-494 [PMID: 31240980 DOI: 10.1080/17453674.2019.1633759]
3 **Bryant D**, Litchfield R, Sandow M, Gartsman GM, Guyatt G, Kirkley A. A comparison of pain, strength, range of motion, and functional outcomes after hemiarthroplasty and total shoulder arthroplasty in patients with osteoarthritis of the shoulder. A systematic review and meta-analysis. *J Bone Joint Surg Am* 2005; **87**: 1947-1956 [PMID: 16140808 DOI: 10.2106/JBJS.D.02854]
4 **Kirsch JM**, Khan M, Thornley P, Gichuru M, Freehill MT, Neviaser A, Moravek J, Miller BS, Bedi A. Platform shoulder arthroplasty: a systematic review. *J Shoulder Elbow Surg* 2018; **27**: 756-763 [PMID: 29046255 DOI: 10.1016/j.jse.2017.08.020]
5 **Christiansen DH**, Frost P, Falla D, Haahr JP, Frich LH, Svendsen SW. Responsiveness and Minimal Clinically Important Change: A Comparison Between 2 Shoulder Outcome Measures. *J Orthop Sports Phys Ther* 2015; **45**: 620-625 [PMID: 26110548 DOI: 10.2519/jospt.2015.5760]
6 **Goutallier D**, Postel JM, Bernageau J, Lavau L, Voisin MC. Fatty muscle degeneration in cuff ruptures. Pre- and postoperative evaluation by CT scan. *Clin Orthop Relat Res* 1994; 78-83 [PMID: 8020238]
7 **Fuchs B**, Weishaupt D, Zanetti M, Hodler J, Gerber C. Fatty degeneration of the muscles of the rotator cuff: assessment by computed tomography *versus* magnetic resonance imaging. *J Shoulder Elbow Surg* 1999; **8**: 599-605 [PMID: 10633896 DOI: 10.1016/s1058-2746(99)90097-6]
8 **Lo IK**, Griffin S, Kirkley A. The development of a disease-specific quality of life measurement tool for osteoarthritis of the shoulder: The Western Ontario Osteoarthritis of the Shoulder (WOOS) index. *Osteoarthritis Cartilage* 2001; **9**: 771-778 [PMID: 11795997 DOI: 10.1053/joca.2001.0474]
9 **Guillemin F**, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. *J Clin Epidemiol* 1993; **46**: 1417-1432 [PMID: 8263569 DOI: 10.1016/0895-4356(93)90142-n]
10 **Rasmussen JV**, Jakobsen J, Olsen BS, Brorson S. Translation and validation of the Western Ontario Osteoarthritis of the Shoulder (WOOS) index - the Danish version. *Patient Relat Outcome Meas* 2013; **4**: 49-54 [PMID: 24133377 DOI: 10.2147/PROM.S50976]
11 **Nyring MRK**, Olsen BS, Amundsen A, Rasmussen JV. Minimal Clinically Important Differences (MCID) for the Western Ontario Osteoarthritis of the Shoulder Index (WOOS) and the Oxford Shoulder Score (OSS). *Patient Relat Outcome Meas* 2021; **12**: 299-306 [PMID: 34588833 DOI: 10.2147/PROM.S316920]
12 **Dawson J**, Fitzpatrick R, Carr A. Questionnaire on the perceptions of patients about shoulder surgery. *J Bone Joint Surg Br* 1996; **78**: 593-600 [PMID: 8682827]
13 **Frich LH**, Noergaard PM, Brorson S. Validation of the Danish version of Oxford Shoulder Score. *Dan Med Bull* 2011; **58**: A4335 [PMID: 22047932]
14 **Ban I**, Troelsen A, Christiansen DH, Svendsen SW, Kristensen MT. Standardised test protocol (Constant Score) for evaluation of functionality in patients with shoulder disorders. *Dan Med J* 2013; **60**: A4608 [PMID: 23651718]
15 **Constant CR**, Gerber C, Emery RJ, Søjbjerg JO, Gohlke F, Boileau P. A review of the Constant score: modifications and guidelines for its use. *J Shoulder Elbow Surg* 2008; **17**: 355-361 [PMID: 18218327 DOI: 10.1016/j.jse.2007.06.022]
16 **Simovitch R**, Flurin PH, Wright T, Zuckerman JD, Roche CP. Quantifying success after total shoulder arthroplasty: the minimal clinically important difference. *J Shoulder Elbow Surg* 2018; **27**: 298-305 [PMID: 29162305 DOI: 10.1016/j.jse.2017.09.013]
17 **Ahmed R**, Lanham NS, Peterson JR, Jobin CM, Levine WN. Characterization of ASES score pain and functional improvement after anatomic total shoulder arthroplasty: a patient-centered perspective. *J Shoulder Elbow Surg* 2022; **31**: 1042-1046 [PMID: 34808350 DOI: 10.1016/j.jse.2021.10.031]
18 **Cohn MR**, Kunze KN, Polce EM, Nemsick M, Garrigues GE, Forsythe B, Nicholson GP, Cole BJ, Verma NN. Establishing clinically significant outcome thresholds for the Single Assessment Numeric Evaluation 2 years following total shoulder arthroplasty. *J Shoulder Elbow Surg* 2021; **30**: e137-e146 [PMID: 32711106 DOI: 10.1016/j.jse.2020.07.011]
19 **Holmgren T**, Oberg B, Adolfsson L, Björnsson Hallgren H, Johansson K. Minimal important changes in the Constant-Murley score in patients with subacromial pain. *J Shoulder Elbow Surg* 2014; **23**: 1083-1090 [PMID: 24726486 DOI: 10.1016/j.jse.2014.01.014]
20 **Mowbray J**, Van Niekerk M, Frampton C, Hirner M. The outcomes of shoulder arthroplasty in those aged ≥70 years with glenohumeral arthritis: a New Zealand Joint Registry study. *J Shoulder Elbow Surg* 2022; **31**: 799-805 [PMID: 34656778 DOI: 10.1016/j.jse.2021.09.006]
21 **Flynn L**, Patrick MR, Roche C, Zuckerman JD, Flurin PH, Crosby L, Friedman R, Wright TW. Anatomical and reverse shoulder arthroplasty utilizing a single implant system with a platform stem: A prospective observational study with midterm follow-up. *Shoulder Elbow* 2020; **12**: 330-337 [PMID: 33123222 DOI: 10.1177/1758573219840675]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 163-169

DOI: 10.5312/wjo.v15.i2.163

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Prospective Study

Effect of ankle versus thigh tourniquets on post-operative pain in foot and ankle surgery

Ashish Mishra, Ahmed Barakat, Jitendra Mangwani, Jakub Kazda, Sagar Tiwatane, Sana Mohammed Aamir Shaikh, Linzy Houchen-Wolloff, Vipul Kaushik

Specialty type: Surgery

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Ewers A, Austria; Vaheb S, Iran

Received: October 19, 2023
Peer-review started: October 19, 2023
First decision: November 23, 2023
Revised: December 19, 2023
Accepted: January 16, 2024
Article in press: January 16, 2024
Published online: February 18, 2024

Ashish Mishra, Department of Trauma and Orthopedics, University Hospitals Leicester, Leicester LE1 5WW, United Kingdom

Ahmed Barakat, Department of Trauma and Orthopedics, Leicester University Hospitals-NHS Trust, Leicester LE1 5WW, Leicestershire, United Kingdom

Jitendra Mangwani, Academic Team of Musculoskeletal Surgery, University Hospitals of Leicester NHS Trust, Leicester LE3 9QP, United Kingdom

Jakub Kazda, Department of Anaesthesia, York & Scarborough Teaching Hospitals NHS Foundation Trust, North Yorkshire YO31 8HE, United Kingdom

Sagar Tiwatane, Department of Anaesthesia, Royal Free London NHS Trust, London NW3 2QG, United Kingdom

Sana Mohammed Aamir Shaikh, Department of Trauma & Orthopaedics, Breach Candy Hospital Trust, Mumbai 400026, India

Linzy Houchen-Wolloff, Department of Physiotherapy, University Hospitals of Leicester NHS Trust, Leicester LE3 9QP, United Kingdom

Vipul Kaushik, Department of Anasthesia, University Hospitals of Leicester NHS Trust, Leicester LE1 5WW, United Kingdom

Corresponding author: Ahmed Barakat, MBChB, MSc, Surgeon, Department of Trauma and Orthopedics, Leicester University Hospitals-NHS Trust, University Hospitals of Leicester Headquarters, Level 3, Balmoral Building, Leicester Royal Infirmary, Infirmary Square, Leicester LE1 5WW, Leicestershire, United Kingdom. ahmedharoonbarakat@gmail.com

Abstract

BACKGROUND

Tourniquets are commonly used in elective extremity orthopaedic surgery to reduce blood loss, improve visualization in the surgical field, and to potentially reduce surgical time. There is a lack of consensus in existing guidelines regarding the optimal tourniquet pressure, placement site, and duration of use. There is a paucity of data on the relationship between the site of a tourniquet and postoperative pain in foot and ankle surgery.

AIM
To explore the relationship between tourniquet site and intensity of post-operative pain scores in patients undergoing elective foot and ankle surgery.

METHODS
Retrospective analysis of prospectively collected data on 201 patients who underwent foot and ankle surgery in a single institution was undertaken. Intraoperative tourniquet duration, tourniquet pressure and site, and postoperative pain scores using Visual Analogue Score were collected in immediate recovery, at six hours and at 24 h post-op. Scatter plots were used to analyse the data and to assess for the statistical correlation between tourniquet pressure, duration, site, and pain scores using Pearson correlation coefficient.

RESULTS
All patients who underwent foot and ankle surgery had tourniquet pressure of 250 mmHg for ankle tourniquet and 300 mmHg for thigh. There was no correlation between the site of the tourniquet and pain scores in recovery, at six hours and after 24 h. There was a weak correlation between tourniquet time and Visual Analogue Score immediately post-op (r = 0.14, P = 0.04) but not at six or 24 h post-operatively.

CONCLUSION
This study shows that there was no statistically significant correlation between tourniquet pressure, site and post-op pain in patients undergoing foot and ankle surgery. The choice of using a tourniquet is based on the surgeon's preference, with the goal of minimizing the duration of its application at the operative site.

Key Words: Lower limb surgery; Tourniquet time; Tourniquet pressure; Tourniquet site; Post-operative pain; Pain scores

Core Tip: Tourniquets are standard in orthopedic extremity surgery, aiding blood loss control and surgical efficiency. However, varying guidelines and a lack of consensus on tourniquet parameters exist. This study prospectively examines tourniquet site and duration effects on post-operative pain scores using data from 201 patients undergoing foot and ankle surgery.

Citation: Mishra A, Barakat A, Mangwani J, Kazda J, Tiwatane S, Shaikh SMA, Houchen-Wolloff L, Kaushik V. Effect of ankle versus thigh tourniquets on post-operative pain in foot and ankle surgery. *World J Orthop* 2024; 15(2): 163-169
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/163.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.163

INTRODUCTION

Tourniquets are frequently employed in orthopaedic procedures involving lower extremities[1]. Their primary purpose is to minimize blood loss, enhance surgical visibility, and streamline the surgical process[2]. Due to their ubiquity within the sphere of lower limb surgery, particularly foot and ankle, their use has been an interest of study to establish protocols and guidelines for their application. Nevertheless, the utilization of tourniquets has been linked to numerous local and systemic complications, one of which is postoperative pain[3].

The choice of tourniquet site and duration can significantly affect post-operative pain, and striking the right balance is essential[4]. The incidence of complications associated with tourniquet usage increases proportionally with the duration of tourniquet application. This is linked to the hypoxic conditions induced by tourniquet inflation, thereby increasing the likelihood of consequential hypoxic and reperfusion damage to soft tissues[3].

In foot and ankle surgery, the usual placement of a tourniquet is at the thigh, calf, or ankle. While thigh tourniquets are effective in minimizing intraoperative blood loss and maintaining a clear surgical field, they have been associated with a slightly higher risk of post-operative pain compared to ankle tourniquets[5]. The duration for which a tourniquet is inflated during surgery is another critical consideration. Prolonged tourniquet application has been associated with ischemic complications, muscle damage, and post-operative pain[6]. The challenge lies in finding the delicate balance between achieving adequate surgical conditions and minimizing tourniquet-associated complications. Other than minimizing tourniquet duration and optimizing occlusion pressure, the aim is to reduce the column of blood confined by the tourniquet use during surgery by utilizing an effective, well-tolerated and distal as possible.

We present the results of a comparative study investigating thigh *vs* ankle tourniquets applied for elective foot and ankle surgery in terms of effect on post-operative pain scores at different time points up to 24 h post-procedure. In addition, patient demographics such as age, gender, relevant medical conditions, and tourniquet time correlation to pain scores at those time points was also evaluated.

MATERIALS AND METHODS

The study was performed at the University Hospitals Leicester, United Kingdom. The study protocol was reviewed and accepted by University Hospitals Leicester as a service evaluation project ensuring compliance with regulatory and ethical guidance.

201 consecutive patients who had elective foot or ankle surgery under tourniquet (ankle and thigh) were included. The recruitment was performed as per the pre-set inclusion and exclusion criteria outlined in the study protocol. The inclusion criteria included patients who had their foot or ankle procedures under thigh or ankle tourniquets. All trauma/fracture procedures were excluded as well as those with peripheral neuropathy or generalized pain disorders (*e.g.*, fibromyalgia rheumatica). Patient demographics such as age, gender, and relevant pre-existing medical conditions such as peripheral vascular disease, cardiac disease, severe hypertension, coagulopathies, diabetes, and smoking status were collected. Patients were assigned to either ankle or thigh tourniquet groups in accordance with the surgeon's discretion. Recruited patients' operative details such as tourniquet site, occlusion pressure, and length of the operative procedure were recorded in the patient's operative records.

A standardized ankle tourniquet (Anetic Aid Ltd, Baildon, United Kingdom) was applied 5-10 cm above the ankle joint (586 mm length × 106 mm width) and thigh tourniquets (Anetic Aid Ltd, Baildon, United Kingdom) at mid-thigh (1074 mm length × 129 mm width). The tourniquet site was well padded in all patients with 3 rolls of 150 mm width cotton roll (Softban Ltd, United Kingdom) and tourniquet site occluded with an impervious U-drape. All limbs were either exsanguinated or elevated before tourniquet inflation; a tourniquet pressure of 250 mmHg for ankle tourniquet and 300 mmHg for thigh was applied. Local anaesthetic depending on the length of the incision and procedure performed (10-20 mLs of 0.5% Levobupivacaine) was injected into the incision site before dressings were applied. Whilst in the recovery bay and as soon as the patient was fully awake and co-operative, visual analogue score (VAS) was recorded in the immediate post-operative, six hours, and 24 h after the operative procedure. Any tourniquet related complications (skin burn and post-tourniquet syndrome) were recorded. The analgesic plan for all the included patients in the first 24 h was standardized with Paracetamol 500 mg and Dihydrocodeine 30 mg prescribed per-orally every 4-6 h and Oromorph 10-20 ug prescribed as required unless patient's specific medical conditions or allergies precludes that.

Statistical analysis was performed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp). The normality of variable distribution was assessed using the Kolmogorov-Smirnov test with mean, standard deviation (SD) and range used to describe normally distributed data. A Kruskal-Wallis test was employed in this study to assess whether there is a statistically significant relationship between the placement of tourniquets at different sites (thigh or ankle) and the reported pain scores at immediate, six-hour, and 24-h post-operative time points. Scatter plots were used to analyse the data and to assess the statistical correlation between tourniquet pressure, duration, site, and pain scores using Pearson correlation coefficient. The significance of the obtained results was established at the 5% level ($P \leq 0.05$) and strong correlation considered for r values > 0.7 while weak correlation for those < 0.3[7].

RESULTS

A total of 201 patients were included in our analysis. There were 116 (57%) males while the remainder 85 (43%) were females. The mean age was 59.4 years (range = 23–95 years, SD = 15.6) with no statistically significant difference between the ankle and the thigh tourniquet groups ($P = 0.4$). The medical records and conditions were available for all patients, with 89 (44%) having a relevant pre-existing medical condition presenting a potential risk factor influencing the outcomes of tourniquet use. The distribution of patient's demographics for the ankle and the thigh tourniquet groups is tabulated in Table 1.

A total of 87 patients (43%) had an ankle tourniquet while 114 patients (57%) had a thigh tourniquet. The average tourniquet time was 73.7 min (range = 10–149 min, SD = 28.7) with no statistical difference between the ankle and the thigh tourniquet groups ($P = 0.12$). There were two occurrences of tourniquet interruption after 120 min due to exceeding the recommended tourniquet time. Both of which happened in the thigh tourniquet group.

The mean immediate postoperative VAS was 3.9 (SD = 3.2, range = 0–10), mean six-hour VAS was 3.6 (SD = 2.6, range = 0-10), and mean 24-hour post-operative VAS was 5.8 (SD = 3.2, range = 0-10). Those patients who had a VAS of 10 at any time point were managed with elevation and escalated analgesia with resolution of their pain. None had any signs of compartment syndrome or concerning clinical findings. There were no reported tourniquet related complications for any of the included patients. Subsequent subgroup analysis showed no statistically significant relationship between the 24 h VAS and the patient's age, gender or pre-existing medical conditions using multivariate regression analysis ($P = 0.35$, $P = 0.18$ and $P = 0.25$ respectively).

A paired t-test showed that there was a significantly higher mean VAS after 24 h as compared to the immediate post-operative ($t = 61.2$, $P < 0.0001$). We postulate that this is due to weaning of the local anaesthetic effect, post-operative oedema, increasing patient activity level and peaking of the inflammatory response[8].

There was a very weak correlation between tourniquet time and recovery pain score ($P = 0.04$). However, the size of the correlation coefficient is rather small ($r = 0.14$). On the other hand, there was no statistically significant correlation between tourniquet time and the six-hour pain score ($r = 0.09$, $P = 0.19$) or the 24-h pain score ($r = 0.01$, $P = 0.81$) (Figure 1).

As for the tourniquet site, Kruskal-Wallis analysis demonstrated no significant difference between immediate post-operative ($P = 0.69$), six-hour ($P = 0.45$) and 24 h ($P = 0.13$) pain scores as opposed to the tourniquet site (thigh *vs* ankle) (Figure 2).

Table 1 Distribution of patient's demographics in terms of number recruited, mean age, gender and pre-existing relevant medical conditions amongst the two tourniquet study groups

Group	No. of patients	Mean age (yr, SD)	Gender (Male/Female)	Pre-existing medical conditions
Ankle tourniquet	87	58.3 (SD = 14.3)	51/36	49
Thigh tourniquet	114	60.2 (SD = 15.8)	65/49	40
Total	201	59.4 (SD = 15.6)	116/85	89

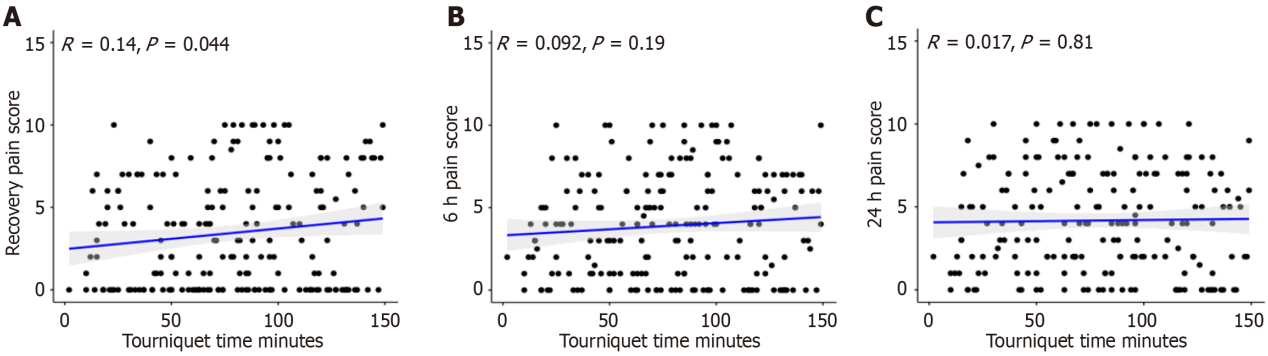


Figure 1 Scatter plots illustrating the correlation (r) between tourniquet time and the immediate post-operative, six-hour, and 24-h pain scores. A: Recovery pain score *vs* tourniquet time minutes; B: 6 h pain score *vs* tourniquet time minutes; C: 24 h pain score *vs* tourniquet time minutes. Note the weak correlation between tourniquet time and immediate post-operative pain scores with the absence of correlation to the six- and 24-h pain scores.

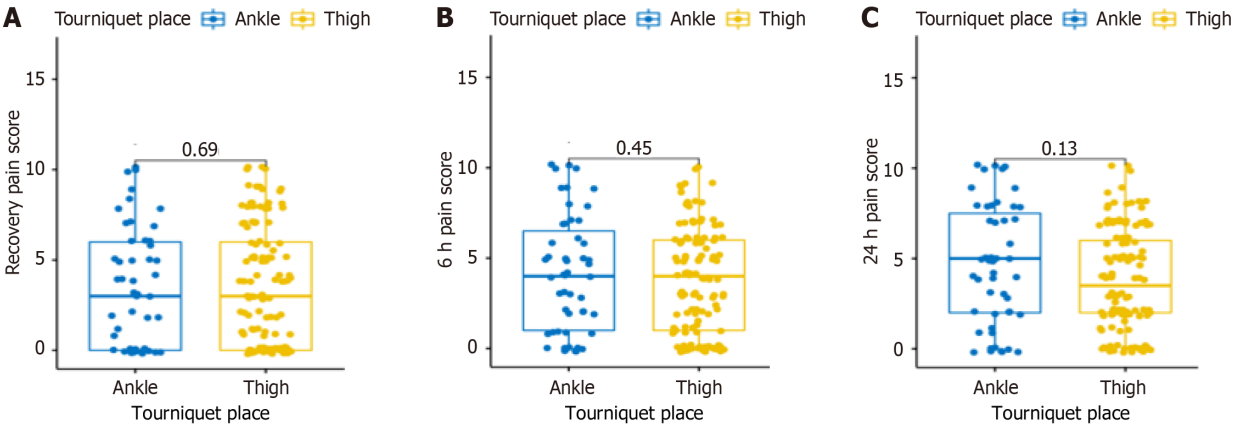


Figure 2 Whisker plot illustrating the absence of significant difference (*P* > 0.05) between immediate post-operative, six-hour, and 24-h pain scores as opposed to the tourniquet site (thigh *vs* ankle). A: Recovery pain score; B: 6 h pain score; C: 24 h pain score.

DISCUSSION

The use of tourniquet offers several potential benefits during foot and ankle surgery, including reducing operative time, minimizing blood loss, and thus improving visualization. However, tourniquet use is associated with well-documented drawbacks, which encompass muscle ischemia, wound complications, neurovascular injuries, deep venous thrombosis[9-11]. The most common side effect remains to be post-operative pain at the tourniquet site[12]. Exploring the effect of tourniquet site and duration on post-operative pain has been investigated in our prospective study.

Mitigating tourniquet related post-operative pain can improve patient rehabilitation and engagement with physiotherapy as well as reducing morbidity and hospital stay. As for tourniquet duration, it has been recommended that tourniquet time should not exceed 120 min for foot and ankle surgery[13,14]. It has been demonstrated that tourniquet-related complications increase as tourniquet time increases attributed to the hypoxic conditions and tissue ischaemia[15,16].

Although we observed no complications directly related to tourniquet use, we did identify a weak correlation between tourniquet duration and immediate post-operative pain scores, this correlation did not extend to the pain scores at six- or 24-hours post-operation. Other studies have observed a similar relationship between tourniquet duration and post-operative pain with even better pain scores when not using a tourniquet. In a randomized trial by Dimnjaković *et al*[17] assessing tourniquet *vs* no tourniquet in 50 consecutive ankle arthroscopy patients, they found less post-operative pain

scores in the no tourniquet group. A systematic review encompassing four studies that investigated tourniquet usage in lower limb surgery yielded consistent results. The findings supported the notion that surgical procedures performed without the use of a tourniquet resulted in a notably shorter hospital stay. Furthermore, these tourniquet-free surgeries were associated with reduced post-operative pain and complication rates, as compared to surgeries where tourniquets were utilized[18].

On the other hand, and contrary to other studies, there was no significant correlation between the choice of tourniquet site—whether at the thigh or the ankle—and the post-operative pain scores at the various time points we assessed. While extensive research exists regarding the immediate consequences of applying a tourniquet at a particular site, there is a notable paucity of high-quality data elucidating the comparative risk profiles associated with tourniquet use at one location *vs* another with only three comparative studies concerned with foot and ankle surgery available. For instance, a comparative study evaluated the impact of calf and ankle tourniquets on pain scores immediately and 30 min after deflation. The results revealed that despite the higher minimal occlusion pressure needed in the ankle tourniquet group, they demonstrated significantly better VAS than the calf tourniquets at the different evaluation time-points[19]. However, it is imperative to note that this conclusion was based on a laboratory experimental study on 63 healthy volunteers with VAS assessed to a maximum of 30 min after tourniquet removal. The other study was a retrospective analysis comparing between using a thigh *vs* ankle tourniquet for calcaneal fracture surgery[20]. It included 42 patients and demonstrated significantly less foot pain in the ankle tourniquet group within two weeks after surgery and higher complications in the thigh tourniquet group. Finally, in a randomized controlled trial, in which 50 elective patients were allocated either to thigh or ankle tourniquet group showed significantly better pain scores for the ankle tourniquet group which was assessed for a maximum of 30 min post-operatively[21].

There are limitations to our study as we did not assess foot and ankle functional scores due to the heterogenicity in the operative procedures included. Furthermore, the allocation of both groups was according to surgeon's preference and not randomized. However, despite these limitation, the authors believe that the findings of this study contribute to the current knowledge on this subject.

CONCLUSION

In conclusion, the use of tourniquet, both at ankle and thigh location, serves to meet the requirement of surgical field in foot and ankle procedures. Tourniquet location does not have a significant bearing on post-operative pain levels but minimizing tourniquet duration does. Future high quality randomized trials are warranted to derive conclusions more reliably about the value of using tourniquets in foot and ankle surgery.

ARTICLE HIGHLIGHTS

Research background

Tourniquet utilization in orthopedic surgery is widespread for its benefits in blood loss reduction and enhanced surgical visibility, yet guidelines lack consensus on optimal pressure, placement, and duration. Despite its common use, there is limited understanding of how tourniquet site relates to postoperative pain in foot and ankle surgeries, highlighting a significant gap in existing knowledge.

Research motivation

The motivation behind this study stems from the existing ambiguity in guidelines regarding tourniquet practices in foot and ankle surgeries and the dearth of data on the connection between tourniquet site and postoperative pain. Understanding this relationship could not only improve patient outcomes but also guide surgical practices by providing evidence-based recommendations.

Research objectives

The primary objective of this study was to investigate the potential correlation between the tourniquet site and the intensity and duration of postoperative pain in patients undergoing foot and ankle surgery.

Research methods

The study analyzed prospectively collected data from 201 patients who underwent foot and ankle surgery in a single institution. Key variables included intra-operative tourniquet duration, pressure, site, and postoperative pain scores assessed through Visual Analogue Score at immediate recovery, six hours, and 24 h post-operation. Data analysis involved scatter plots and statistical testing using Pearson correlation.

Research results

There was no correlation between tourniquet pressure, site, and postoperative pain in foot and ankle surgery patients. All patients had standardized tourniquet pressures, and the weak correlation found between tourniquet time and immediate postoperative pain did not persist at six or 24 h post-operatively.

Research conclusions

The study demonstrates that tourniquet pressure and site do not significantly influence postoperative pain in foot and ankle surgery.

Research perspectives

The absence of a correlation suggests that the surgeon's preference in choosing a tourniquet is not necessarily tied to minimizing postoperative pain.

FOOTNOTES

Co-first authors: Ahmed Barakat and Ashish Mishra.

Author contributions: Mangwani J envisaged the research question and designed the study. Barakat A, Mishra A, Kazda J, Tiwatane S, Shaikh SMA, Kaushik V, and Houchen-Wolloff L collected the results. Both Barakat A and Mishra A were equally involved in results collections, results analysis, drafting and proof-reading the manuscript; All authors read and approved the manuscript prior to submission; Both Barakat A and Mishra A were equally involved in results collections, results analysis, drafting and proof-reading the manuscript.

Institutional review board statement: This study was reviewed and approved by the Leicester University Hospitals - NHS Trust as a service evaluation project.

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

Conflict-of-interest statement: All the authors declare that they have no conflict of interest.

Data sharing statement: Source data is available upon request.

Country/Territory of origin: United Kingdom

ORCID number: Ahmed Barakat 0000-0002-7742-7059; Sana Mohammed Aamir Shaikh 0000-0002-6676-9942; Linzy Houchen-Wolloff 0000-0003-4940-8835; Jitendra Mangwani 0000-0002-3960-3023.

Corresponding Author's Membership in Professional Societies: British Orthopedic Association, 38006.

S-Editor: Liu JH
L-Editor: A
P-Editor: Zhao S

REFERENCES

1 **Younger AS**, Kalla TP, McEwen JA, Inkpen K. Survey of tourniquet use in orthopaedic foot and ankle surgery. *Foot Ankle Int* 2005; **26**: 208-217 [PMID: 15766423 DOI: 10.1177/107110070502600305]
2 **Lau B**, Kothari V, Trowbridge S, Lewis TL, Ray R. Tourniquet use in ankle arthroscopy: A systematic review. *Foot Ankle Surg* 2024; **30**: 50-56 [PMID: 37866989 DOI: 10.1016/j.fas.2023.09.005]
3 **Jensen J**, Hicks RW, Labovitz J. Understanding and Optimizing Tourniquet Use During Extremity Surgery. *AORN J* 2019; **109**: 171-182 [PMID: 30694553 DOI: 10.1002/aorn.12579]
4 **Wilson AG**. Current Insights and Recommendations For Tourniquet Use In Foot And Ankle Surgery–Part 3: Recommendations. *Podiatry Today* 2021; **34** [DOI: 10.1186/1757-1146-6-s1-p1]
5 **Hamad F**, Rossiter N. Tourniquet use in trauma and orthopaedics, how and when: current evidence. *Surgery (Oxford)* 2023 [DOI: 10.1016/j.mpsur.2023.08.008]
6 **Gangadharan R**, Roslee C, Kelsall N, Taylor H. Retrospective review of complications following long tourniquet time in foot and ankle surgery. *J Clin Orthop Trauma* 2021; **16**: 189-194 [PMID: 33717956 DOI: 10.1016/j.jcot.2020.12.023]
7 **Mukaka MM**. Statistics corner: A guide to appropriate use of correlation coefficient in medical research. *Malawi Med J* 2012; **24**: 69-71 [PMID: 23638278]
8 **Gan TJ**. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *J Pain Res* 2017; **10**: 2287-2298 [PMID: 29026331 DOI: 10.2147/JPR.S144066]
9 **Kim YH**, Kim JS, Kim DY. Clinical outcome and rate of complications after primary total knee replacement performed with quadriceps-sparing or standard arthrotomy. *J Bone Joint Surg Br* 2007; **89**: 467-470 [PMID: 17463113 DOI: 10.1302/0301-620X.89B4.18663]

10 **Huang HT**, Su JY, Chang JK, Chen CH, Wang GJ. The early clinical outcome of minimally invasive quadriceps-sparing total knee arthroplasty: report of a 2-year follow-up. *J Arthroplasty* 2007; **22**: 1007-1012 [PMID: 17920473 DOI: 10.1016/j.arth.2007.03.021]

11 **Li B**, Wen Y, Wu H, Qian Q, Lin X, Zhao H. The effect of tourniquet use on hidden blood loss in total knee arthroplasty. *Int Orthop* 2009; **33**: 1263-1268 [PMID: 18751703 DOI: 10.1007/s00264-008-0647-3]

12 **Farhan-Alanie MM**, Dhaif F, Trompeter A, Underwood M, Yeung J, Parsons N, Metcalfe A, Wall PDH. The risks associated with tourniquet use in lower limb trauma surgery: a systematic review and meta-analysis. *Eur J Orthop Surg Traumatol* 2021; **31**: 967-979 [PMID: 33792771 DOI: 10.1007/s00590-021-02957-7]

13 **Dosani S**, Devarakonda S. 104 Audit on Adherence to the BOAST Guidelines on the Safe Use of Intraoperative Tourniquets. *Br J Surg* 2023; **110** Suppl 7: znad258-648 [DOI: 10.1093/bjs/znad258.648]

14 **Fitzgibbons PG**, Digiovanni C, Hares S, Akelman E. Safe tourniquet use: a review of the evidence. *J Am Acad Orthop Surg* 2012; **20**: 310-319 [PMID: 22553103 DOI: 10.5435/JAAOS-20-05-310]

15 **Noordin S**, McEwen JA, Kragh JF Jr, Eisen A, Masri BA. Surgical tourniquets in orthopaedics. *J Bone Joint Surg Am* 2009; **91**: 2958-2967 [PMID: 19952261 DOI: 10.2106/JBJS.I.00634]

16 **Altin R**, Yesil M, Ozcan O, Karaca C, Sen S, Firat F. An investigation into the cellular-level adverse effects of tourniquet use on the infrapatellar fat pad in primary total knee arthroplasty: A prospective randomized study. *Acta Orthop Traumatol Turc* 2023; **57**: 283-288 [PMID: 37823743 DOI: 10.5152/j.aott.2023.22164]

17 **Dimnjaković D**, Hrabač P, Bojanić I. Value of Tourniquet Use in Anterior Ankle Arthroscopy: A Randomized Controlled Trial. *Foot Ankle Int* 2017; **38**: 716-722 [PMID: 28399633 DOI: 10.1177/1071100717702461]

18 **Smith TO**, Hing CB. The efficacy of the tourniquet in foot and ankle surgery? A systematic review and meta-analysis. *Foot Ankle Surg* 2010; **16**: 3-8 [PMID: 20152747 DOI: 10.1016/j.fas.2009.03.006]

19 **Piyavunno C**, Mahaisavariya B. Tourniquet pain: calf versus ankle tourniquet. *J Med Assoc Thai* 2012; **95** Suppl 9: S110-S113 [PMID: 23326992]

20 **Xu FL**, Yao Y, Zhang Y, Zhou LY, Shi TT, Fan J, Yu GR. Analysis of curative effect of low position tourniquet in calcaneal fracture surgery [DOI: 10.21203/rs.3.rs-1511901/v1]

21 **Finsen V**, Kasseth AM. Tourniquets in forefoot surgery: less pain when placed at the ankle. *J Bone Joint Surg Br* 1997; **79**: 99-101 [PMID: 9020454 DOI: 10.1302/0301-620x.79b1.7069]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 170-179

DOI: 10.5312/wjo.v15.i2.170

ISSN 2218-5836 (online)

ORIGINAL ARTICLE

Prospective Study

Assessment of the effectiveness of weight-adjusted antibiotic administration, for reduced duration, in surgical prophylaxis of primary hip and knee arthroplasty

Tosan Okoro, Michael Wan, Takura Darlington Mukabeta, Ella Malev, Marketa Gross, Claudia Williams, Muhammad Manjra, Jan Herman Kuiper, John Murnaghan

Specialty type: Orthopedics

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Mohapatra S, India

Received: November 8, 2023
Peer-review started: November 8, 2023
First decision: November 29, 2023
Revised: December 8, 2023
Accepted: January 5, 2024
Article in press: January 5, 2024
Published online: February 18, 2024

Tosan Okoro, Department of Arthroplasty, Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust, Oswestry SY10 7AG, United Kingdom

Tosan Okoro, School of Medicine, Keele University, Staffordshire ST5 5BG, United Kingdom

Michael Wan, St Joseph's Health Centre, Unity Health Toronto, Toronto M6R 1B5, Canada

Takura Darlington Mukabeta, Department of Arthroplasty, The Royal London Hospital, Barts Health NHS Trust, London E1 1BB, United Kingdom

Ella Malev, Marketa Gross, Claudia Williams, Muhammad Manjra, John Murnaghan, Department of Arthroplasty, Sunnybrook Holland Orthopaedic and Arthritis Centre, Toronto M4Y 1H1, Canada

Jan Herman Kuiper, Institute for Science and Technology in Medicine, Keele University, Staffordshire ST5 1BG, United Kingdom

Corresponding author: Tosan Okoro, BSc, MBChB, PhD, FRCS, Consultant Trauma and Orthopaedic Surgeon, Honorary Senior Clinical Lecturer, Department of Arthroplasty, Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust, Gobowen, Oswestry SY10 7AG, United Kingdom. tosanwumi@hotmail.com

Abstract

BACKGROUND

Prophylactic antibiotics have significantly led to a reduction in the risk of post-operative surgical site infections (SSI) in orthopaedic surgery. The aim of using antibiotics for this purpose is to achieve serum and tissue drug levels that exceed, for the duration of the operation, the minimum inhibitory concentration of the likely organisms that are encountered. Prophylactic antibiotics reduce the rate of SSIs in lower limb arthroplasty from between 4% and 8% to between 1% and 3%. Controversy, however, still surrounds the optimal frequency and dosing of anti-biotic administration.

AIM

To evaluate the impact of introduction of a weight-adjusted antibiotic prophylaxis

regime, combined with a reduction in the duration of administration of post-operative antibiotics on SSI incidence during the 2 years following primary elective total hip and knee arthroplasty

METHODS

Following ethical approval, patients undergoing primary total hip arthroplasty (THA)/total knee arthroplasty (TKA) with the old regime (OR) of a preoperative dose [cefazolin 2 g intravenously (IV)], and two subsequent doses (2 h and 8 h), were compared to those after a change to a new regime (NR) of a weight-adjusted preoperative dose (cefazolin 2 g IV for patients < 120 kg; cefazolin 3g IV for patients > 120 kg) and a post-operative dose at 2 h. The primary outcome in both groups was SSI rates during the 2 years post-operatively.

RESULTS

A total of n = 1273 operations (THA n = 534, TKA n = 739) were performed in n = 1264 patients. There was no statistically significant difference in the rate of deep (OR 0.74% (5/675) *vs* NR 0.50% (3/598); fishers exact test P = 0.72), nor superficial SSIs (OR 2.07% (14/675) *vs* NR 1.50% (9/598); chi-squared test P = 0.44) at 2 years post-operatively. With propensity score weighting and an interrupted time series analysis, there was also no difference in SSI rates between both groups [RR 0.88 (95%CI 0.61 to 1.30) P = 0.46].

CONCLUSION

A weight-adjusted regime, with a reduction in number of post-operative doses had no adverse impact on SSI incidence in this population.

Key Words: Antibiotics; Weight-adjusted; Hip and knee arthroplasty; Surgical site infection

Core Tip: For patients in the study population undergoing primary lower limb arthroplasty, reducing the number of post-operative antibiotic doses had no adverse impact on surgical site infections incidence, at 2 years following surgery, if a weight-adjusted regime is used.

Citation: Okoro T, Wan M, Mukabeta TD, Malev E, Gross M, Williams C, Manjra M, Kuiper JH, Murnaghan J. Assessment of the effectiveness of weight-adjusted antibiotic administration, for reduced duration, in surgical prophylaxis of primary hip and knee arthroplasty. *World J Orthop* 2024; 15(2): 170-179
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/170.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.170

INTRODUCTION

Prophylactic antibiotics have significantly led to a reduction in the risk of post-operative surgical site infections (SSI) in orthopaedic surgery[1,2]. The aim of using antibiotics for this purpose is to achieve serum and tissue drug levels that exceed, for the duration of the operation, the minimum inhibitory concentration of the likely organisms that are encountered[3]. Prophylactic antibiotics reduce the rate of SSIs in lower limb arthroplasty from between 4% and 8% to between 1% and 3%[4]. Controversy, however, still surrounds the optimal frequency and dosing of antibiotic administration[5].

Periprosthetic joint infection (PJI) occurs following 1% to 2% of primary lower limb arthroplasties[6,7]. This complication is associated with significant morbidity for patients and the need for complex multidisciplinary treatment strategies[8]. In Canada, deep incisional and organ-space PJI rates are 0.96% for primary total hip arthroplasty (THA) and 0.71% for primary total knee arthroplasty (TKA)[9]. Ninety three percent of THA PJIs and 92% of TKA PJIs tend to be identified within 90 days following surgery, with an average diagnosis time of 21 d[9].

Various studies have analyzed the effect of antibiotic duration and infection, however, no benefit has been demonstrated beyond 24 h[10,11]. Prolonged postoperative prophylactic antibiotic administration should be discouraged due to the risk of additional toxicity, production of resistant organisms, and unnecessary expense incurred[12]. These findings are supported by guidance from the American Association (Academy) of Orthopedic Surgeons which recommend that the duration of prophylactic antibiotic administration should not exceed 24 h[13]. In the United Kingdom, the National Institute for Health and Care Excellence (NICE) recommends a single intravenous dose of antibiotic prophylaxis on induction of anesthesia, with a repeat dose if the surgical duration is longer than the half-life of the antibiotic, or if blood loss is significant[14]. The World Health Organization (WHO) also recommends against the prolongation of surgical antibiotic prophylaxis administration after completion of the operation for the purpose of preventing SSIs[15].

Obesity in patients represents a significant risk factor for SSI[16,17]. In 2016, a report from the WHO indicated that more than 39% of adults in world were considered overweight and of this group, around a third would be considered obese[18]. This report also highlighted that obese and overweight individuals represent a significant proportion of patients undergoing surgery worldwide[18]. However, dosing guidelines for antibiotic prophylaxis do not recommend adjustments based on weight[13-15]. The rationale for this is that the use of standardized doses is considered safe, effective, and convenient for the majority of the adult population[19]. Studies have suggested that doubling the dose of antibiotic prophylaxis for morbidly obese patients weighing at least 120 kg, or with a body mass index (BMI) of 40 kg/m^2 or higher may reduce the risk of SSI[20,21]. According to the Centers for Disease Control and Prevention guidelines for SSI prevention, the issue of weight-adjusted antibiotic prophylaxis dosing is still considered unresolved[22].

At the time this study was conceived, the antibiotic prophylaxis regime at the study institution, a tertiary elective arthroplasty unit, comprised a single preoperative dose of cefazolin 2 g (irrespective of patient weight) followed by two postoperative doses within the first 24 h following surgery.

The aim of this study was to evaluate the impact of introduction of a weight-adjusted antibiotic prophylaxis regime, combined with a reduction in the duration of administration of post-operative antibiotics on SSI incidence during the 2 years following primary elective total hip and knee arthroplasty.

MATERIALS AND METHODS

Following approval of the quality improvement project by the Sunnybrook Health Sciences Centre, Toronto, Research Ethics Board (September 2018), a prospective cohort study was performed. This study was granted an exemption from requiring informed consent by the Sunnybrook Health Sciences Centre Research Ethics Board.

A cohort of arthroplasty patients undergoing primary THA/TKA with a single pre-operative dose and two post-operative antibiotic doses (old regime, OR; September to December 2018), was compared to a group of patients undergoing primary THA/TKA after the regime had been changed to a weight-adjusted pre-operative dose and a single post-operative dose [new regime, (NR); January to April 2019].

In order to implement change to achieve the stated aims above, prescription order sets were developed with the NR of antibiotics, and this was performed with engagement of appropriate stakeholders to ensure buy-in. The involved stakeholders included Orthopedic Surgery, Pharmacy, Nursing, Anesthesia, Antimicrobial Stewardship and Infection Prevention and Control (IP&C). The majority of the discussions occurred *via* email. The previous antibiotic prophylaxis order-set had been in use since 2012. The group worked on developing a modified order set; with the main changes for the purpose of this QI project being the removal of the second post-operative dose of cefazolin, and the introduction of a weight-adjusted dosage regime for the pre-operative cefazolin that is administered. The modified order set was submitted for review and subsequently approved by the Forms Committee in November 2018. There was an active drive to notify all service areas, with communication sent to staff groups about the proposed change.

The old regime (OR) for antibiotic prophylaxis consisted of a single preoperative dose [cefazolin 2 g intravenously (IV)], and two subsequent antibiotic doses (cefazolin 2 g IV at 2 h and cefazolin 1g IV at 8 h). This was changed to the NR; which comprised a weight-adjusted preoperative dose (cefazolin 2 g IV for patients < 120 kg; cefazolin 3 g IV for patients > 120 kg) and a single subsequent dose (cefazolin 2 g IV at 2 h).

Inclusion and exclusion criteria

We included all adult patients undergoing primary hip or knee arthroplasty (THA/TKA) at our institution. Patients were also included if undergoing another primary THA/TKA within the study period. Patients undergoing revision arthroplasty surgery or return to theatre following primary procedures were not included in this cohort.

Outcome measures

The primary outcome assessed in both groups was the incidence of SSI in the 2 years following the index operation. Surgical site infection for the purposes of this study was diagnosed as being superficial incisional, deep incisional, or organ-space in origin (Figure 1)[19,20].

Demographic information including age, sex, BMI, was also collected for every enrolled patient in each assessed group (OR and NR). Patient records were also interrogated for information on American Association of Anesthesiologists (ASA) grade, presence of diabetes mellitus and use of oral anticoagulants at the time of surgery.

Statistical analysis

SSI rates were compared directly between the two regimes using Fisher's exact test (where observed SSI infections < 5) or chi-squared tests (observed SSI infections > 5). We also used a covariate-balancing propensity score weighting method to reduce biases from baseline differences in our comparison between the two regimes[23]. In determining the propensity score, we used age, sex, joint (knee or hip), ASA grade, BMI, weight, anticoagulant use (yes or no), diabetes, inflammatory arthritis, previous surgery and number of comorbidities as covariates. Missing covariate values were imputed using a single imputation with added prediction error and parameter uncertainty (SI+PE+PU), a recommended method when comparing two treatments[24]. We used the standardized difference (SMD) to assess covariate balance and assumed that any imbalance above 10% would indicate a meaningful imbalance[25]. The average treatment effects were then estimated using a log-binomial model with a robust (sandwich) variance estimator. An inverse probability treatment weighting was used to implement the propensity weights[25]. The SSI rates under the old and NR were also analyzed as an interrupted time series, which was implemented as a segmented log-binomial regression with patient number ordered by operation

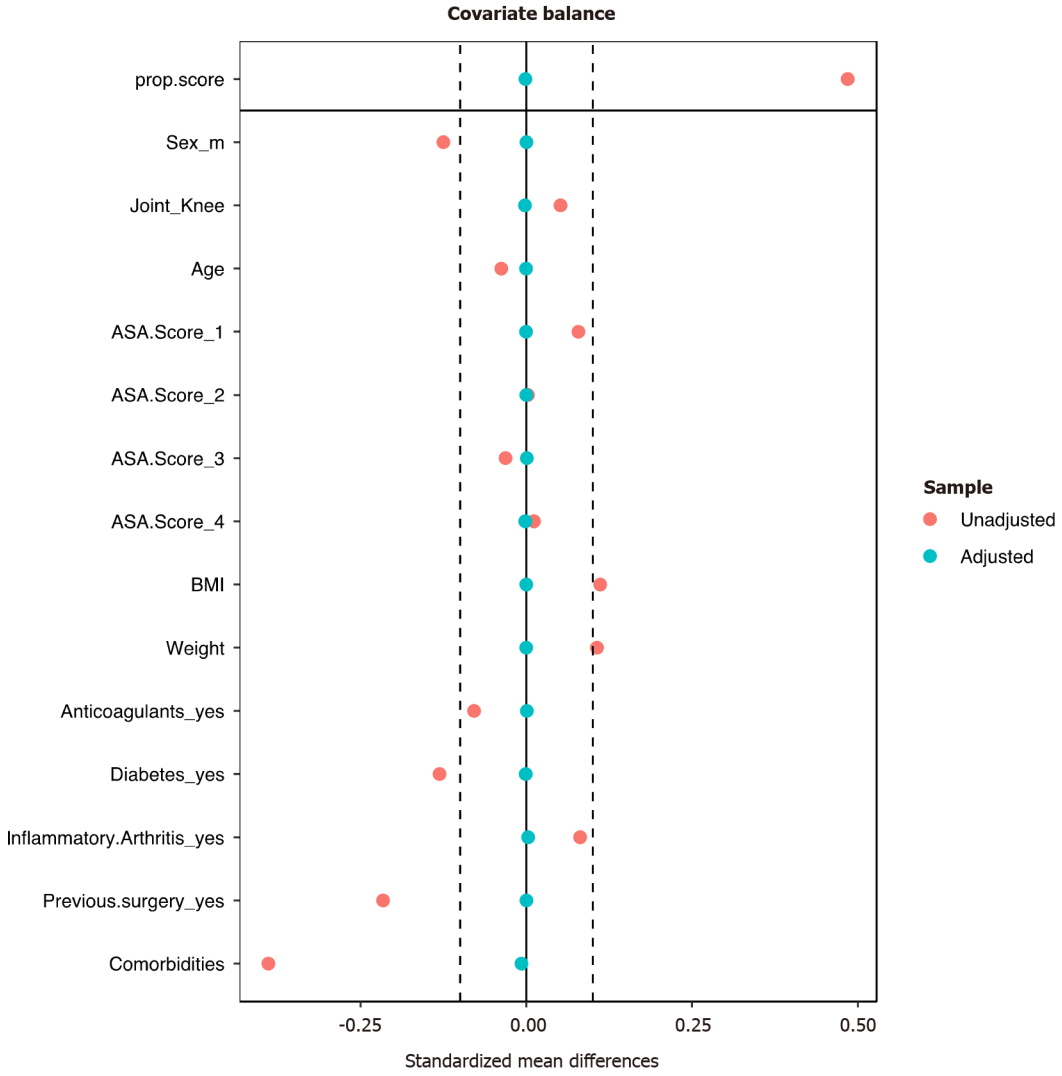


Figure 1 Balance plot showing standardized mean differences in covariate values between the two regimes before (unadjusted) and after (adjusted) propensity score weighting. The vertical dashed lines represent the boundary of meaningful baseline bias.

time as independent variable[26]. Our hypothesis was that the introduction of a weight-adjusted regime of shorter duration in the NR would not lead to a change in the incidence of all SSI when compared to the old regime (OR). Statistical analysis was performed using 'Jamovi' (Version 1.6); retrieved from https://www.jamovi.org, and using R *vs* 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria) for the propensity score analysis (packages CBPS and mice) and the interrupted time series analysis. For all analyses, a *P* value below 0.05 was assumed to denote statistical significance.

RESULTS

A total of 1273 operations (THA *n* = 534, TKA *n* = 739) were performed over the study period in *n* = 1264 patients (males *n* = 493, females *n* = 771). Six hundred and sixty-nine (*n* = 669) patients had surgery under the old antibiotic prophylaxis regime (OR) whilst *n* = 595 had surgery under the NR. In the OR group the mean age was 69.3 years (SD ± 11.9), whilst for the NR cohort, the mean age was 68.8 years (SD ± 10.5). Table 1 illustrates the demographic characteristics of both groups in further detail. Complete data (demographic information, ASA grading, presence of diabetes mellitus, use of anticoagulation) was available for *n* = 310 patients in the OR group and *n* = 458 patients in the NR group (Table 2).

At final follow-up, there had been 5 episodes of deep incisional or organ space infection (5/675; 0.74%) in the OR cohort and 14 episodes of superficial incisional infection (14/675; 2.07%). For the NR group, at 2 years following surgery, there had been 3 episodes of deep incisional or organ space infection (3/598; 0.50%) and 9 episodes of superficial incisional infection (9/598; 1.67%). There was no statistically significant difference in the rate of deep incisional or organ space infection between the OR and NR groups (0.74% *vs* 0.50%; Fisher's exact test *P* = 0.73), nor in the superficial incisional infection rate between the OR and NR groups (2.07% *vs* 1.67%; chi-squared test *P* = 0.44); Table 3. For the subgroup with complete demographic data, there was no significant difference in the rates of superficial (OR 2.6% *vs* NR 1.5%; chi-squared test *P* = 0.30) and deep infection (OR 0.3% *vs* NR 0.5%; Fisher's exact test *P* = 1.0) between the OR and

Table 1 Demographic information for patients treated with the old regime and new regime of perioperative antibiotic prophylaxis, *n* (%)

	Old regime	New regime
	***n* = 669 patients**	***n* = 595 patients**
Age (mean ± SD)	69.3 ± 11.9 yr	68.8 ± 10.5 yr
Gender (male)	279 (41.7)	214 (40.0%)
BMI (mean ± SD)	32.2 ± 11.0	31.8 ± 7.4
Operation performed		
THA	THA, *n* = 291 (43.1)	THA, *n* = 243 (40.6)
TKA	TKA, *n* = 384 (56.9)	TKA, *n* = 355 (59.4)

BMI: Body mass index; SD: Standard deviation; THA: Total hip arthroplasty; TKA: Total knee arthroplasty.

Table 2 Demographic information for patients treated with the old regime and new regime of perioperative antibiotic prophylaxis (complete data)

	Old regime, *n* (%)	New regime, *n* (%)
	***n* = 310**	***n* = 458**
Age (mean ± SD)	67.5 ± 10.9 yr	67.0 ± 10.5 yr
Gender (male)	132 (42.6)	165 (36.0)
Weight (kg; mean ± SD)	84.82 ± 20.9	87.73 ± 22.3
Weight > 120 kg	19 (6.1)	44 (9.6)
Operation performed		
Total hip arthroplasty	124 (40.0)	198 (43.2)
Total knee arthroplasty	186 (60.0)	260 (56.8)
Comorbidities		
ASA grade		
1	5 (1.6)	12 (2.6)
2	154 (49.7)	212 (46.3)
3	148 47.7)	227 (50.0)
4	3 (1.0)	7 (1.5)
Diabetes mellitus		
Yes	49 (15.8)	48 (10.5)
No	261 (84.2)	410 (89.5)
Anticoagulation on admission		
Yes	27 (8.7)	29 (6.3)
No	283 (91.3)	429 (93.7)
Antibiotic prophylaxis		
Cefazolin	342 (50.7)	449 (98.0)
Clindamycin	11 (1.6)	8 (1.7)
Vancomycin	1 (0.1)	1 (0.3)
Dose appropriate for weight?		
Yes	340 (50.3)	458 (100)
No	13 (2.0)	0 (0.0)

ASA: American society of anaesthesiology.

Table 3 Incidence of superficial and deep surgical site infections after 2 years follow up in patients undergoing elective primary total hip and knee arthroplasty

	Old regime, *n* = 669 patients	New regime, *n* = 595 patients
	(*n* = 675 THA/TKA)	(*n* = 598 THA/TKA)
Superficial infection, *n* (%)	14 (2.07)	9 (1.50)
	THA, *n* = 6	THA, *n* = 2
	TKA, *n* = 8	TKA, *n* = 7
Deep/organ space infection, *n* (%)	5 (0.74)	3 (0.50)
	THA, *n* = 1	THA, *n* = 2
	TKA, *n* = 4	TKA, *n* = 1

TKA: Total knee arthroplasty; THA: Total hip arthroplasty.

Table 4 Incidence of superficial and deep surgical site infections after 2 years follow up in patients undergoing elective primary total hip and knee arthroplasty (THA/TKA; Complete demographic data subgroup)

	Old regime	New regime
	n = 310 joints	*n* = 458 joints
Total number of infections, *n* (%)	9 (2.9)	9 (2.0)
Superficial infections, *n* (%)	8 (2.6)	7 (1.5)
	THA, *n* = 2	THA, *n* = 1
	TKA, *n* = 6	TKA, *n* = 6
Deep/organ space infections	1 (0.3)	2 (0.5)
	THA, *n* = 1	THA, *n* = 2

THA: Total hip arthroplasty; TKA: Total knee arthroplasty.

NR groups; Table 4. Supplementary Tables 1 and 2 provide further information on the patients in the whole cohort diagnosed with SSIs, whilst Supplementary Tables 3 and 4 provide the same for patients with SSIs from the subgroup with complete demographic information.

Analysis using propensity score weighting and interrupted time series

Before propensity score weighting, the dataset had meaningful imbalances (over 10% SMD) in the distribution of sex, BMI, weight, diabetes, previous surgery and the number of comorbidities (Figure 1). Propensity score weighting achieved a balanced dataset. The relative risks of overall or deep SSI were however comparable between the original and weighted dataset, with clearly overlapping 95% confidence intervals between the two types of analyses (Table 5).

When analyzed as an interrupted time series, the overall infection rate in the original dataset seems constant under the old regime, whereas under the NR it seems to drop with patient number (Figure 2A). In the weighted dataset, the infection rate already seemed to drop under the old regime and after an initial rise continued to drop under the NR (Figure 2B). However, it is important to realize that none of the rate coefficients differed significantly from zero (Table 6), as can also be judged by the wide confidence intervals in the graphs.

DISCUSSION

Weight-adjusted antibiotic prophylaxis dosing has not been evaluated in large patient cohorts and there is limited evidence for its use in SSI prophylaxis[13-15]. The findings from this study are in agreement with our null hypothesis that using a weight based antibiotic prophylaxis regime and shortening the duration of administered antibiotics, would not lead to a statistically significant increase in deep incisional/organ space SSI rates between the OR and NR groups. The

Table 5 Relative risks for all and deep surgical site infections in original dataset and after propensity score weighting

Infection	Original dataset		Weighted dataset	
	RR (95%CI)	*P* value	RR (95%CI)	*P* value
Overall infection	0.69 (0.34 to 1.4)	0.31[1]	0.66 (0.32 to 1.4)	0.27[3]
Deep infection	0.66 (0.16 to 2.7)	0.73[2]	0.55 (0.13 to 2.4)	0.43[3]

[1]Chi-squared test.
[2]Fisher's exact test.
[3]Weighted log-binomial regression using robust variance estimator.
RR: Relative risk (old regime/new regime).

Table 6 Coefficient values (converted to relative risks) for interrupted time series analysis of overall infection rate over time

Parameter	Original dataset		Weighted dataset	
	RR (95%CI)	*P* value	RR (95%CI)	*P* value
Slope of infection rate per 100 patients, old regime	0.99 (0.79 to 1.3)	0.98	0.95 (0.76 to 1.2)	0.62
Jump in infection rate, new *vs* old	1.16 (0.30 to 4.4)	0.82	1.3 (0.39 to 4.5)	0.66
Change in slope of infection rate per 100 patients, new *vs* old	0.83 (0.55 to 1.2)	0.37	0.88 (0.61 to 1.3)	0.46

RR: Relative risk.

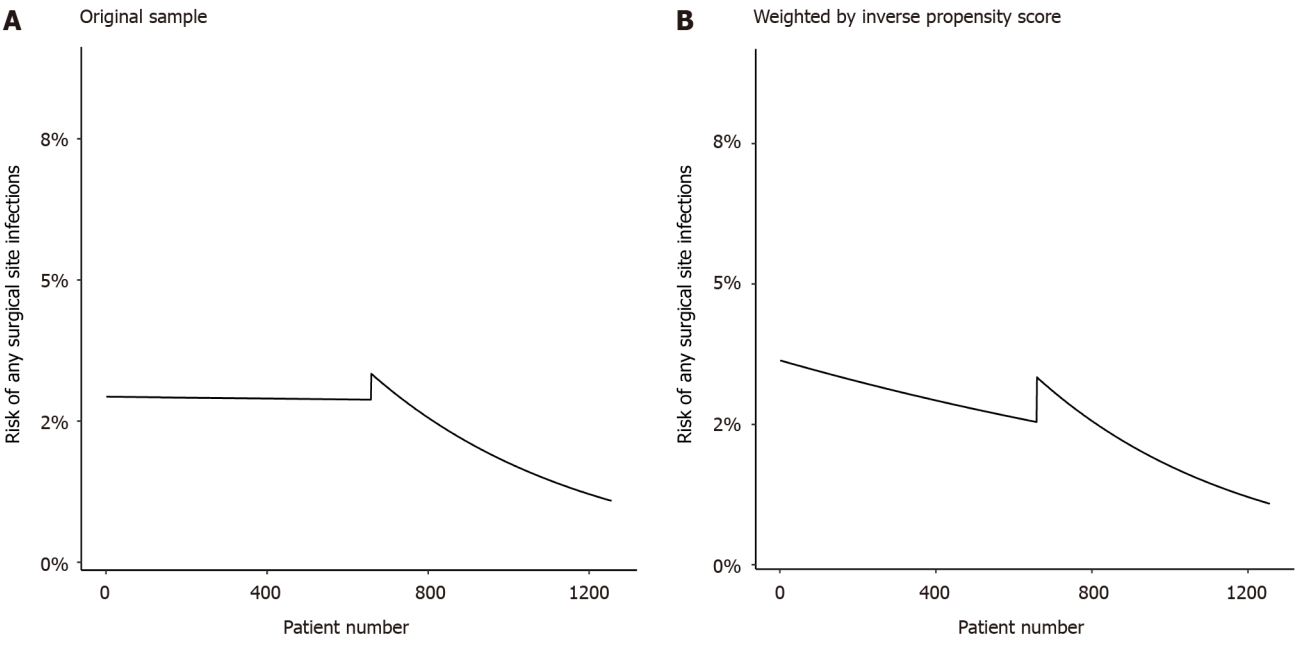


Figure 2 Interrupted time series analysis for risk of overall infection. A: Original sample; B: Propensity score-weighted sample.

use of a weight-adjusted regime led to a reduction in the rates of superficial SSIs [NR (1.67%) *vs* OR (2.07%)] but this was not found to be statistically significant. The incidence of superficial SSIs in TKAs were found to be greater than in THAs and this is likely to be due to the fact that there is less soft tissue overlying the operated joint in TKA as opposed to THA. Because of the oedema in the operated limb following surgery, TKA patients are perhaps more likely to be diagnosed and treated for a superficial SSI by their family care physician in the community.

No randomized trials exist in the literature comparing variable duration antibiotic prophylaxis in patients undergoing lower limb arthroplasty. In one study comparing a one-day regime of cefuroxime with a three-day regime in a prospective, double blinded, there was no significant difference in the prevalence of wound infections between the two groups (deep infection rate with cefuroxime 0.5% (THA), 0.6% (TKA) *vs* cefazolin 1.2% (THA), 1.4% (TKA)[17]. Another study that compared a single preoperative dose of either cefazolin or nafcillin with a 48-h regimen found no difference in infection prevalence, although the study lacked power to compare the one dose and the more than one dose categories,

and had a small sample size (n = 466 over 4 years)[18].

Evaluations of pre-and post-intervention periods have also been used to assess the impact of antibiotic duration on surgical prophylaxis. One such study showed that a change from one preoperative and two post-operative doses of intravenous cefuroxime every 8 h to a single preoperative dose of intravenous cefazolin for all clean orthopedic surgeries led to a deep wound infection rate of 1.1% for THA (95%CI 0%-3.3%), and 1.6% for TKA (95%CI 0%-3.8%) in the cefuroxime group, *vs* 1.1% for THA (95%CI 0%-2.2%) and 1.0% for TKA (95%CI 0.3%-1.7%) in the cefazolin group, with no statistically significant difference[27].

Obesity is associated with systemic low-grade inflammation, and this can be characterized by increased serum levels of pro-inflammatory cytokines, potentially resulting in an impaired immune response[28]. Conditions such as type 2 diabetes and dyslipidaemia, which are associated with obesity, may also increase the risk of postoperative infections[29]. Technical difficulties associated with surgery in obese patients may also result in prolonged operations, which are associated with higher SSI rates[30]. Standardized antibiotic prophylaxis doses do tend to provide lower antibiotic concentrations per kilogram in overweight and obese patients compared with patients of normal bodyweight. Various studies however, have suggested no difference in infection rates between standardized and weight-adjusted regimes[31, 32]. We have used a weight-adjusted regime in this study and there appears to be a trend to reduction in the number of superficial SSIs, which is more likely to occur in TKA patients.

LIMITATIONS

There were limitations to this study. Firstly, the data was derived from the observational analysis of a large cohort and, as such, the findings are subject to selection bias. However, the sample size was sufficient to yield meaningful analysis. Based on post priori-power calculation; the current power of the study is 11% *vs* 80% which would be the ideal scenario. Based on a difference between OR and NR regimes of 0.94%, for statistical power of 80%, to demonstrate a difference (or reduction in incidence of SSI) between the groups, n = 8862 patients would be required per group; a total of n = 17724. Such a number would be impractical to recruit to, and observational cohorts such as described in this study are the most pragmatic method to study SSI incidence because of the low rates typically observed. Another limitation is the missing demographic data (approximately 40%). However, the analysis of the subgroup data in terms of SSI incidence, yielded similar results in comparison to the whole cohort data.

CONCLUSION

In conclusion, reducing the number of post-operative antibiotic doses had no adverse impact on SSI incidence, at 2 years following surgery, in this patient population. A weight-adjusted regime appears to have a benefit (not statistically significant) in reducing the rate of superficial SSIs.

ARTICLE HIGHLIGHTS

Research background

Antibiotic stewardship is important in everyday orthopaedic practice. Preventing surgical site infection (SSIs) with the use of prophylactic antibiotics has to take into account the impact of obesity. There is a growing consensus that a weight based regime may be efficacious in dealing with SSIs in everyday practice.

Research motivation

This study aimed to evaluate the impact of a weight based regime administered for a shorter duration, on the incidence of SSIs in a cohort of patients undergoing elective primary total hip and knee arthroplasty (THA/TKA).

Research objectives

The main objective of the study was to evaluate if there was no reduction in levels of prophylaxis for a weight based antibiotic regime, administered for a shorter duration, *vs* a standard regime in prevention of SSIs in a cohort of patients undergoing elective primary THA/TKA.

Research methods

A cohort of arthroplasty patients undergoing primary THA/TKA with a single pre-operative dose and two post-operative antibiotic doses (old regime, OR; September to December 2018), was compared to a group of patients undergoing primary THA/TKA after the regime had been changed to a weight-adjusted pre-operative dose and a single post-operative dose [new regime, (NR); January to April 2019]. Our hypothesis was that the introduction of a weight-adjusted regime of shorter duration in the NR would not lead to a change in the incidence of all SSI when compared to the old regime (OR).

Research results

The findings from this study are in agreement with our null hypothesis that using a weight based antibiotic prophylaxis regime and shortening the duration of administered antibiotics, would not lead to a statistically significant increase in deep incisional/organ space SSI rates between the OR and NR groups. The use of a weight-adjusted regime led to a reduction in the rates of superficial SSIs [NR (1.67%) *vs* OR (2.07%)] but this was not found to be statistically significant.

Research conclusions

It is important to consider use of a weight based regime for a shorter duration in patients undergoing elective primary THA/TKA as there is no increased SSI risk.

Research perspectives

More studies on antibiotic prophylaxis stewardship for this group of patients is required.

ACKNOWLEDGEMENTS

Mr. Peter Craig and Mr. Caesar Wek for help in data collation and data analysis respectively. Research Staff at Sunnybrook Holland Orthopaedic and Arthritic Center, Toronto, for help in data collation.

FOOTNOTES

Author contributions: Okoro T, Murnaghan J designed the research study; Okoro T, Wan M, Mukabeta TD, Williams C, Malev E, Manjra M, Gross M performed the research; Okoro T, Kuiper JH performed the statistical analysis; Okoro T, Kuiper JH, Murnaghan J analyzed the data and wrote the manuscript; All authors have read and approve the final manuscript.

Institutional review board statement: This study was approved by the Sunnybrook Health Sciences Centre, Toronto, Research Ethics Board in September 2018.

Clinical trial registration statement: The clinical trial is registered with ClinicalTrials.gov, using identifier NCT00526890. Details can be found at https://clinicaltrials.gov/ct2/show/NCT00526890?term=NCT00526890&rank=1.

Informed consent statement: I wish to confirm that the above study was performed after approval as a quality improvement project by the Sunnybrook Health Sciences Research Department without the need for formal ethics committee approval and therefore did not require informed consent from the patients.

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

Data sharing statement: No additional data are available.

Country/Territory of origin: Canada

ORCID number: Tosan Okoro 0000-0003-0432-0936; Takura Darlington Mukabeta 0000-0002-6581-5660.

S-Editor: Liu JH
L-Editor: A
P-Editor: Yuan YY

REFERENCES

1 **Lidwell OM**. The cost implications of clean air systems and antibiotic prophylaxis in operations for total joint replacement. *Infect Control* 1984; **5**: 36-37 [PMID: 6557084 DOI: 10.1017/S0195941700058781]
2 **Page CP**, Bohnen JM, Fletcher JR, McManus AT, Solomkin JS, Wittmann DH. Antimicrobial prophylaxis for surgical wounds. Guidelines for clinical care. *Arch Surg* 1993; **128**: 79-88 [PMID: 8418785 DOI: 10.1001/archsurg.1993.01420130087014]
3 **Bratzler DW**, Houck PM; Surgical Infection Prevention Guideline Writers Workgroup. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Am J Surg* 2005; **189**: 395-404 [PMID: 15820449 DOI: 10.1016/j.amjsurg.2005.01.015]
4 **Uçkay I**, Hoffmeyer P, Lew D, Pittet D. Prevention of surgical site infections in orthopaedic surgery and bone trauma: state-of-the-art update. *J Hosp Infect* 2013; **84**: 5-12 [PMID: 23414705 DOI: 10.1016/j.jhin.2012.12.014]

5 **Bryson DJ**, Morris DL, Shivji FS, Rollins KR, Snape S, Ollivere BJ. Antibiotic prophylaxis in orthopaedic surgery: difficult decisions in an era of evolving antibiotic resistance. *Bone Joint J* 2016; **98-B**: 1014-1019 [PMID: 27482011 DOI: 10.1302/0301-620X.98B8.37359]

6 **Nehrer S**, Thalhammer F, Schwameis E, Breyer S, Kotz R. Teicoplanin in the prevention of infection in total hip replacement. *Arch Orthop Trauma Surg* 1998; **118**: 32-36 [PMID: 9833102 DOI: 10.1007/s004020050306]

7 **Zimmerli W**, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med* 2004; **351**: 1645-1654 [PMID: 15483283 DOI: 10.1056/nejmra040181]

8 **Izakovicova P**, Borens O, Trampuz A. Periprosthetic joint infection: current concepts and outlook. *EFORT Open Rev* 2019; **4**: 482-494 [PMID: 31423332 DOI: 10.1302/2058-5241.4.180092]

9 **Roth VR**, Mitchell R, Vachon J, Alexandre S, Amaratunga K, Smith S, Vearncombe M, Davis I, Mertz D, Henderson E, John M, Johnston L, Lemieux C, Pelude L, Gravel D; Canadian Nosocomial Infection Surveillance Program. Periprosthetic Infection following Primary Hip and Knee Arthroplasty: The Impact of Limiting the Postoperative Surveillance Period. *Infect Control Hosp Epidemiol* 2017; **38**: 147-153 [PMID: 27834161 DOI: 10.1017/ice.2016.256]

10 **Turano A**. New clinical data on the prophylaxis of infections in abdominal, gynecologic, and urologic surgery. Multicenter Study Group. *Am J Surg* 1992; **164**: 16S-20S [PMID: 1443354 DOI: 10.1016/s0002-9610(06)80052-8]

11 **Niederhäuser U**, Vogt M, Vogt P, Genoni M, Künzli A, Turina MI. Cardiac surgery in a high-risk group of patients: is prolonged postoperative antibiotic prophylaxis effective? *J Thorac Cardiovasc Surg* 1997; **114**: 162-168 [PMID: 9270631 DOI: 10.1016/s0022-5223(97)70140-5]

12 **Enzler MJ**, Berbari E, Osmon DR. Antimicrobial prophylaxis in adults. *Mayo Clin Proc* 2011; **86**: 686-701 [PMID: 21719623 DOI: 10.4065/mcp.2011.0012]

13 AAOS. Recommendations for the Use of Intravenous Antibiotic Prophylaxis in Primary Total Joint Arthroplasty. *Am Acad Orthop Surg* 2014 [DOI: 10.5435/jaaos-d-23-00434]

14 **National Institute for Health and Care Excellence**. Surgical site infections: prevention and treatment NICE guideline (NG125). Published online 2019. Available from: https://www.nice.org.uk/guidance/ng125/resources/surgical-site-infections-prevention-and-treatment-pdf-66141660564421

15 **Allegranzi B**, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, Gomes SM, Gans S, Wallert ED, Wu X, Abbas M, Boermeester MA, Dellinger EP, Egger M, Gastmeier P, Guirao X, Ren J, Pittet D, Solomkin JS; WHO Guidelines Development Group. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis* 2016; **16**: e288-e303 [PMID: 27816414 DOI: 10.1016/S1473-3099(16)30402-9]

16 **Thelwall S**, Harrington P, Sheridan E, Lamagni T. Impact of obesity on the risk of wound infection following surgery: results from a nationwide prospective multicentre cohort study in England. *Clin Microbiol Infect* 2015; **21**: 1008.e1-1008.e8 [PMID: 26197212 DOI: 10.1016/j.cmi.2015.07.003]

17 **Rondon AJ**, Kheir MM, Tan TL, Shohat N, Greenky MR, Parvizi J. Cefazolin Prophylaxis for Total Joint Arthroplasty: Obese Patients Are Frequently Underdosed and at Increased Risk of Periprosthetic Joint Infection. *J Arthroplasty* 2018; **33**: 3551-3554 [PMID: 30093266 DOI: 10.1016/j.arth.2018.06.037]

18 WHO. World Health Organization (WHO): Obesity and overweight. World Health Organization 2021. Accessed 21st December 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

19 **Bratzler DW**, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm* 2013; **70**: 195-283 [PMID: 23327981 DOI: 10.2146/ajhp120568]

20 **Decker BK**, Nagrebetsky A, Lipsett PA, Wiener-Kronish JP, O'Grady NP. Controversies in Perioperative Antimicrobial Prophylaxis. *Anesthesiology* 2020; **132**: 586-597 [PMID: 31841446 DOI: 10.1097/ALN.0000000000003075]

21 **Edmiston CE**, Krepel C, Kelly H, Larson J, Andris D, Hennen C, Nakeeb A, Wallace JR. Perioperative antibiotic prophylaxis in the gastric bypass patient: do we achieve therapeutic levels? *Surgery* 2004; **136**: 738-747 [PMID: 15467657 DOI: 10.1016/j.surg.2004.06.022]

22 **Siddiqi A**, Forte SA, Docter S, Bryant D, Sheth NP, Chen AF. Perioperative Antibiotic Prophylaxis in Total Joint Arthroplasty: A Systematic Review and Meta-Analysis. *J Bone Joint Surg Am* 2019; **101**: 828-842 [PMID: 31045673 DOI: 10.2106/JBJS.18.00990]

23 **Floor-Westerdijk M**, Colier W, van der Burght R. Letter to the editor: re: "a new automated assessment method for contrast-detail images by applying support vector machine and its robustness to non-linear image processing" by Takei T, Ikeda M, Imai K, Yamauchi-Kawaura C, Kato K, Isoda H., APESM 36(3), pp 313-322, DOI 10.1007/s13246-013-0215-z. *Australas Phys Eng Sci Med* 2014; **37**: 471-472 [PMID: 25103997 DOI: 10.1007/s13246-014-0290-9]

24 **Coffman DL**, Zhou J, Cai X. Comparison of methods for handling covariate missingness in propensity score estimation with a binary exposure. *BMC Med Res Methodol* 2020; **20**: 168 [PMID: 32586271 DOI: 10.1186/s12874-020-01053-4]

25 **Austin PC**, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Stat Med* 2015; **34**: 3661-3679 [PMID: 26238958 DOI: 10.1002/sim.6607]

26 **Mascha EJ**, Sessler DI. Segmented Regression and Difference-in-Difference Methods: Assessing the Impact of Systemic Changes in Health Care. *Anesth Analg* 2019; **129**: 618-633 [PMID: 31008746 DOI: 10.1213/ANE.0000000000004153]

27 **Tang WM**, Chiu KY, Ng TP, Yau WP, Ching PT, Seto WH. Efficacy of a single dose of cefazolin as a prophylactic antibiotic in primary arthroplasty. *J Arthroplasty* 2003; **18**: 714-718 [PMID: 14513443 DOI: 10.1016/S0883-5403(03)00201-8]

28 **Jin C**, Henao-Mejia J, Flavell RA. Innate immune receptors: key regulators of metabolic disease progression. *Cell Metab* 2013; **17**: 873-882 [PMID: 23747246 DOI: 10.1016/j.cmet.2013.05.011]

29 **Peleg AY**, Weerarathna T, McCarthy JS, Davis TM. Common infections in diabetes: pathogenesis, management and relationship to glycaemic control. *Diabetes Metab Res Rev* 2007; **23**: 3-13 [PMID: 16960917 DOI: 10.1002/dmrr.682]

30 **Cheng H**, Chen BP, Soleas IM, Ferko NC, Cameron CG, Hinoul P. Prolonged Operative Duration Increases Risk of Surgical Site Infections: A Systematic Review. *Surg Infect (Larchmt)* 2017; **18**: 722-735 [PMID: 28832271 DOI: 10.1089/sur.2017.089]

31 **Ho VP**, Nicolau DP, Dakin GF, Pomp A, Rich BS, Towe CW, Barie PS. Cefazolin dosing for surgical prophylaxis in morbidly obese patients. *Surg Infect (Larchmt)* 2012; **13**: 33-37 [PMID: 22316145 DOI: 10.1089/sur.2010.097]

32 **Banoub M**, Curless MS, Smith JM, Jarrell AS, Cosgrove SE, Rock C, Avdic E. Higher versus Lower Dose of Cefotetan or Cefoxitin for Surgical Prophylaxis in Patients Weighing One Hundred Twenty Kilograms or More. *Surg Infect (Larchmt)* 2018; **19**: 504-509 [PMID: 29717917 DOI: 10.1089/sur.2017.296]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 180-191

DOI: 10.5312/wjo.v15.i2.180

ISSN 2218-5836 (online)

META-ANALYSIS

Meta-analysis of factors influencing anterior knee pain after total knee arthroplasty

Hui Feng, Ming-Li Feng, Jing-Bo Cheng, Xiang Zhang, Hai-Cheng Tao

Specialty type: Orthopedics

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Ng BW, Malaysia; Velázquez-Saornil J, Spain

Received: October 25, 2023
Peer-review started: October 25, 2023
First decision: December 11, 2023
Revised: December 20, 2023
Accepted: January 22, 2024
Article in press: January 22, 2024
Published online: February 18, 2024

Hui Feng, Ming-Li Feng, Jing-Bo Cheng, Xiang Zhang, Hai-Cheng Tao, Department of Orthopaedic Surgery, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

Corresponding author: Ming-Li Feng, MD, Chief Physician, Department of Orthopaedic Surgery, Xuanwu Hospital, Capital Medical University, No. 45 Changchun Ave, Xicheng District, Beijing 100053, China. fengmingli6666@163.com

Abstract

BACKGROUND

Total knee arthroplasty (TKA) is a mature procedure recommended for correcting knee osteoarthritis deformity, relieving pain, and restoring normal biomechanics. Although TKA is a successful and cost-effective procedure, patient dissatisfaction is as high as 50%. Knee pain after TKA is a significant cause of patient dissatisfaction; the most common location for residual pain is the anterior region. Between 4% and 40% of patients have anterior knee pain (AKP).

AIM

To investigate the effect of various TKA procedures on postoperative AKP.

METHODS

We searched PubMed, EMBASE, and Cochrane from January 2000 to September 2022. Randomized controlled trials with one intervention in the experimental group and no corresponding intervention (or other interventions) in the control group were collected. Two researchers independently read the title and abstract of the studies, preliminarily screened the articles, and read the full text in detail according to the selection criteria. Conflicts were resolved by consultation with a third researcher. And relevant data from the included studies were extracted and analyzed using Review Manager 5.4 software.

RESULTS

There were 25 randomized controlled trials; 13 were comparative studies with or without patellar resurfacing. The meta-analysis showed no significant difference between the experimental and control groups (P = 0.61). Six studies were comparative studies of circumpatellar denervation *vs* non-denervation, divided into three subgroups for meta-analysis. The two-subgroup meta-analysis showed no significant difference between the experimental and the control groups (P = 0.31, P = 0.50). One subgroup meta-analysis showed a significant difference between the experimental and control groups (P = 0.001). Two studies compared fixed-bearing TKA and mobile-bearing TKA; the results meta-analysis showed no

significant difference between the experimental and control groups (P = 0.630). Two studies compared lateral retinacular release *vs* non-release; the meta-analysis showed a significant difference between the experimental and control groups (P = 0.002); two other studies compared other factors.

CONCLUSION
Patellar resurfacing, mobile-bearing TKA, and fixed-bearing TKA do not reduce the incidence of AKP. Lateral retinacular release can reduce AKP; however, whether circumpatellar denervation can reduce AKP is controversial.

Key Words: Total knee arthroplasty; Anterior knee pain; Knee osteoarthritis; Interventions; Meta-analysis

Core Tip: In our meta-analysis, we searched PubMed, EMBASE, and Cochrane from January 2000 to September 2022, and we included only high level randomized controlled trials in order to get more accurate results. We discussed the influence of multiple factors on anterior knee pain after total knee arthroplasty, with different results from previous studies.

Citation: Feng H, Feng ML, Cheng JB, Zhang X, Tao HC. Meta-analysis of factors influencing anterior knee pain after total knee arthroplasty. *World J Orthop* 2024; 15(2): 180-191
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/180.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.180

INTRODUCTION

Knee osteoarthritis is a chronic joint disease characterized by articular cartilage degeneration and secondary hyperosteogeny[1]. The primary symptom is pain during knee joint weight-bearing and activity, severely affecting the quality of life. In the early stage, conservative treatment with medication is effective; however, in the middle and late stages (especially in the end stage), knee pain is severe, and the effective treatment is knee replacement[2,3]. Total knee arthroplasty (TKA) is a mature procedure recommended for correcting knee osteoarthritis deformity, relieving pain, and restoring normal biomechanics[4]. The patients enjoy excellent long-term survival[5-8]. Although TKA is a successful and cost-effective procedure, patient dissatisfaction is as high as 50%. Knee pain after TKA is a significant cause of patient dissatisfaction; the most common location for residual pain is the anterior region[9]. Between 4% and 40% of patients have anterior knee pain (AKP)[10-12]. In this review, we searched PubMed, EMBASE, and the Cochrane database for randomized controlled trials related to AKP after TKA to explore the effects of various TKA approaches on AKP.

MATERIALS AND METHODS

Eligibility criteria and outcome definitions

Studies were selected based on the following inclusion criteria: (1) Type of studies: A randomized controlled trial; (2) subjects: Patients undergoing TKA for the first time; (3) intervention: Not limited; (4) control group: Intervention different from the experimental group or no intervention; and (5) evaluation indicators: Occurrence of AKP (incidence and pain degree). The exclusion criteria were as follows: Patellar surgery, fracture history, high tibial osteotomy, no AKP, review or expert reports, cadaveric studies, model studies, and case reports.

Information sources and search strategy

PubMed, EMBASE, and the Cochrane Library were searched from January 2000 to September 2022. The keywords were "Total Knee Arthroplasty", "Anterior Knee Pain", and other related Medline search heading terms or expressions.

Study selection and data extraction

Two researchers independently read the title and abstract of the studies, preliminarily screened the articles, and read the full text in detail according to the selection criteria. Conflicts were resolved by consultation with a third researcher. We retrieved 294 articles from three databases. After reading the title and abstract, 67 articles were identified. After reading the full text, articles without AKP were excluded, and the controversies were resolved. Finally, 25 articles were included in this review. A flowchart of the studies considered for inclusion is shown in Figure 1.

Quality assessment

According to the Cochrane Risk of Bias tool, the risk of bias of each randomized controlled trial was graded as low, high, or unclear based on: (1) Random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting, and (7) other bias.

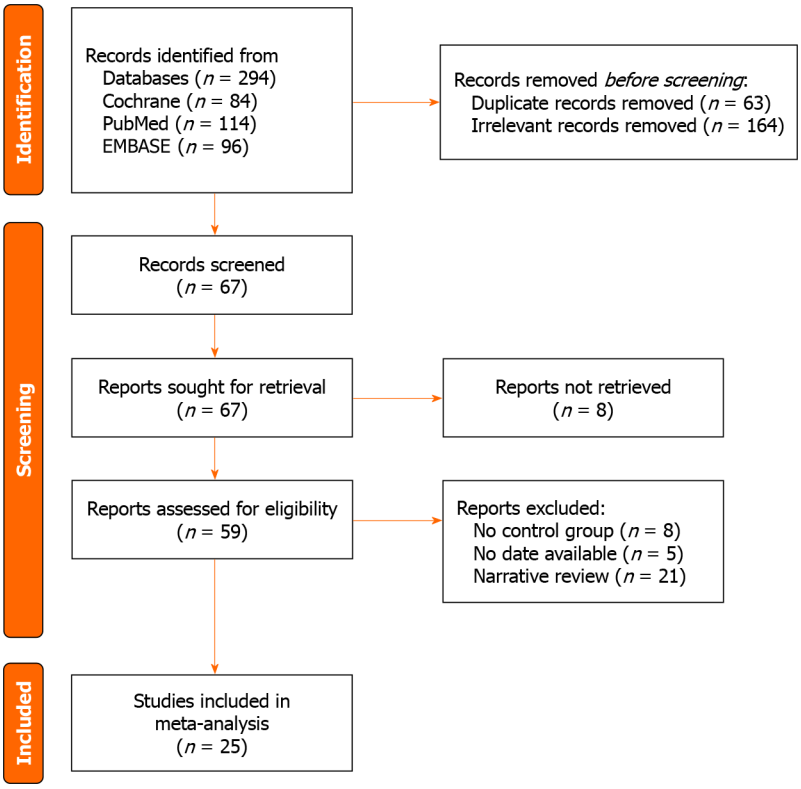


Figure 1 Flowchart of included studies.

The risk of bias assessments is shown in Figures 2 and 3.

Data synthesis and analysis

Data on study design, study population, interventions, and outcomes were extracted from the included articles' text, figures, and tables. Dichotomous outcomes were expressed as risk ratios with 95% confidence intervals (95%CIs), while continuous outcomes were expressed as mean or standard mean differences with 95%CI. Heterogeneity was expressed as P and I^2. This value of I^2 ranges from 0% (complete consistency) to 100% (complete inconsistency). If the P value of the heterogeneity test was < 0.1 or I^2 > 50%, a random-effects model was used in place of the fixed modality.

Publication bias was tested using funnel plots. Forest plots were used to graphically present the results of individual studies and the respective pooled effect size estimate. All statistical analyses were performed using Review Manager version 5.4.

RESULTS

Effect of patellar resurfacing on AKP

We included 13 studies on the effect of patellar replacement on AKP after TKA[4,13-24]. Ten reported the number of patients with AKP in each group, and the remaining three evaluated AKP using a visual analog scale (VAS) and hospital for special surgeries patellar score. These three studies did not conduct meta-analyses. There were 1197 TKA patients in these ten studies, including 586 TKA patients with patellar resurfacing (121 AKP) and 611 TKA patients without patellar resurfacing (100 AKP). The basic information of the ten studies (Table 1) and the forest plot (Figure 4) and funnel plot (Figure 5) of the meta-analysis are as follows (I^2 = 0%, using the fixed modality, P = 0.13, suggesting that there was no significant difference between the two groups. The funnel plot was symmetrical, suggesting no publication bias).

Effect of circumpatellar denervation on AKP

Six studies[25-30] compared circumpatellar denervation with non-denervation in TKA. The patellofemoral Feller score (PFS) was used to evaluate postoperative AKP in two studies, VAS was used in two studies, and the remaining two reported the number of cases of AKP in each group; therefore, they were divided into three subgroups for meta-analysis. The basic information of the six articles is presented in Tables 2 and 3.

PFS score subgroup

There were two studies[25,26] with 138 cases in the denervation group and 131 in the non-denervation group. The meta-analysis forest plot is shown in Figure 6A (I^2 = 66%, using the random-effects model, P = 0.31, suggesting no significant difference between the groups).

Table 1 Basic information (*e.g.*, patellar resurfacing *vs* no patellar resurfacing)

Ref.	Follow-up time	Patients included (resurfacing/non-resurfacing)	Resurfacing		Non-resurfacing	
			Patients with AKP	Patients available	Patients with AKP	Patients available
Koh *et al*[16], 2019	5 yr	49/49	29	49	30	49
Thiengwittayaporn *et al*[15], 2019	1 yr	42/42	0	41	2	39
Ha *et al*[17], 2019	5 yr	66/66	1	60	1	60
Deroche *et al*[13], 2022	18.0 months (mean)	123/123	14	116	15	105
Agarwala *et al*[4], 2018	19.0 months	60/60	7	60	9	60
Zou *et al*[19], 2011	16.5 months (mean)	64/64	7	64	9	64
Burnett *et al*[22], 2004	10 yr	50/50	7	19	5	20
Burnett *et al*[20], 2009	10 yr	59/59	8	38	6	40
Barrack *et al*[24], 2001	70.5 months	59/59	9	47	8	46
Wood *et al*[23], 2002	48.0 months (mean)	110/110	15	91	39	127

AKP: Anterior knee pain.

Table 2 The basic information of the studies (with or without circumpatellar denervation)

Ref.	Follow-up time	Patients included (denervation/non-denervation)	Denervation		Non-denervation	
			Patients with AKP	Patients available	Patients with AKP	Patients available
Jonbergen *et al*[29], 2011	1 yr	150/150	25	131	42	131
Pulavarti *et al*[28], 2014	2 yr	63/63	53	61	51	58

AKP: Anterior knee pain.

Table 3 The basic information of the studies (with or without circumpatellar denervation)

Ref.	Follow-up time	Patients available (denervation/non-denervation)	Score	Denervation		Non-denervation	
				Mean	SD	Mean	SD
Kwon *et al*[26], 2015	5 yr	50/50	PFS	14.10	1.00	14.20	1.20
Goicoechea *et al*[25], 2021	1 yr	88/81	PFS	12.60	3.50	13.60	2.70
Altay *et al*[27], 2012	3 yr	35/35	VAS	2.20	1.10	2.82	1.20
Deekshith *et al*[30], 2020	2 yr	50/49	VAS	1.34	0.47	1.60	0.53

VAS: Visual analog scale; PFS: Patellofemoral Feller score.

VAS score subgroup

There were two studies with 85 patients in the denervation group and 84 in the non-denervation group[27,30]. The meta-analysis forest plot is shown in Figure 6B (I^2 = 34%, using the fixed modality, P = 0.001, suggesting that the difference between the groups was statistically significant).

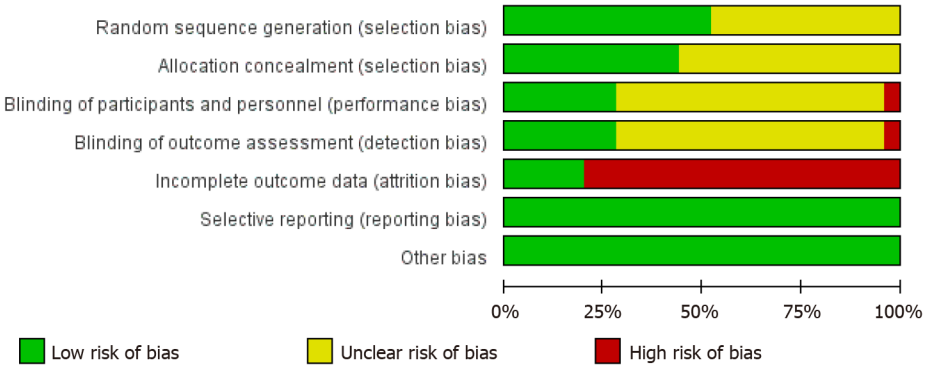


Figure 2 Proportions in the methodological quality assessment.

Subgroup of the number of patients with AKP

There were two studies with 213 patients in the denervation group and 213 in the non-denervation group[28,29]. The meta-analysis forest plot is shown in Figure 6C (I^2 = 90%, using the random-effects model, P = 0.50, suggesting no significant difference between the groups).

Effects of using fixed or mobile-bearing TKA on AKP

There were two studies comparing mobile-bearing and fixed-bearing designs. There were 88 cases of fixed-bearing and 71 of mobile-bearing[31,32]. The basic information of the studies (Table 4) and the forest plot of meta-analysis (Figure 6D) are as follows (I^2 = 12%, using the fixed modality, P = 0.63, suggesting that there was no significant difference between the two groups).

Effect of lateral retinacular release on AKP

We included two comparative studies of lateral retinacular release and non-release, with 135 cases in the release group and 130 in the non-release group[33,34]. The basic information of the two studies (Table 5) and the forest plot of meta-analysis (Figure 6E) are as follows (I^2 = 0%, using the fixed modality, P = 0.002, suggesting that the difference between the two groups was statistically significant).

Effect of other factors on AKP

Yuan *et al*[35] reported differences in patellofemoral function, clinical outcomes, and radiographic parameters between the freehand and cutting guide patellar resection techniques in patients undergoing TKA. The authors randomly assigned 100 patients to the freehand technique group and the cutting guide technique group, with 50 patients in each group. Finally, 42 patients in the cutting guide technique group and 44 patients in the freehand technique group were available for analysis. AKP occurred in 7.14% of the patients in the cutting guide technique group and 9.09% in the freehand technique group. There was no significant difference between the two groups. Fahmy *et al*[36] randomized into an experimental group, including patients with complete excision of the infrapatellar pad of fat (IPFP) and the control group with IPFP preservation. The authors randomly assigned 90 patients to the experimental and the control groups. At 6 months follow-up, 10 knees and 14 knees had AKP in IPFP preservation and excision group patients, respectively. The pain decreased during the follow-up period until the number of cases was almost equal at the final visit. There was no significant difference in AKP between the groups. Each group's mean VAS pain scores were comparable throughout the recorded follow-up period.

DISCUSSION

Effect of patellar resurfacing on AKP

Patellar resurfacing in TKA has long been controversial; some authors believe that patellar resurfacing can improve patient satisfaction, reduce postoperative AKP, and reduce the revision rate[37-40], while others hold the opposite view [41,42]. We analyzed 13 randomized controlled trials of patellar resurfacing and non-resurfacing. Of these, 12 showed no significant difference in postoperative AKP between the groups. Wood *et al*[23] showed that postoperative AKP was lower in the patellar resurfacing group than in the non-resurfacing group. In that study, surgery was performed by one of six experienced surgeons or their trainees under their supervision, and the follow-up time varied substantially (36-79 months, mean 48 months). Different surgeons have different surgical preferences, and the postoperative results also show substantial differences. The patients were followed up for a minimum of 36 months and a maximum of 79 months. The incidence of AKP and the severity of pain after TKA decreased with time. Therefore, comparing results at 36 and 79 months is not appropriate. These reasons may explain the different results between Wood *et al*[23] and other studies

Our meta-analysis showed no significant difference in the incidence of postoperative AKP between the patellar resurfacing group and the non-resurfacing group. Patellar resurfacing increases the operative time and blood loss.

Table 4 The basic information of the studies (effects of using fixed or mobile-bearing total knee arthroplasty)

Ref.	Follow-up time	Fixed		Mobile	
		Patients with AKP	Patients available	Patients with AKP	Patients available
Feczko *et al*[31], 2017	5.0 yr	11	48	6	42
Breugem *et al*[32], 2014	7.9 yr	5	40	5	29

AKP: Anterior knee pain.

Table 5 The basic information of the studies (lateral retinacular release *vs* non-release)

Ref.	Follow-up time	Lateral retinacular release		Non-release	
		Patients with AKP	Patients available	Patients with AKP	Patients available
Zhu *et al*[33], 2017	5 years	4	64	12	62
Zha *et al*[34], 2014	7.9 years	4	71	14	68

AKP: Anterior knee pain.

Furthermore, the patella in Asians is generally thin, leading to an increased risk of postoperative patellar fracture[41,42]. Therefore, we do not recommend patellar resurfacing in TKA.

Effect of circumpatellar denervation on AKP

The peripatellar soft tissue and retropatellar fat pad have been reported to be the source of AKP[43,44]. Immunohistochemical studies of nerve distribution in this area have shown the presence of substance-p nociceptive fibers in the peripatellar soft tissue[45]. Electrocautery disables these pain receptors and achieves desensitization or denervation of the anterior knee region. Thus, postoperative AKP can be reduced[46,47]. In our review, six studies compared circumpatellar denervation and non-denervation in TKA. Due to the inconsistency of the indicators to evaluate postoperative AKP, the meta-analysis was divided into three subgroups.

The results of the PFS score subgroup with AKP showed no significant difference between the denervation and non-denervation groups, while the VAS score subgroup showed that denervation was superior to non-denervation. Due to the large incision of TKA, peripatellar soft tissue and retropatellar fat pad are injured to a greater extent; therefore, achieving the surgical goal by performing only circumpatellar denervation is challenging. The heterogeneity among the six studies was considerable. The sample size was small, and the power of meta-analysis was weak; therefore, more studies are needed.

Effects of fixed or mobile-bearing TKA on AKP

The theoretical advantage of the mobile-bearing TKA is the ability to self-align and accommodate minor mismatches[32]. The design of the mobile-bearing TKA could lead to a better range of motion during knee flexion activities[48]. Breugem *et al*[12] found that over a one-year follow-up, the incidence of postoperative AKP of mobile-bearing TKA was lower than that of fixed-bearing TKA. However, postoperative AKP tended to be the same over time[32]. This result is similar to other studies[49,50]. This review included two studies comparing fixed-bearing TKA and mobile-bearing TKA, with follow-up times of 5.0 and 7.9 years, respectively. The meta-analysis showed no difference in the incidence of AKP between the groups. Therefore, the advantage of mobile-bearing TKA might decrease over time.

Effect of lateral retinacular release on AKP

Theoretically, proper lateral retinacular release improves patellar tracking and reduces patellofemoral contact pressure. These factors have been reported to be closely related to AKP[51,52]. In a prospective cohort study of 271 patients, Lee *et al*[51] found that patients who underwent patellar decompression had less AKP than those who did not. Wilson *et al*[52] found that patients with AKP had abnormal patellar tracking compared with patients without AKP. This review included two studies comparing lateral retinacular release and non-release in TKA. The meta-analysis showed that lateral retinacular release reduced AKP. No studies reported that lateral retinacular release produces adverse postoperative complications. Proper lateral retinacular release increases the intraoperative field of vision, which is conducive to successful outcomes.

Effect of other factors on AKP

In patellar resections when conducting TKA, a number of principles should be considered including restoring patellar height, performing a symmetric resection, avoiding under-resection, and minimizing over-stuffing of the patellofemoral joint[53]. Reasonable patellar excision is more beneficial to the installation of patellar components. At the same time, reasonable excision can reduce AKP, patellar fracture and patellar injury[54,55]. This review included one study

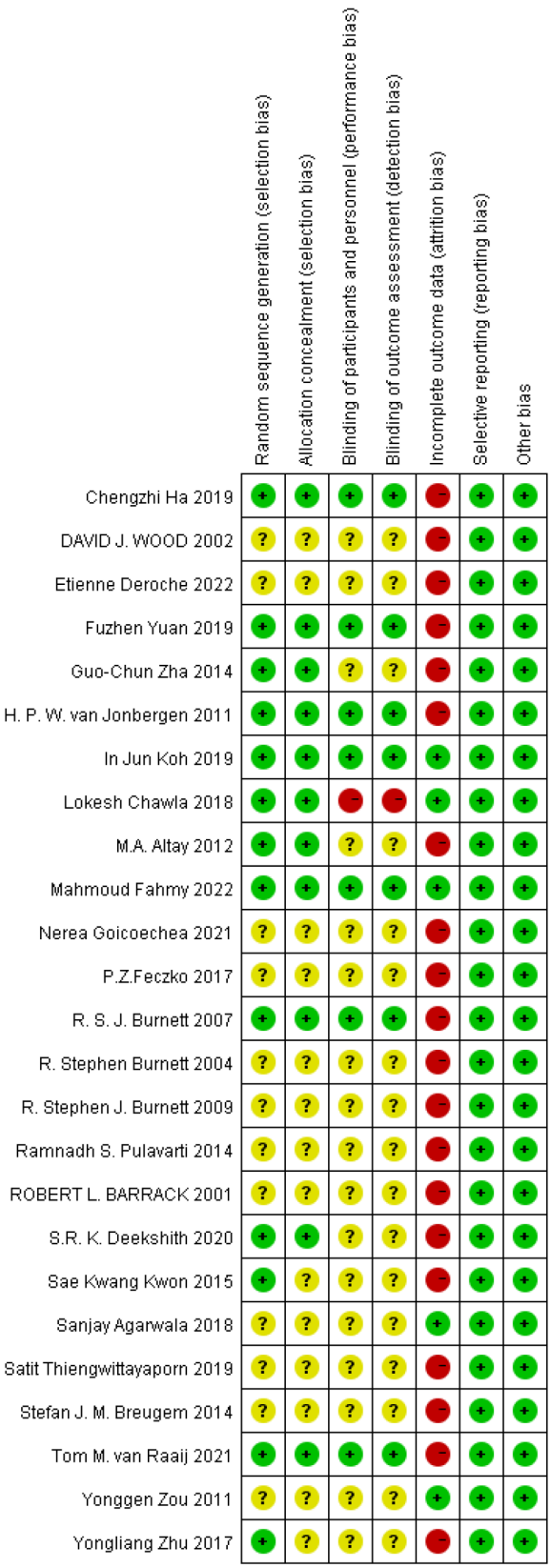


Figure 3 Methodological quality.

comparing freehand and cutting guide patellar resection techniques in TKA. In their prospective randomized controlled trial, no statistically significant difference was observed in the incidence of AKP between the two groups. Therefore, better knee function may be more related to basic principles, including excellent lower limb alignment, proper prosthetic placement, intact ligaments, and greater lower limb strength[35].

The IPFP is a piece of fat tissue located between the patellar ligament, the inferior patellar end, and the proximal tibia. Anatomically, it is considered to be an intraarticular extrasynovial compartment that may support effective joint

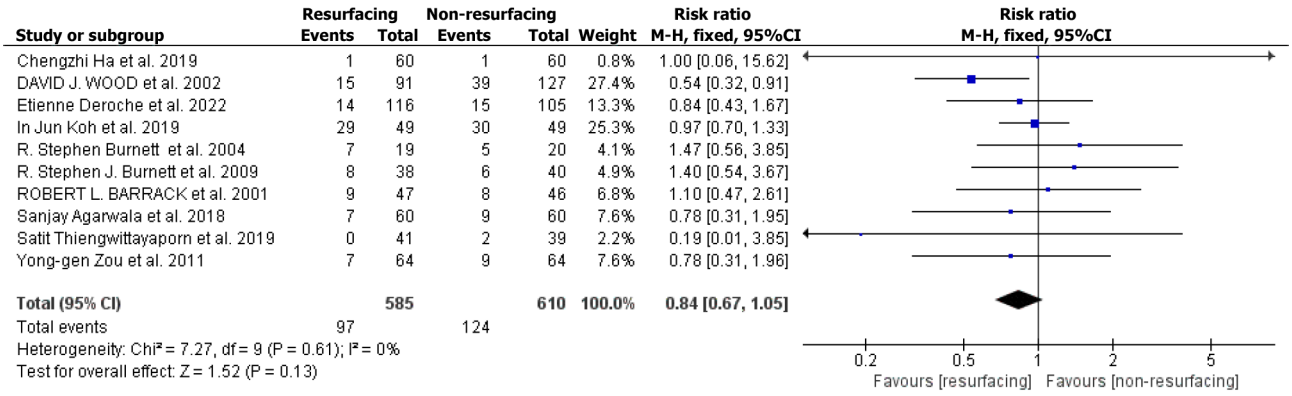


Figure 4 Forest plot for patellar resurfacing *vs* no resurfacing. 95%CI: 95% confidence interval.

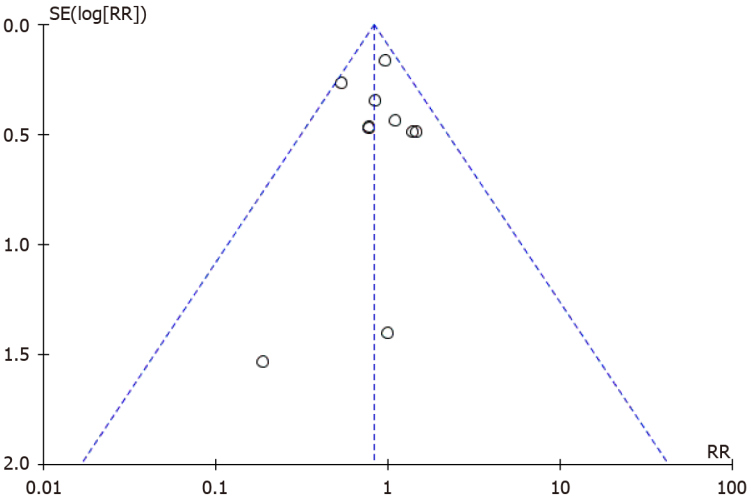


Figure 5 Funnel plot for patellar resurfacing *vs* no resurfacing.

lubrication[56]. The sufficient surgical exposure often prompts many surgeons to remove it during surgery, as there is debate about the effectiveness of its removal, but there is not complete agreement. In the study of Fahmy *et al*[36], the difference of the postoperative AKP, range of motion, oxford knee score and the clinical outcomes whether infrapatellar fat pad was excised or not were statistically insignificant. Therefore, surgeons had better to save the IPFP if conventional exposure can be reached; otherwise, resection is preferred to improve exposure.

The exact pathogenesis of AKP may be multifactorial. Laubach *et al*[57] concluded that quadriceps muscle strength, inlay thickness, and the patella position might be of particular relevance in avoiding postsurgical AKP. The results of another study suggest that the successful repair of the medial patellofemoral ligament after using a medial parapatellar approach in TKA could reduce the high rate of postoperative AKP[58]. There are many other factors that may be related to AKP after TKA[59-61]. Due to the lack of randomized controlled trials in the exploration of these factors, they were not included in the meta-analysis of this study.

Our meta-analysis had several strengths. First, it resulted in a different conclusion from the 2 reached in earlier meta-analyses[62,63]. In the study by Duan *et al*[62], the results showed that patellar resurfacing had a significant protective effect on AKP with low heterogeneity and robust results. In our analysis, the incidence of AKP was not statistically significant with or without patellar replacement in TKA. A meta-analysis conducted by Xie *et al*[63]. concluded that patellar denervation could significantly relieve AKP during follow-up up to 12 months, but not beyond 12 months. We found that the results of different assessment methods for AKP were different. Second, only randomized controlled trials were included in our study, and the results obtained were more accurate. Third, the studies we included were screened independently by two researchers according to inclusion and exclusion criteria, we used Cochrane Risk of Bias tool to assess publication bias, and these results indicated that publication bias was well controlled. This meta-analysis also had limitations. First, only a small number of trials was analyzed since we only included randomized controlled trials. Second, there is no single definition of AKP, and distinguishing patellofemoral pain syndrome is difficult. Third, the studies included in the meta-analysis applied different techniques and diagnostic criteria to AKP, which could lead to performance bias. Given these limitations, more high-level research is still needed in the future.

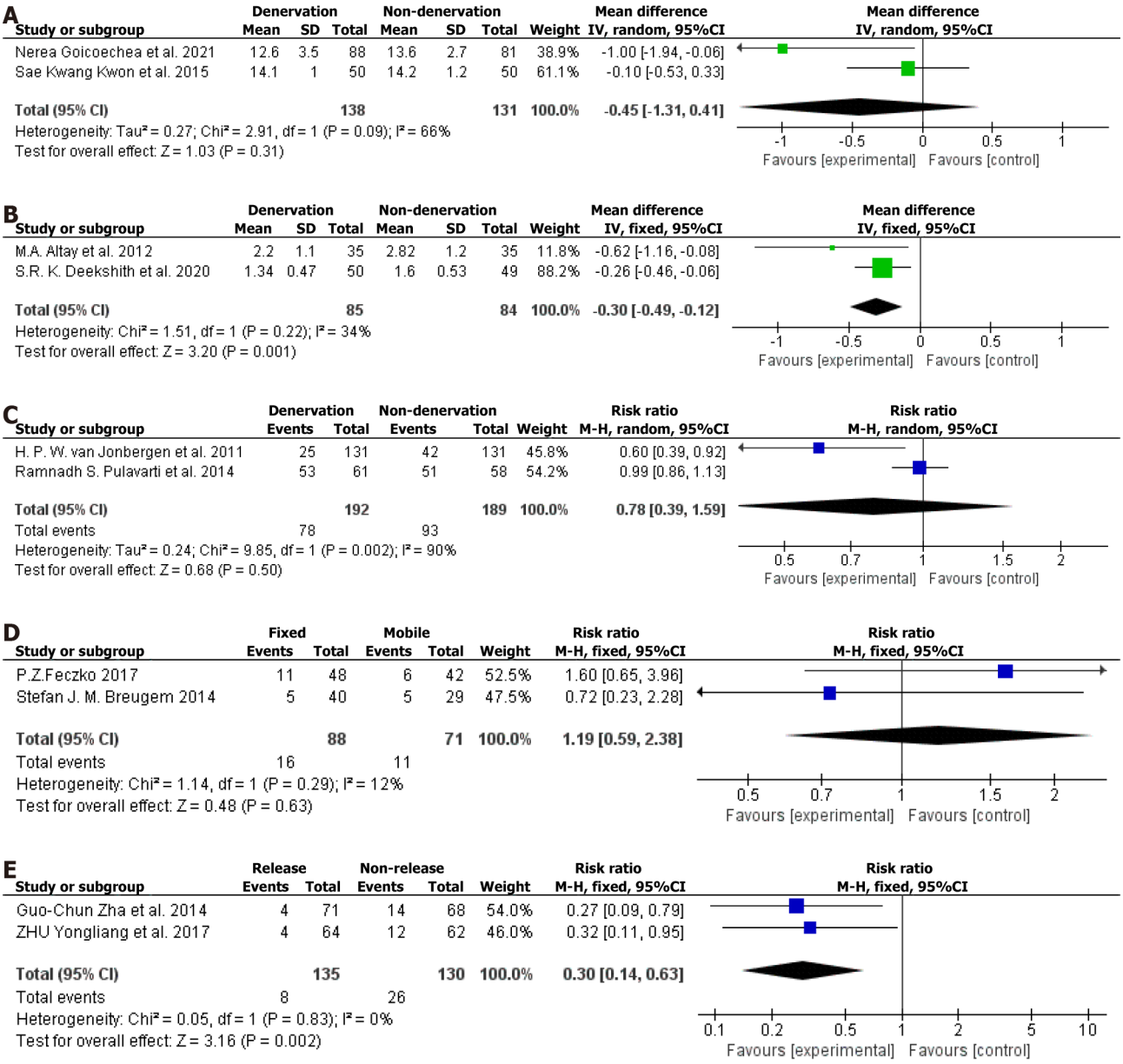


Figure 6 Forest plot. A: Forest plot for patellofemoral Feller score subgroups; B: Forest plot for the visual analog scale score subgroup; C: Forest plot for the subgroup of patients with anterior knee pain; D: Forest plot for using fixed or mobile-bearing total knee arthroplasty; E: Forest plot for lateral retinacular release *vs* non-release. 95%CI: 95% confidence interval.

CONCLUSION

This meta-analysis of currently available evidence indicates that patellar resurfacing, mobile-bearing TKA, and fixed-bearing TKA can't relieve AKP postoperatively after TKA. We do not recommend patellar replacement in TKA unless patellar replacement is necessary. In evaluating the effect of patellar denervation on TKA, the results of different assessment methods for AKP were different. Therefore, future high-level research is warranted for validation. Besides, lateral retinacular release in TKA is recommended because it is safe and result in good clinical outcomes in controlling AKP.

ARTICLE HIGHLIGHTS

Research background

Knee osteoarthritis seriously affects the quality of life of the elderly. Total knee arthroplasty (TKA) is an effective treatment for end-stage osteoarthritis. Anterior knee pain (AKP) after TKA is the main cause of dissatisfaction in the elderly. The management of AKP after total knee replacement is very important.

Research motivation

Although total knee replacement is very successful, postoperative AKP is common and a major cause of patient dissatisfaction. By studying the influencing factors of AKP after TKA, we can improve the quality of life of patients and improve the surgical methods.

Research objectives

To study the influencing factors of AKP after TKA. We identified certain intraoperative factors that may improve the occurrence of postoperative AKP. It provides some help for the management of AKP after TKA.

Research methods

This study is a meta-analysis. We combined some previous randomized controlled trials to get new conclusions. We analyzed the influence of several different factors on AKP after TKA.

Research results

There are few randomized controlled trials for many factors, and more high-quality studies are needed to further explore.

Research conclusions

We found that patellar replacement or not did not affect the incidence of postoperative AKP. We found that different assessment methods for AKP may produce different results.

Research perspectives

More randomized controlled trials are needed for further validation in the future.

FOOTNOTES

Author contributions: Feng H contributed to conceptualization, methodology, investigation, formal analysis, writing-original draft; Feng ML contributed to conceptualization, funding acquisition, resources, supervision, writing-review, and editing; Cheng JB contributed to data curation and writing-original draft; Tao HC contributed to visualization and investigation; Zhang X contributed to visualization and investigation.

Supported by the Capital Fund Project for Clinical Diagnosis and Treatment Technology Research and Translational Application, No. Z201100005520091; and Beijing Traditional Chinese Medicine Science and Technology Development Fund Project, No. JJ-2020-67.

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

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

Country/Territory of origin: China

ORCID number: Ming-Li Feng 0000-0002-4676-4570.

S-Editor: Chen YL
L-Editor: A
P-Editor: Yuan YY

REFERENCES

1 **Hussain SM**, Neilly DW, Baliga S, Patil S, Meek R. Knee osteoarthritis: a review of management options. *Scott Med J* 2016; **61**: 7-16 [PMID: 27330013 DOI: 10.1177/0036933015619588]

2 **Jang S**, Lee K, Ju JH. Recent Updates of Diagnosis, Pathophysiology, and Treatment on Osteoarthritis of the Knee. *Int J Mol Sci* 2021; **22** [PMID: 33807695 DOI: 10.3390/ijms22052619]

3 **Michael JW**, Schlüter-Brust KU, Eysel P. The epidemiology, etiology, diagnosis, and treatment of osteoarthritis of the knee. *Dtsch Arztebl Int* 2010; **107**: 152-162 [PMID: 20305774 DOI: 10.3238/arztebl.2010.0152]

4 **Agarwala S**, Shetty V, Karumuri LK, Vijayvargiya M. Patellar Resurfacing versus Nonresurfacing with Patellaplasty in Total Knee Arthroplasty. *Indian J Orthop* 2018; **52**: 393-398 [PMID: 30078898 DOI: 10.4103/ortho.IJOrtho_512_16]

5 **Gill GS**, Joshi AB. Long-term results of cemented, posterior cruciate ligament-retaining total knee arthroplasty in osteoarthritis. *Am J Knee Surg* 2001; **14**: 209-214 [PMID: 11703032]

6 **Pavone V**, Boettner F, Fickert S, Sculco TP. Total condylar knee arthroplasty: a long-term followup. *Clin Orthop Relat Res* 2001; 18-25 [PMID: 11451118 DOI: 10.1097/00003086-200107000-00005]

7 **Rodriguez JA**, Bhende H, Ranawat CS. Total condylar knee replacement: a 20-year followup study. *Clin Orthop Relat Res* 2001; 10-17 [PMID: 11451106 DOI: 10.1097/00003086-200107000-00004]

8 **Ritter MA**, Faris PM, Keating EM, Meding JB. Postoperative alignment of total knee replacement. Its effect on survival. *Clin Orthop Relat Res* 1994; 153-156 [PMID: 8119010 DOI: 10.1097/00003086-199402000-00021]

9 **Park CN**, White PB, Meftah M, Ranawat AS, Ranawat CS. Diagnostic Algorithm for Residual Pain After Total Knee Arthroplasty. *Orthopedics* 2016; **39**: e246-e252 [PMID: 26811953 DOI: 10.3928/01477447-20160119-06]

10 **Popovic N**, Lemaire R. Anterior knee pain with a posterior-stabilized mobile-bearing knee prosthesis: the effect of femoral component design. *J Arthroplasty* 2003; **18**: 396-400 [PMID: 12820079 DOI: 10.1016/S0883-5403(03)00059-7]

11 **Waters TS**, Bentley G. Patellar resurfacing in total knee arthroplasty. A prospective, randomized study. *J Bone Joint Surg Am* 2003; **85**: 212-217 [PMID: 12571296 DOI: 10.2106/00004623-200302000-00005]

12 **Breugem SJ**, Sierevelt IN, Schafroth MU, Blankevoort L, Schaap GR, van Dijk CN. Less anterior knee pain with a mobile-bearing prosthesis compared with a fixed-bearing prosthesis. *Clin Orthop Relat Res* 2008; **466**: 1959-1965 [PMID: 18523833 DOI: 10.1007/s11999-008-0320-6]

13 **Deroche E**, Batailler C, Swan J, Sappey-Marinier E, Neyret P, Servien E, Lustig S. No difference between resurfaced and non-resurfaced patellae with a modern prosthesis design: a prospective randomized study of 250 total knee arthroplasties. *Knee Surg Sports Traumatol Arthrosc* 2022; **30**: 1025-1038 [PMID: 33661323 DOI: 10.1007/s00167-021-06521-y]

14 **Raaij TMV**, Meij EV, Vries AJ, Raay JJAMV. Patellar Resurfacing Does Not Improve Clinical Outcome in Patients with Symptomatic Tricompartmental Knee Osteoarthritis. An RCT Study of 40 Patients Receiving Primary Cruciate Retaining Total Knee Arthroplasty. *J Knee Surg* 2021; **34**: 1503-1509 [PMID: 32434236 DOI: 10.1055/s-0040-1710369]

15 **Thiengwittayaporn S**, Srungboonmee K, Chiamtrakool B. Resurfacing in a Posterior-Stabilized Total Knee Arthroplasty Reduces Patellar Crepitus Complication: A Randomized, Controlled Trial. *J Arthroplasty* 2019; **34**: 1969-1974 [PMID: 31126775 DOI: 10.1016/j.arth.2019.04.050]

16 **Koh IJ**, Kim MS, Sohn S, Song KY, Choi NY, In Y. Patients undergoing total knee arthroplasty using a contemporary patella-friendly implant are unaware of any differences due to patellar resurfacing. *Knee Surg Sports Traumatol Arthrosc* 2019; **27**: 1156-1164 [PMID: 30132051 DOI: 10.1007/s00167-018-5120-2]

17 **Ha C**, Wang B, Li W, Sun K, Wang D, Li Q. Resurfacing versus not-resurfacing the patella in one-stage bilateral total knee arthroplasty: a prospective randomized clinical trial. *Int Orthop* 2019; **43**: 2519-2527 [PMID: 31227852 DOI: 10.1007/s00264-019-04361-7]

18 **Chawla L**, Bandekar S M, Dixit V, Ambareesh P, Krishnamoorthi A, Mummigatti S. Functional outcome of patellar resurfacing vs non resurfacing in Total Knee Arthoplasty in elderly: a prospective five year follow-up study. *Journal Arthrosc Jt Surg* 2019; **6**: 65-69 [DOI: 10.1016/j.jajs.2018.09.006]

19 **Zou YG**, Chen ZW, Feng ZQ, Xing JS. Factors related to anterior knee pain after total knee arthroplasty. *Nan Fang Yi Ke Da Xue Xue Bao* 2011; **31**: 1428-1430 [PMID: 21868338]

20 **Burnett RS**, Boone JL, Rosenzweig SD, Steger-May K, Barrack RL. Patellar resurfacing compared with nonresurfacing in total knee arthroplasty. A concise follow-up of a randomized trial. *J Bone Joint Surg Am* 2009; **91**: 2562-2567 [PMID: 19884428 DOI: 10.2106/JBJS.H.00109]

21 **Burnett RS**, Boone JL, McCarthy KP, Rosenzweig S, Barrack RL. A prospective randomized clinical trial of patellar resurfacing and nonresurfacing in bilateral TKA. *Clin Orthop Relat Res* 2007; **464**: 65-72 [PMID: 17589364 DOI: 10.1097/BLO.0b013e31812f783b]

22 **Burnett RS**, Haydon CM, Rorabeck CH, Bourne RB. Patella resurfacing versus nonresurfacing in total knee arthroplasty: results of a randomized controlled clinical trial at a minimum of 10 years' followup. *Clin Orthop Relat Res* 2004; 12-25 [PMID: 15534514 DOI: 10.1097/01.blo.0000148594.05443.a3]

23 **Wood DJ**, Smith AJ, Collopy D, White B, Brankov B, Bulsara MK. Patellar resurfacing in total knee arthroplasty: a prospective, randomized trial. *J Bone Joint Surg Am* 2002; **84**: 187-193 [PMID: 11861723 DOI: 10.2106/00004623-200202000-00004]

24 **Barrack RL**, Bertot AJ, Wolfe MW, Waldman DA, Milicic M, Myers L. Patellar resurfacing in total knee arthroplasty. A prospective, randomized, double-blind study with five to seven years of follow-up. *J Bone Joint Surg Am* 2001; **83**: 1376-1381 [PMID: 11568201 DOI: 10.2106/00004623-200109000-00013]

25 **Goicoechea N**, Hinarejos P, Torres-Claramunt R, Leal-Blanquet J, Sánchez-Soler J, Monllau JC. Patellar denervation does not reduce post-operative anterior knee pain after primary total knee arthroplasty with patellar resurfacing. *Knee Surg Sports Traumatol Arthrosc* 2021; **29**: 3346-3351 [PMID: 32761276 DOI: 10.1007/s00167-020-06164-5]

26 **Kwon SK**, Nguku L, Han CD, Koh YG, Kim DW, Park KK. Is Electrocautery of Patella Useful in Patella Non-Resurfacing Total Knee Arthroplasty?: A Prospective Randomized Controlled Study. *J Arthroplasty* 2015; **30**: 2125-2127 [PMID: 26100474 DOI: 10.1016/j.arth.2015.05.057]

27 **Altay MA**, Ertürk C, Altay N, Akmeşe R, Işıkan UE. Patellar denervation in total knee arthroplasty without patellar resurfacing: a prospective, randomized controlled study. *Orthop Traumatol Surg Res* 2012; **98**: 421-425 [PMID: 22552314 DOI: 10.1016/j.otsr.2012.03.002]

28 **Pulavarti RS**, Raut VV, McLauchlan GJ. Patella denervation in primary total knee arthroplasty - a randomized controlled trial with 2 years of follow-up. *J Arthroplasty* 2014; **29**: 977-981 [PMID: 24291230 DOI: 10.1016/j.arth.2013.10.017]

29 **van Jonbergen HP**, Scholtes VA, van Kampen A, Poolman RW. A randomised, controlled trial of circumpatellar electrocautery in total knee replacement without patellar resurfacing. *J Bone Joint Surg Br* 2011; **93**: 1054-1059 [PMID: 21768628 DOI: 10.1302/0301-620X.93B8.26560]

30 **Deekshith SRK**, Reddy KJ, Raviteja R. RETRACTED ARTICLE: Patelloplasty in total knee arthroplasty with circumpatellar denervation versus without denervation - a randomized prospective study. *Arthroplasty* 2020; **2**: 26 [PMID: 35236444 DOI: 10.1186/s42836-020-00044-6]

31 **Feczko PZ**, Jutten LM, van Steyn MJ, Deckers P, Emans PJ, Arts JJ. Comparison of fixed and mobile-bearing total knee arthroplasty in terms of patellofemoral pain and function: a prospective, randomised, controlled trial. *BMC Musculoskelet Disord* 2017; **18**: 279 [PMID: 28662692 DOI: 10.1186/s12891-017-1635-9]

32 **Breugem SJ**, van Ooij B, Haverkamp D, Sierevelt IN, van Dijk CN. No difference in anterior knee pain between a fixed and a mobile posterior stabilized total knee arthroplasty after 7.9 years. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 509-516 [PMID: 23124601 DOI: 10.1007/s00167-012-2281-2]

33 **Zhu Y**, Li Y, Yan C, Du X, Xing Z, Chen P. Influence of lateral retinacular release on anterior knee pain following total knee arthroplasty. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 2017; **31**: 541-546 [PMID: 29798542 DOI: 10.7507/1002-1892.201701052]

34 **Zha GC**, Sun JY, Dong SJ. Less anterior knee pain with a routine lateral release in total knee arthroplasty without patellar resurfacing: a

prospective, randomized study. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 517-525 [PMID: 24288077 DOI: 10.1007/s00167-013-2789-0]
35 **Yuan F**, Sun Z, Wang H, Chen Y, Yu J. Clinical and radiologic outcomes of two patellar resection techniques during total knee arthroplasty: a prospective randomized controlled study. *Int Orthop* 2019; **43**: 2293-2301 [PMID: 30539221 DOI: 10.1007/s00264-018-4264-5]
36 **Fahmy M**, Seifeldin AF. The impact of infrapatellar fat pad excision vs preservation after total knee replacement on anterior knee pain, functional outcome and patellar height: Randomized controlled trial. *J Orthop, Trau and Rehabil* 2022; **29** [DOI: 10.1177/22104917221085723]
37 **Adravanti P**, Tecame A, de Girolamo L, Ampollini A, Papalia R. Patella Resurfacing in Total Knee Arthroplasty: A Series of 1280 Patients at Midterm Follow-Up. *J Arthroplasty* 2018; **33**: 696-699 [PMID: 29074323 DOI: 10.1016/j.arth.2017.09.050]
38 **Longo UG**, Ciuffreda M, Mannering N, D'Andrea V, Cimmino M, Denaro V. Patellar Resurfacing in Total Knee Arthroplasty: Systematic Review and Meta-Analysis. *J Arthroplasty* 2018; **33**: 620-632 [PMID: 29032861 DOI: 10.1016/j.arth.2017.08.041]
39 **Maney AJ**, Koh CK, Frampton CM, Young SW. Usually, Selectively, or Rarely Resurfacing the Patella During Primary Total Knee Arthroplasty: Determining the Best Strategy. *J Bone Joint Surg Am* 2019; **101**: 412-420 [PMID: 30845035 DOI: 10.2106/JBJS.18.00389]
40 **Migliorini F**, Eschweiler J, Niewiera M, El Mansy Y, Tingart M, Rath B. Better outcomes with patellar resurfacing during primary total knee arthroplasty: a meta-analysis study. *Arch Orthop Trauma Surg* 2019; **139**: 1445-1454 [PMID: 31367842 DOI: 10.1007/s00402-019-03246-z]
41 **Allen W**, Eichinger J, Friedman R. Resurfaced versus Non-Resurfaced Patella in Total Knee Arthroplasty. *J Knee Surg* 2019; **32**: 611-615 [PMID: 30812045 DOI: 10.1055/s-0039-1681077]
42 **Grassi A**, Compagnoni R, Ferrua P, Zaffagnini S, Berruto M, Samuelsson K, Svantesson E, Randelli P. Patellar resurfacing versus patellar retention in primary total knee arthroplasty: a systematic review of overlapping meta-analyses. *Knee Surg Sports Traumatol Arthrosc* 2018; **26**: 3206-3218 [PMID: 29335747 DOI: 10.1007/s00167-018-4831-8]
43 **Maculé F**, Sastre S, Lasurt S, Sala P, Segur JM, Mallofré C. Hoffa's fat pad resection in total knee arthroplasty. *Acta Orthop Belg* 2005; **71**: 714-717 [PMID: 16459863]
44 **Lehner B**, Koeck FX, Capellino S, Schubert TE, Hofbauer R, Straub RH. Preponderance of sensory versus sympathetic nerve fibers and increased cellularity in the infrapatellar fat pad in anterior knee pain patients after primary arthroplasty. *J Orthop Res* 2008; **26**: 342-350 [PMID: 17902175 DOI: 10.1002/jor.20498]
45 **Wojtys EM**, Beaman DN, Glover RA, Janda D. Innervation of the human knee joint by substance-P fibers. *Arthroscopy* 1990; **6**: 254-263 [PMID: 1702291 DOI: 10.1016/0749-8063(90)90054-H]
46 **Maralcan G**, Kuru I, Issi S, Esmer AF, Tekdemir I, Evcik D. The innervation of patella: anatomical and clinical study. *Surg Radiol Anat* 2005; **27**: 331-335 [PMID: 16172870 DOI: 10.1007/s00276-005-0334-7]
47 **Vega J**, Golanó P, Pérez-Carro L. Electrosurgical arthroscopic patellar denervation. *Arthroscopy* 2006; **22**: 1028.e1-1028.e3 [PMID: 16952734 DOI: 10.1016/j.arthro.2006.01.023]
48 **Haas BD**, Komistek RD, Stiehl JB, Anderson DT, Northcut EJ. Kinematic comparison of posterior cruciate sacrifice versus substitution in a mobile bearing total knee arthroplasty. *J Arthroplasty* 2002; **17**: 685-692 [PMID: 12216020 DOI: 10.1054/arth.2002.33550]
49 **Pagnano MW**, Trousdale RT, Stuart MJ, Hanssen AD, Jacofsky DJ. Rotating platform knees did not improve patellar tracking: a prospective, randomized study of 240 primary total knee arthroplasties. *Clin Orthop Relat Res* 2004; 221-227 [PMID: 15534546 DOI: 10.1097/01.blo.0000148892.31464.81]
50 **Aglietti P**, Baldini A, Buzzi R, Lup D, De Luca L. Comparison of mobile-bearing and fixed-bearing total knee arthroplasty: a prospective randomized study. *J Arthroplasty* 2005; **20**: 145-153 [PMID: 15902852 DOI: 10.1016/j.arth.2004.09.032]
51 **Lee GW**, Lee SM, Jang SJ, Son JH. The efficacy of patellar decompression for improving anterior knee pain following total knee arthroplasty without patellar resurfacing. *Arch Orthop Trauma Surg* 2013; **133**: 561-567 [PMID: 23435648 DOI: 10.1007/s00402-013-1702-0]
52 **Wilson NA**, Press JM, Koh JL, Hendrix RW, Zhang LQ. In vivo noninvasive evaluation of abnormal patellar tracking during squatting in patients with patellofemoral pain. *J Bone Joint Surg Am* 2009; **91**: 558-566 [PMID: 19255215 DOI: 10.2106/JBJS.G.00572]
53 **Rand JA**. Patellar resurfacing in total knee arthroplasty. *Clin Orthop Relat Res* 1990; 110-117 [PMID: 2225612]
54 **Fu C**, Wai J, Lee E, Myden C, Batuyong E, Hutchison CR, Anglin C. Computer-assisted patellar resection for total knee arthroplasty. *Comput Aided Surg* 2012; **17**: 21-28 [PMID: 22145788 DOI: 10.3109/10929088.2011.638399]
55 **Pagnano MW**, Trousdale RT. Asymmetric patella resurfacing in total knee arthroplasty. *Am J Knee Surg* 2000; **13**: 228-233 [PMID: 11269543]
56 **Yao B**, Samuel LT, Acuña AJ, Faour M, Roth A, Kamath AF, Mont MA. Infrapatellar Fat Pad Resection or Preservation during Total Knee Arthroplasty: A Systematic Review. *J Knee Surg* 2021; **34**: 415-421 [PMID: 31505700 DOI: 10.1055/s-0039-1696692]
57 **Laubach M**, Hellmann JT, Dirrichs T, Gatz M, Quack V, Tingart M, Betsch M. Anterior knee pain after total knee arthroplasty: A multifactorial analysis. *J Orthop Surg (Hong Kong)* 2020; **28**: 2309499020918947 [PMID: 32338135 DOI: 10.1177/2309499020918947]
58 **Keshmiri A**, Dotzauer F, Baier C, Maderbacher G, Grifka J, Sendtner E. Stability of capsule closure and postoperative anterior knee pain after medial parapatellar approach in TKA. *Arch Orthop Trauma Surg* 2017; **137**: 1019-1024 [PMID: 28493040 DOI: 10.1007/s00402-017-2706-y]
59 **Aliyev O**, Sarıkaş M, Uçan V, Uzer G, Tuncay İ, Yıldız F. Sagittal Patellar Offset Ratio Can Be a Predictor of Anterior Knee Pain after Primary Total Knee Arthroplasty without Patella Resurfacing. *Z Orthop Unfall* 2022 [PMID: 35654392 DOI: 10.1055/a-1823-1463]
60 **Antinolfi P**, Manfreda F, Ricchiuto I, Petruccelli R, Caraffa A. Role of positioning of femoral component in the anterior-posterior direction on postoperative anterior pain in TKA. *Eur J Orthop Surg Traumatol* 2020; **30**: 1049-1056 [PMID: 32277295 DOI: 10.1007/s00590-020-02666-7]
61 **Ertürk C**, Altay MA, Işikan UE. Patelloplasty with patellar decompression to relieve anterior knee pain in total knee arthroplasty. *Acta Orthop Traumatol Turc* 2011; **45**: 425-430 [PMID: 22245819 DOI: 10.3944/AOTT.2011.2590]
62 **Duan G**, Liu C, Lin W, Shao J, Fu K, Niu Y, Wang F. Different Factors Conduct Anterior Knee Pain Following Primary Total Knee Arthroplasty: A Systematic Review and Meta-Analysis. *J Arthroplasty* 2018; **33**: 1962-1971.e3 [PMID: 29398258 DOI: 10.1016/j.arth.2017.12.024]
63 **Xie X**, Pei F, Huang Z, Tan Z, Yang Z, Kang P. Does patellar denervation reduce post-operative anterior knee pain after total knee arthroplasty? *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 1808-1815 [PMID: 25758982 DOI: 10.1007/s00167-015-3566-z]

World Journal of Orthopedics

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

World J Orthop 2024 February 18; 15(2): 192-200

DOI: 10.5312/wjo.v15.i2.192

ISSN 2218-5836 (online)

LETTER TO THE EDITOR

Adenylate cyclase activates the cAMP signalling pathway to enhance platelet-rich plasma-treated Achilles tendon disease, a theoretical bioinformatics-based study

Jing-Yi Sun, Cai Li, Feng-Ying Du

Specialty type: Orthopedics

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Nezhady MAM, Iran

Received: October 26, 2023
Peer-review started: October 26, 2023
First decision: December 12, 2023
Revised: December 29, 2023
Accepted: January 16, 2024
Article in press: January 16, 2024
Published online: February 18, 2024

Jing-Yi Sun, Cai Li, College of Basic Medical Science, Qilu Medical University, Zibo 255300, Shandong Province, China

Feng-Ying Du, Department of Gastroenterological Surgery, Shandong Provincial Hospital of Shandong First Medical University, Jinan 250021, Shandong Province, China

Corresponding author: Feng-Ying Du, MD, Doctor, Department of Gastroenterological Surgery, Shandong Provincial Hospital of Shandong First Medical University, No. 324 Jingwu Road, Jinan 250021, Shandong Province, China. sdudfy@126.com

Abstract

The effectiveness of platelet-rich plasma (PRP) for the treatment of Achilles tendon disorders still needs to be evaluated through a series of prospective studies, but genomic analysis can reveal the existence of complementary PRP treatment options. Based on the 96 platelet activation-related genes in the Kyoto Encyclopedia of Genes and Genomes (KEGG) database, we performed Gene Ontology functional enrichment analysis and KEGG enrichment analysis, pathway correlation analysis, and enrichment mapping to determine the enrichment results of the gene set enrichment analysis and found that the cAMP signalling pathway may be the key to enhancing the effectiveness of PRP treatment. The cAMP signalling pathway interacts with the Rap1 signalling pathway and cGMP-PKG signalling pathway to mediate the entire pathophy-siological process of Achilles tendon disease. Moreover, ADCY1-9 may be the key to the activation of the cAMP signalling network. Further based on the data in the Gene Expression Omnibus database, it was found that ADCY4 and ADCY7 may be the players that play a major role, associated with the STAT4-ADCY4-LAMA5 axis and the GRbeta-ADCY7-SEMA3C axis, which is expected to be a complementary target for enhancing the efficacy of PRP in the treatment of Achilles tendon disease.

Key Words: Platelet-rich plasma; Achilles tendon disease; cAMP; Adenylate cyclase; Complementary target

Core Tip: The cAMP signalling pathway may be the key to enhancing the effectiveness of platelet-rich plasma (PRP) in the treatment of Achilles tendon disease. ADCY1-9 may be the key to activating the cAMP signalling network and is expected to be a complementary target for enhancing the effectiveness of PRP in the treatment of Achilles tendon disease.

Citation: Sun JY, Li C, Du FY. Adenylate cyclase activates the cAMP signalling pathway to enhance platelet-rich plasma-treated Achilles tendon disease, a theoretical bioinformatics-based study. *World J Orthop* 2024; 15(2): 192-200
URL: https://www.wjgnet.com/2218-5836/full/v15/i2/192.htm
DOI: https://dx.doi.org/10.5312/wjo.v15.i2.192

TO THE EDITOR

We read with great interest the study by Huang *et al*[1], which reported that platelet-rich plasma (PRP) injections alone had no significant efficacy on patients who suffered Achilles tendon rupture or Achilles tendinopathy and that PRP alone improved ankle mobility after 12 months of treatment. Moreover, Dan's team suggested that the method of PRP preparation and the active ingredient, frequency of injection, injection dose, and injection site may be factors influencing the uncertainty of clinical outcomes.

We agree with the authors that the assessment of the effectiveness of PRP in the treatment of Achilles tendinopathy needs to be advanced by a series of prospective studies, which require blinding, randomization, and control of variables. In theory, the pathophysiologic process of Achilles tendinopathy is associated with localized inflammation of the Achilles tendon, with further degenerative lesions leading to complete Achilles tendon rupture[2,3]. PRP, obtained by centrifugation of whole blood, allows the inclusion of supraphysiologic concentrations of growth factors. The release of these growth factors is effectively activated, leading to increased regeneration and healing at the site of injection[4,5]. Moreover, PRP also treats tendon tissue by inducing type I collagen and glycosaminoglycan deposition[5]. The central key to these beneficial biological processes in the treatment of Achilles tendon disease is platelet activation, and the inability to effectively activate platelets may be one of the reasons why PRP is so ineffective in treating this disease. As the field of genomics has developed and transformed, it has allowed us to more accurately understand the keys to complex biological processes, facilitating the development of more precise and effective therapeutic regimens. With respect to the relevant genes in the "map04611: Platelet activation" (https://www.genome.jp/entry/pathway+map04611) pathway in the Kyoto Encyclopedia of Genes and Genomes (KEGG) database, we used bioinformatics analysis to provide a theoretical basis for the potential activation of platelets in PRP.

Gene ontology (GO) annotation of 96 genes in the "platelet activation" signalling pathways using the "enrichGO" function of the "clusterProfiler" R package[6] revealed that, under the classification of biological processes, in addition to platelet activation-related pathways (Figure 1A), the "wound healing", "homotypic cell-cell adhesion" and "cAMP biosynthetic process" pathways were significantly enriched. In terms of cellular components, cell membrane-related pathways were more enriched, which may be a prerequisite for the activation of "cell-substrate junction" pathways. In terms of molecular function, the phosphatidylinositol-related pathway was activated, which may be a preparation for "scaffold protein binding". Furthermore, using the "pairwise_termsim" function of the "enrichplot" R package to calculate the correlation between the enriched GO pathways and the enrichment map for the enrichment results of the gene set enrichment analysis by the "emapplot" function revealed that "platelet activation" was correlated with "wound healing", "vascular process in circulatory system", "cell-matrix-substrate adhesion", and other biological functions closely related to Achilles tendon recovery (Figure 1B). In addition, cAMP biosynthesis and metabolism appear to constitute another functional subgroup resulting from platelet activation. Plotting the Gene-Concept Network using the "cnetplot" function revealed that none of the pathways, such as "wound healing" and "cAMP biosynthetic process", had common genes but were associated with "regulation of body fluid levels" (Figure 1C). However, in the KEGG database, all 96 genes were identified as related to "platelet activation". This result suggested that the specific role of cAMP-related functions in platelet activation is unclear. The cAMP signalling pathway, one of the well-known is the protein kinase A (PKA) system, is a type of cyclic nucleotide system that regulates key physiological processes such as nodal metabolism, secretion, calcium homeostasis, muscle contraction, cell fate and gene transcription[7]. These processes are closely related to the local inflammatory response and immune response of the Achilles tendon, the metabolism and differentiation of fibroblasts, and the senescence and apoptosis of fibroblasts[2,8,9]. Overall, these physiological conditions are known to characterize Achilles tendon inflammation, Achilles tendon recovery, and degenerative Achilles tendon disease.

The "enrichKEGG" function was used to analyse the KEGG pathways associated with these 96 platelet activation-related genes (Figure 2A), and the Rap1, cGMP-PKG, and cAMP signalling pathways were found to be enriched. This further verified the results of the GO analysis, suggesting that cAMP-related functions might be involved in the alteration of low platelet activation. The enrichment map generated by the "emapplot" function shown in Figure 2B reveals that platelet activation and the signalling pathways of Rap1, cGMP-PKG, and cAMP are strongly associated and do not exist in relatively large subgroups of the pathways. The Rap1 signalling pathway is involved mainly in the regulation of cell adhesion and cell junctions, as well as the processes of cell migration, polarization, proliferation, and survival[10,11]. In Achilles tendon disease, regulation of the Rap1 signalling pathway may involve aspects of fibroblast metabolism, differentiation, and repair, thereby affecting Achilles tendon development and repair. The second messenger cAMP stimulates Epac1, a Rap guanylate exchange factor. cAMP activates Epac1 migration to the plasma membrane, activates Epac-Rap1

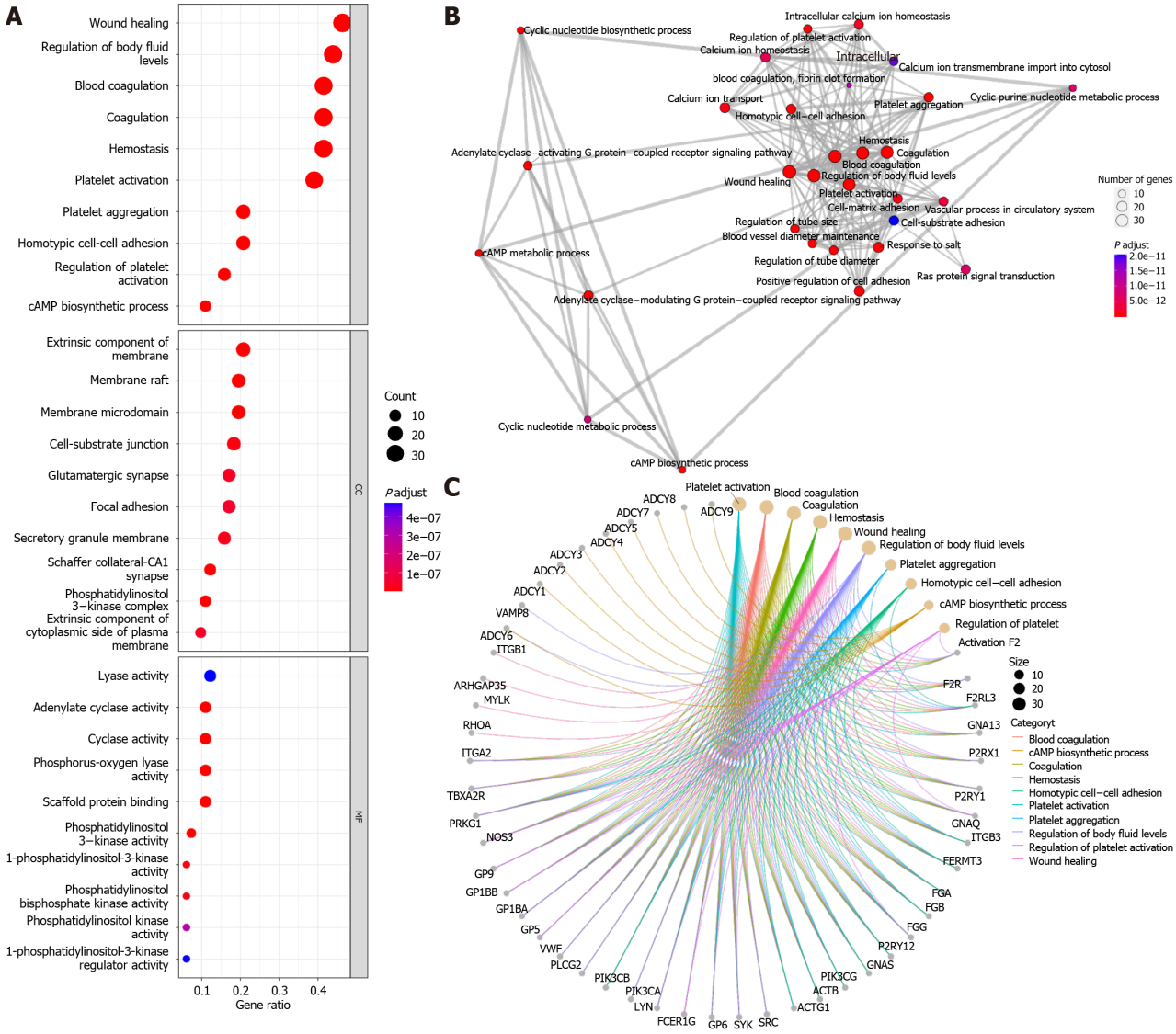


Figure 1 Gene ontology enrichment analysis of 96 platelet activation-associated genes. A: Bubble plot of gene ontology (GO) functional enrichment analysis; B: Association network between GO terms that were enriched; C: Enrichment maps between GO terms and genes.

signalling, and enhances integrin-mediated cell adhesion[12,13]. The regulation of the cGMP-PKG signalling pathway may involve inflammatory responses, immune responses, and apoptosis, thus affecting the pathogenesis and pathological processes of diseases such as Achilles tendonitis, Achilles tendon rupture, and Achilles tendon degeneration. The cross-interaction between ATP and GTP also leads to the interaction of cGMP with cAMP, which are also second messengers [14]. Gene-concept network analysis revealed that ADCY1-9 were common genes for platelet activation, Rap1, cGMP-PKG, cAMP, and cytokine activation (Figure 2C), which was also consistent with the results of the GO analysis (Figure 1C). These results suggest that ADCY1-9 may be key to the cAMP pathway and platelet activation pathway and are closely related to a large functional subgroup of the GO pathway beyond "platelet activation". Interaction network analysis of these 96 platelet-related genes using the STRING database (https://string-db.org/) revealed that ADCY1-9 may be the upstream genes of AKT1 (Figure 3), which may be the key to ameliorating the inability of platelets to be activated efficiently.

The adenylate cyclase (ADCY) family of genes encodes a membrane-associated enzyme that catalyses the formation of cAMP[15], which is in complete agreement with the results of GO and KEGG enrichment analyses. We can further speculate that if activated, ADCY1-9 stimulate the cAMP signalling pathway, which in turn leads to the upregulation of the Rap1 and cGMP-PKG signalling pathways, ultimately completing the global mobilization of the "platelet activation" pathway. ADCY1-9 can be used as an adjunctive target for RPR therapy to enhance its effectiveness in treating Achilles tendon disorders, such as Achilles tendon rupture, Achilles tendonitis, and degenerative Achilles tendon diseases.

Further, we searched the Gene Expression Omnibus (GEO) database for data on healthy human platelets sequenced in the GSE178158 cohort[16], and 65 samples from the GSE178158 cohort were included, with 100 healthy human whole blood samples from the GSE134080 cohort used as controls[17]. Comparison of the differences in the expression levels of ADCY1-9 in platelets and whole blood revealed (Figure 4A) that ADCY2, 6, and 8 were highly expressed in platelets, while ADCY4, 5, 7, and 9 were lowly expressed in platelets, and the rest did not differ. Cartilage tissue sequencing data from the GEO database for osteoarthritic diseases were also obtained, which included 40 osteoarthritic disease samples

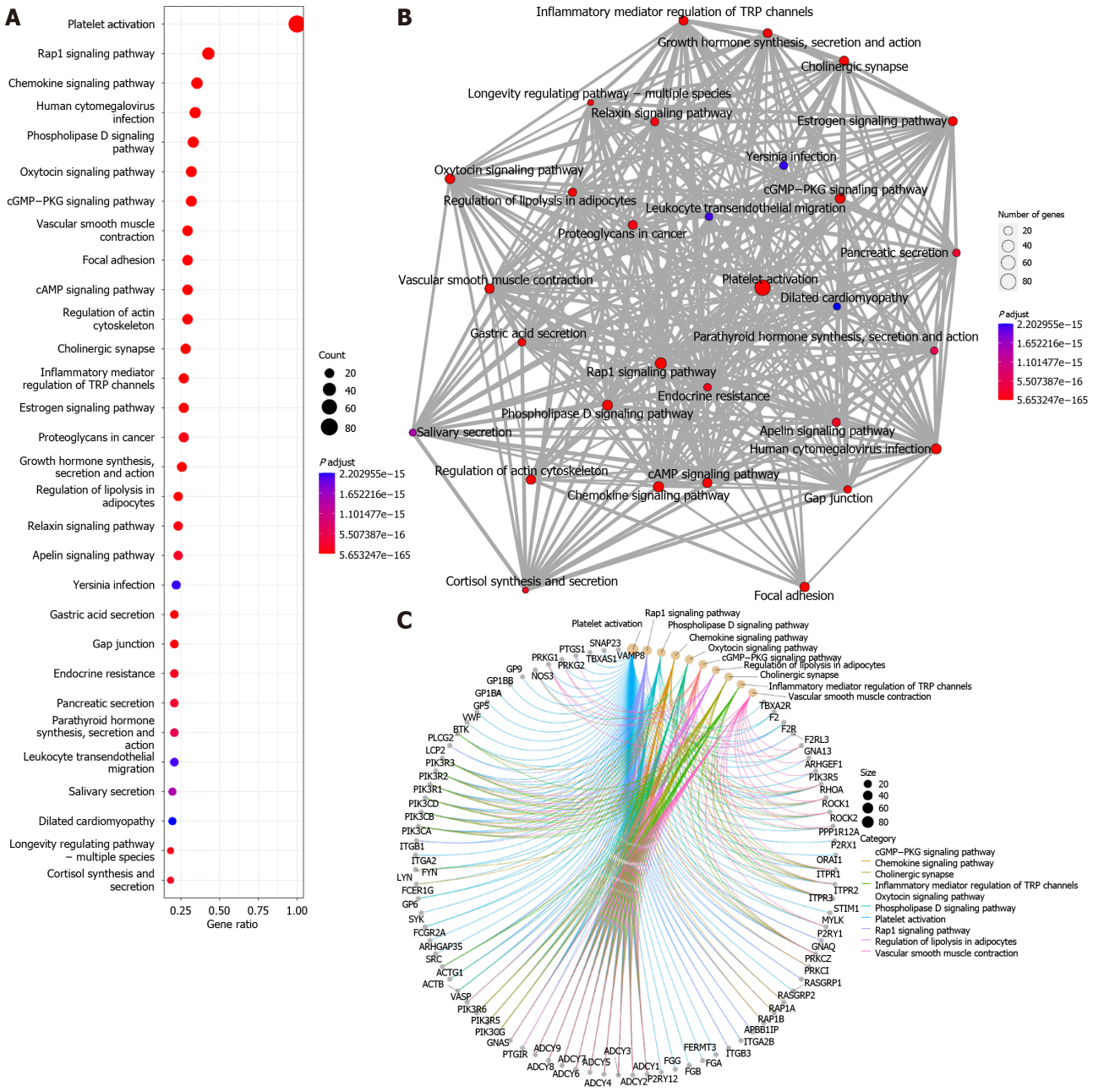


Figure 2 Kyoto Encyclopedia of Genes and Genomes enrichment analysis of 96 platelet activation-associated genes. A: Bubble plot of the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis; B: Association network between KEGG pathways that were enriched; C: Enrichment maps between KEGG signalling pathways and genes.

and 10 healthy cartilage tissue samples from the GSE51588 cohort[18], and 20 osteoarthritic disease samples and 18 healthy cartilage tissue samples from the GSE114007 cohort were also included[19]. Comparative analysis revealed (Figure 4B and 4C) that ADCY1, 4, and 7 were all highly expressed in osteoarthritic disease samples, while ADCY3 was all highly expressed in healthy cartilage tissue samples. Correlation analysis of ADCY 1-9 expression levels and clustering by the ward.D2 method (Figure 4D) showed that the expression level of adenylate cyclase was synergistic in both blood samples and cartilage tissue samples, which was mainly represented by ADCY 4 and ADCY 7. The low expression of ADCY 4 and ADCY 7 in platelets is consistent with healthy cartilage tissue, and they may be the Achilles heel of osteoarthritic diseases. The promoter sequences of ADCY4 (chr14: 24, 318, 359-24, 335, 071) and ADCY7 (chr16: 50, 266, 551-50, 318, 135) were searched in the UCSC database (https://genome.ucsc.edu/), and the 2000 nt region upstream of the transcriptional start site was set as the selected promoter region. The obtained sequences were entered into the PROMO database (https://alggen.lsi.upc.es/cgi-bin/promo_v3/promo/promoinit.cgi?dirDB=TF_8.3)[20,21], with species selection of Homo sapiens and tolerance set at 5% to retrieve site-bound transcription factors. As shown in Figure 4E and F, 48 transcription factors were retrieved for ADCY4, whereas 56 were retrieved for ADCY7. Differential expression analysis in platelets *vs* whole blood and correlation analysis in the osteoarthritic disease cohort revealed (Figure 4G) that STAT4 is either the upstream transcription factor of ADCY4, while the upstream transcription factor of ADCY7 may be GR-beta. By The Human Protein Atlas (https://www.proteinatlas.org/) searching which proteins could

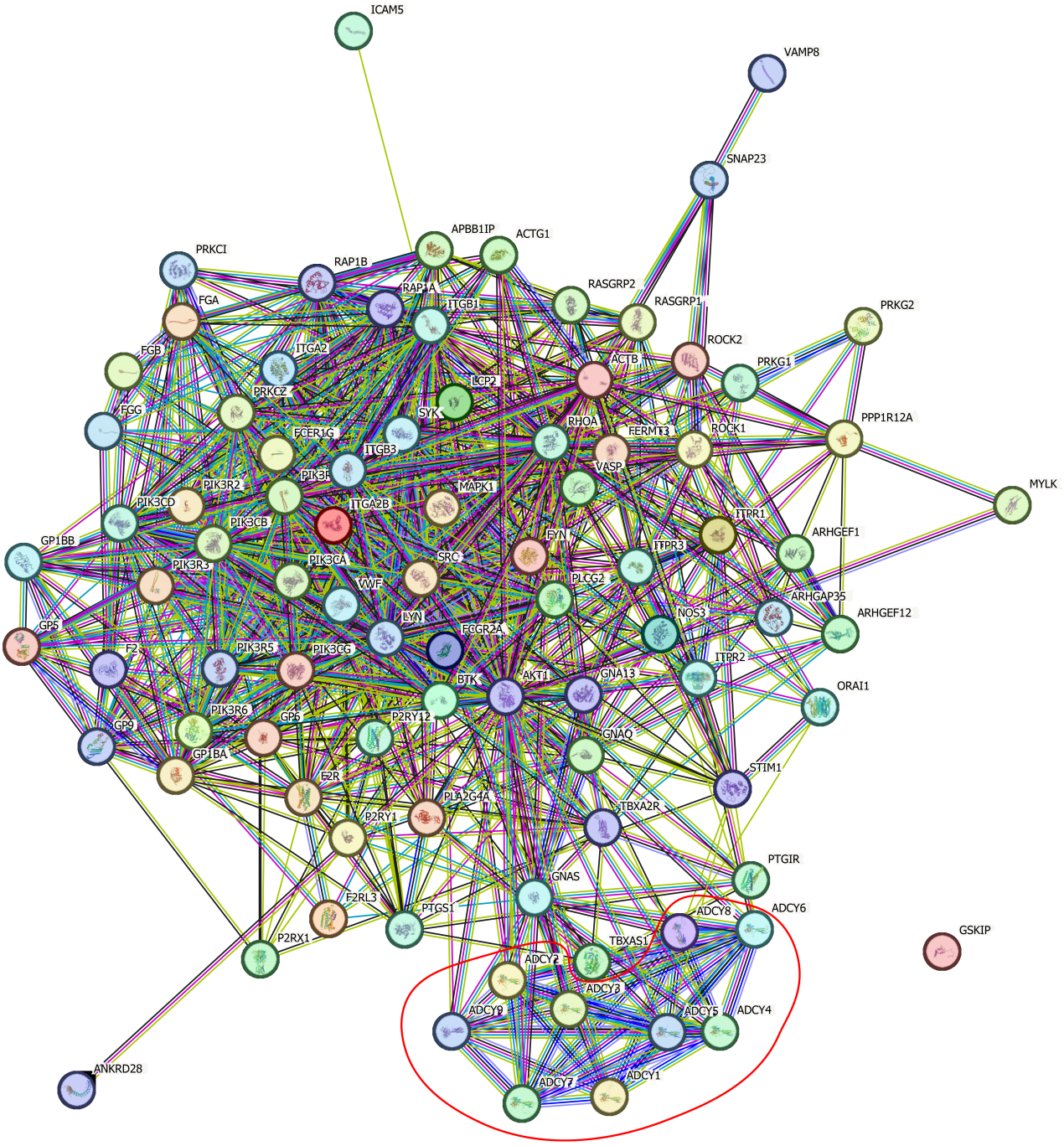
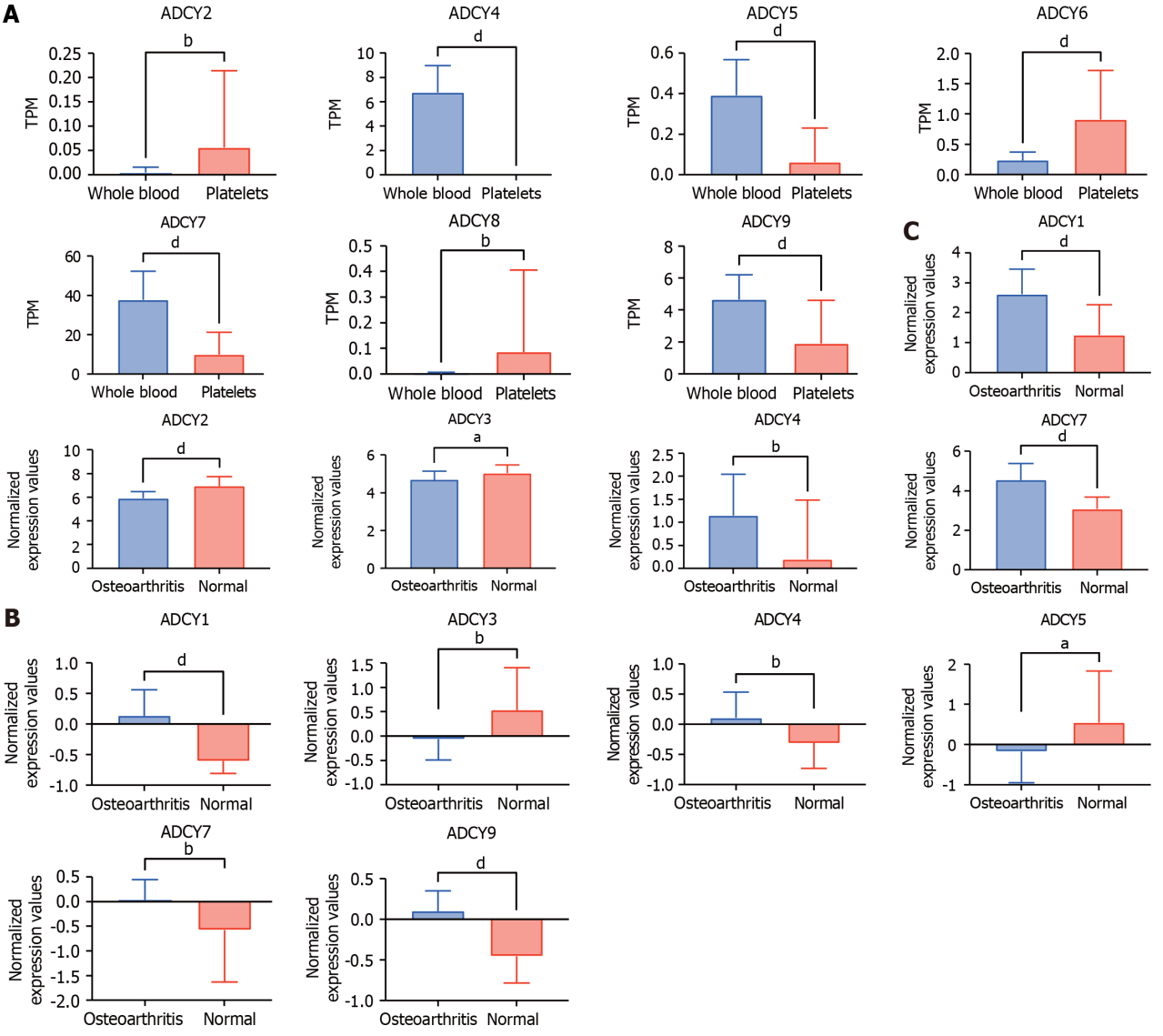
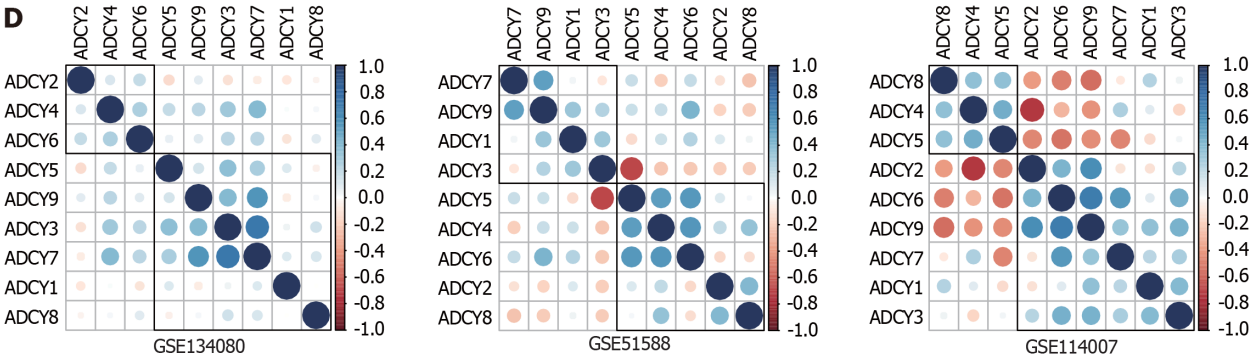


Figure 3 Protein-protein interaction network of 96 platelet activation-related genes.

be secreted and analyzing the correlation of all secreted proteins (Figure 4H)[22], we concluded that ADCY 4 may cause increased secretion of LAMA 5, while ADCY 7 caused SEMA3C. Surprisingly, as shown in Figure 4I, both LAMA 5 and SEMA3C were highly expressed in the osteoarthritic disease samples. These results prove that the STAT 4-ADCY 4-LAMA 5 axis and the GRbeta-ADCY 7-SEMA3C axis may regulate the occurrence in osteoarthritic diseases.

Based on the above bioinformatics analysis, we speculate that the role of adenylate cyclase in osteoarthritic disease is very important, and the poor treatment effect of Achilles tendon disease may be that the cAMP signaling pathway is not effectively activated, and the key point may lie in ADCY 4 and ADCY 7. Both STAT 4-ADCY 4-LAMA 5 axis and GRbeta-ADCY 7-SEMA3C axis are suspected to mediate the occurrence of osteoarthritic disease, and the relevant treatment options can be explored as a theoretical basis.





E

Factors predicted within a dissimilarity margin less or equal than 5% for ADCY4:

0 TBP [T00794]	1 GR-beta [T01920]	2 TFII-I [T00824]	3 C/EBPbeta [T00581]	4 FOXP3 [T04280]	5 GR-alpha [T00337]	6 AP-2alphaA [T00035]	7 PXR-1:RXR-alpha [T05671]
8 RXR-alpha [T01345]	9 YY1 [T00915]	10 STAT4 [T01577]	11 c-Ets-1 [T00112]	12 GATA-1 [T00306]	13 TFIID [T00820]	14 IRF-1 [T00423]	15 SRY [T00997]
16 NF-AT1 [T01948]	17 GR [T05076]	18 RAR-beta [T00721]	19 HNF-1A [T00368]	20 c-Myb [T00137]	21 Pax-5 [T00070]	22 p53 [T00671]	23 NF-1 [T00539]
24 Elk-1 [T00250]	25 ER-alpha [T00261]	26 AP-1 [T00029]	27 c-Jun [T00133]	28 c-Fos [T00123]	29 c-Ets-2 [T00113]	30 ENKTF-1 [T00255]	31 XBP-1 [T00902]
32 PR B [T00696]	33 PR A [T01661]	34 NFI/CTF [T00094]	35 ETF [T00270]	36 Sp1 [T00759]	37 T3R-beta1 [T00851]	38 C/EBPalpha [T00105]	39 NF-Y [T00150]
40 AR [T00040]	41 GCF [T00320]	42 VDR [T00885]	43 IRF-2 [T01491]	44 GATA-2 [T00308]	45 E2F-1 [T01542]	46 LEF-1 [T02905]	47 MAZ [T00490]

F

Factors predicted within a dissimilarity margin less or equal than 5% for ADCY7:

0 YY1 [T00915]	1 TFII-I [T00824]	2 STAT4 [T01577]	3 C/EBPbeta [T00581]	4 FOXP3 [T04280]	5 PR B [T00696]	6 PR A [T01661]	7 GR-beta [T01920]
8 GATA-1 [T00306]	9 MITF [T01553]	10 C/EBPalpha [T00105]	11 NF-Y [T00150]	12 LEF-1 [T02905]	13 NF-1 [T00539]	14 p53 [T00671]	15 AP-2alphaA [T00035]
16 IRF-2 [T01491]	17 GR-alpha [T00337]	18 STAT5A [T04683]	19 Sp1 [T00759]	20 c-Jun [T00133]	21 c-Ets-1 [T00112]	22 NF-kappaB1 [T00593]	23 RXR-alpha [T01345]
24 XBP-1 [T00902]	25 USF2 [T00878]	26 T3R-beta1 [T00851]	27 ER-alpha [T00261]	28 c-Ets-2 [T00113]	29 Pax-5 [T00070]	30 IRF-1 [T00423]	31 TCF-4 [T02918]
32 TFIID [T00820]	33 HNF-3alpha [T02512]	34 NF-AT1 [T01948]	35 STAT1beta [T01573]	36 Elk-1 [T00250]	37 MAZ [T00490]	38 HOXD9 [T01424]	39 HOXD10 [T01425]
40 GR [T05076]	41 ETF [T00270]	42 GCF [T00320]	43 GATA-2 [T00308]	44 COUP-TF1 [T00149]	45 RAR-beta [T00721]	46 ENKTF-1 [T00255]	47 PEA3 [T00685]
48 AR [T00040]	49 EBF [T05427]	50 PPAR-alpha:RXR-alpha [T05221]	51 TBP [T00794]	52 PITX2 [T02413]	53 Ik-1 [T02702]	54 PXR-1:RXR-alpha [T05671]	55 SRY [T00997]

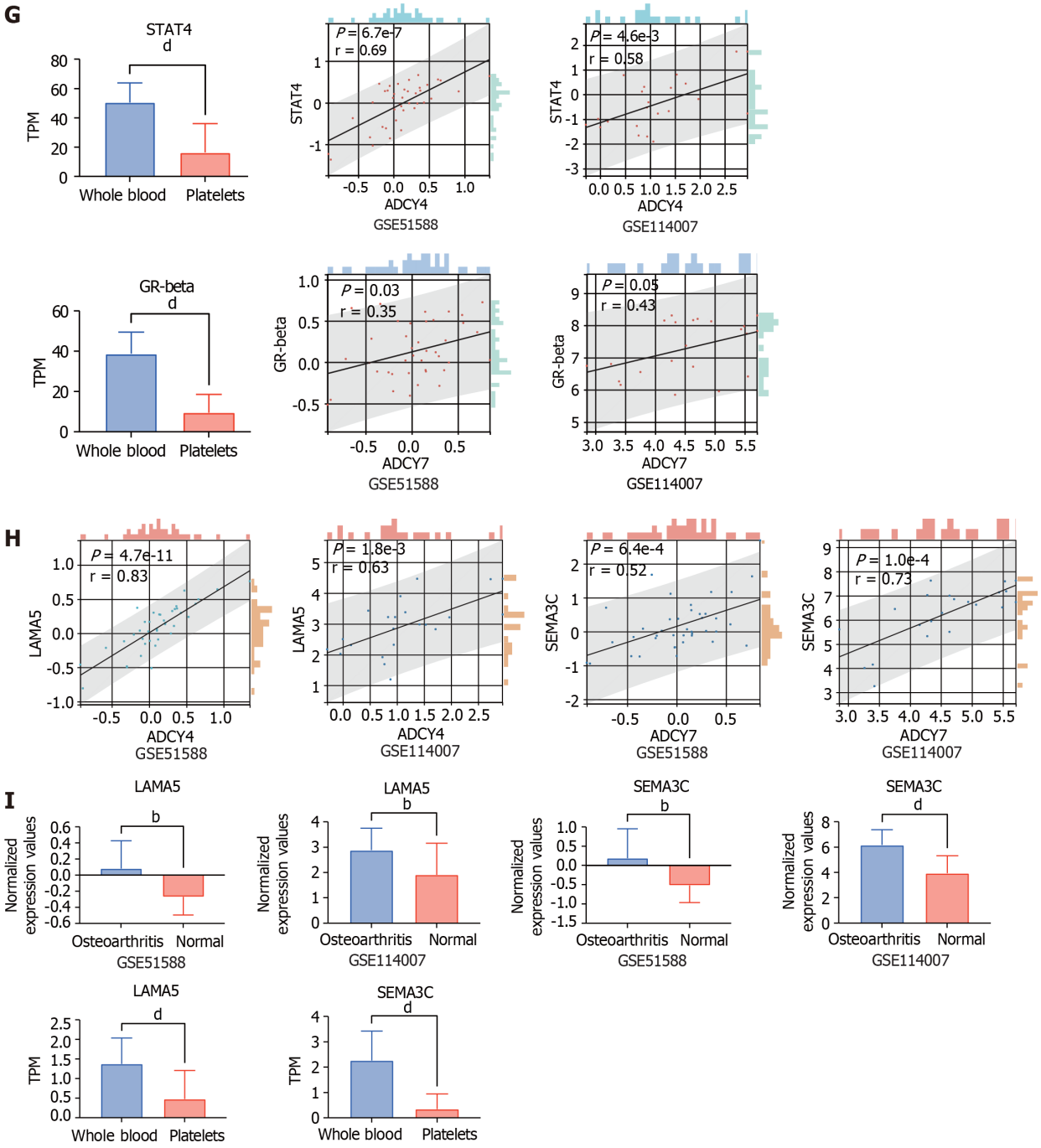


Figure 4 The STAT4-ADCY4-LAMA5 axis and the GRbeta-ADCY7-SEMA3C axis are either key to osteoarthritic diseases. A: Differential expression levels of adenylate cyclase in platelets and whole blood (data from GSE178158, GSE134080 cohorts); B: Differential expression levels of adenylate cyclase in platelets and whole blood (data from GSE51588 cohort); C: Adenylate cyclase expression level difference exists in platelets and whole blood (data from GSE114007 cohort); D: There is a very strong correlation between the expression level of adenylate cyclase (left: GSE134080 cohort, center: GSE51588 cohort, right: GSE114007 cohort); E: Can be combined with the ADCY4 promoter region; F: Transcription factors that can bind to ADCY7 promoter region; G: There is an extremely strong positive correlation between STAT4 and ADCY4 expression levels, and between GR-beta and ADCY7 expression levels; H: There is an extremely strong positive correlation between LAMA5 and ADCY4 expression levels, and between SEMA3C and ADCY7 expression levels; I: Both LAMA5 and SEMA3C were highly expressed in osteoarthritic disease samples. $^{a}P < 0.05$, $^{b}P < 0.01$, $^{c}P < 0.001$, and $^{d}P < 0.0001$.

FOOTNOTES

Author contributions: Du FY designed the study; Du FY and Sun JY performed the research; Du FY and Sun JY analysed the data; Sun JY and Li C wrote the manuscript; Du FY and Li C revised the manuscript.

Conflict-of-interest statement: All the authors declare no conflicts of interest.

Country/Territory of origin: China

ORCID number: Jing-Yi Sun 0009-0004-8221-0622; Feng-Ying Du 0000-0002-2767-1301.

S-Editor: Liu JH
L-Editor: A
P-Editor: Zhao S

REFERENCES

1 **Huang D**, Vithran DTA, Gong HL, Zeng M, Tang ZW, Rao ZZ, Wen J, Xiao S. Effectiveness of platelet-rich plasma in the treatment of Achilles tendon disease. *World J Orthop* 2023; **14**: 485-501 [PMID: 37377997 DOI: 10.5312/wjo.v14.i6.485]
2 **Millar NL**, Silbernagel KG, Thorborg K, Kirwan PD, Galatz LM, Abrams GD, Murrell GAC, McInnes IB, Rodeo SA. Tendinopathy. Nat Rev Dis Primers 2021; 7: 1 [PMID: 33414454 DOI: 10.1038/s41572-020-00234-1]
3 **Dakin SG**, Newton J, Martinez FO, Hedley R, Gwilym S, Jones N, Reid HAB, Wood S, Wells G, Appleton L, Wheway K, Watkins B, Carr AJ. Chronic inflammation is a feature of Achilles tendinopathy and rupture. *Br J Sports Med* 2018; **52**: 359-367 [PMID: 29118051 DOI: 10.1136/bjsports-2017-098161]
4 **Everts P**, Onishi K, Jayaram P, Lana JF, Mautner K. Platelet-Rich Plasma: New Performance Understandings and Therapeutic Considerations in 2020. *Int J Mol Sci* 2020; **21** [PMID: 33096812 DOI: 10.3390/ijms21207794]
5 **van Buul GM**, Koevoet WL, Kops N, Bos PK, Verhaar JA, Weinans H, Bernsen MR, van Osch GJ. Platelet-rich plasma releasate inhibits inflammatory processes in osteoarthritic chondrocytes. *Am J Sports Med* 2011; **39**: 2362-2370 [PMID: 21856929 DOI: 10.1177/0363546511419278]
6 **Wu T**, Hu E, Xu S, Chen M, Guo P, Dai Z, Feng T, Zhou L, Tang W, Zhan L, Fu X, Liu S, Bo X, Yu G. clusterProfiler 4.0: A universal enrichment tool for interpreting omics data. *Innovation (Camb)* 2021; **2**: 100141 [PMID: 34557778 DOI: 10.1016/j.xinn.2021.100141]
7 **Ould Amer Y**, Hebert-Chatelain E. Mitochondrial cAMP-PKA signaling: What do we really know? *Biochim Biophys Acta Bioenerg* 2018; **1859**: 868-877 [PMID: 29694829 DOI: 10.1016/j.bbabio.2018.04.005]
8 **Rho JH**, Ko IG, Jin JJ, Hwang L, Kim SH, Chung JY, Hwang TJ, Han JH. Polydeoxyribonucleotide Ameliorates Inflammation and Apoptosis in Achilles Tendon-Injury Rats. *Int Neurourol J* 2020; **24**: 79-87 [PMID: 33271004 DOI: 10.5213/inj.2040428.214]
9 **Paula DR**, França MS, Leão LKR, Maciel AA, Moura TAA, Moraes SAS, Bahia CP, Borges RS, Batista EJO, Passos ACF, Oliveira KRHM, Herculano AM. Total rupture of Achilles tendon induces inflammatory response and glial activation on the spinal cord of mice. *Braz J Med Biol Res* 2023; **56**: e12391 [PMID: 37851789 DOI: 10.1590/1414-431X2023e12391]
10 **Shah S**, Brock EJ, Ji K, Mattingly RR. Ras and Rap1: A tale of two GTPases. *Semin Cancer Biol* 2019; **54**: 29-39 [PMID: 29621614 DOI: 10.1016/j.semcancer.2018.03.005]
11 **Stefanini L**, Bergmeier W. RAP1-GTPase signaling and platelet function. *J Mol Med (Berl)* 2016; **94**: 13-19 [PMID: 26423530 DOI: 10.1007/s00109-015-1346-3]
12 **Korayem AH**, Mujica PE, Aramoto H, Durán RG, Nepali PR, Kim DD, Harris AL, Sánchez FA, Durán WN. Endothelial cAMP deactivates ischemia-reperfusion-induced microvascular hyperpermeability *via* Rap1-mediated mechanisms. *Am J Physiol Heart Circ Physiol* 2017; **313**: H179-H189 [PMID: 28476918 DOI: 10.1152/ajpheart.00002.2017]
13 **Pannekoek WJ**, Vliem MJ, Bos JL. Multiple Rap1 effectors control Epac1-mediated tightening of endothelial junctions. *Small GTPases* 2020; **11**: 346-353 [PMID: 29388865 DOI: 10.1080/21541248.2018.1431512]
14 **Smolenski A**. Novel roles of cAMP/cGMP-dependent signaling in platelets. *J Thromb Haemost* 2012; **10**: 167-176 [PMID: 22136590 DOI: 10.1111/j.1538-7836.2011.04576.x]
15 **Sanchez-Collado J**, Lopez JJ, Jardin I, Salido GM, Rosado JA. Cross-Talk Between the Adenylyl Cyclase/cAMP Pathway and Ca(2+) Homeostasis. *Rev Physiol Biochem Pharmacol* 2021; **179**: 73-116 [PMID: 33398503 DOI: 10.1007/112_2020_55]
16 **Konstorum A**, Mohanty S, Zhao Y, Melillo A, Vander Wyk B, Nelson A, Tsang S, Blevins TP, Belshe RB, Chawla DG, Rondina MT, Gill TM, Montgomery RR, Allore HG, Kleinstein SH, Shaw AC. Platelet response to influenza vaccination reflects effects of aging. *Aging Cell* 2023; **22**: e13749 [PMID: 36656789 DOI: 10.1111/acel.13749]
17 **Aguirre-Gamboa R**, de Klein N, di Tommaso J, Claringbould A, van der Wijst MG, de Vries D, Brugge H, Oelen R, Võsa U, Zorro MM, Chu X, Bakker OB, Borek Z, Ricaño-Ponce I, Deelen P, Xu CJ, Swertz M, Jonkers I, Withoff S, Joosten I, Sanna S, Kumar V, Koenen HJPM, Joosten LAB, Netea MG, Wijmenga C; BIOS Consortium, Franke L, Li Y. Deconvolution of bulk blood eQTL effects into immune cell subpopulations. *BMC Bioinformatics* 2020; **21**: 243 [PMID: 32532224 DOI: 10.1186/s12859-020-03576-5]
18 **Chou CH**, Wu CC, Song IW, Chuang HP, Lu LS, Chang JH, Kuo SY, Lee CH, Wu JY, Chen YT, Kraus VB, Lee MT. Genome-wide expression profiles of subchondral bone in osteoarthritis. *Arthritis Res Ther* 2013; **15**: R190 [PMID: 24229462 DOI: 10.1186/ar4380]
19 **Fisch KM**, Gamini R, Alvarez-Garcia O, Akagi R, Saito M, Muramatsu Y, Sasho T, Koziol JA, Su AI, Lotz MK. Identification of transcription factors responsible for dysregulated networks in human osteoarthritis cartilage by global gene expression analysis. *Osteoarthritis Cartilage* 2018; **26**: 1531-1538 [PMID: 30081074 DOI: 10.1016/j.joca.2018.07.012]
20 **Messeguer X**, Escudero R, Farré D, Núñez O, Martínez J, Albà MM. PROMO: detection of known transcription regulatory elements using species-tailored searches. *Bioinformatics* 2002; **18**: 333-334 [PMID: 11847087 DOI: 10.1093/bioinformatics/18.2.333]
21 **Farré D**, Roset R, Huerta M, Adsuara JE, Roselló L, Albà MM, Messeguer X. Identification of patterns in biological sequences at the ALGGEN server: PROMO and MALGEN. *Nucleic Acids Res* 2003; **31**: 3651-3653 [PMID: 12824386 DOI: 10.1093/nar/gkg605]
22 **Uhlén M**, Karlsson MJ, Hober A, Svensson AS, Scheffel J, Kotol D, Zhong W, Tebani A, Strandberg L, Edfors F, Sjöstedt E, Mulder J, Mardinoglu A, Berling A, Ekblad S, Dannemeyer M, Kanje S, Rockberg J, Lundqvist M, Malm M, Volk AL, Nilsson P, Månberg A, Dodig-Crnkovic T, Pin E, Zwahlen M, Oksvold P, von Feilitzen K, Häussler RS, Hong MG, Lindskog C, Ponten F, Katona B, Vuu J, Lindström E,

Nielsen J, Robinson J, Ayoglu B, Mahdessian D, Sullivan D, Thul P, Danielsson F, Stadler C, Lundberg E, Bergström G, Gummesson A, Voldborg BG, Tegel H, Hober S, Forsström B, Schwenk JM, Fagerberg L, Sivertsson Å. The human secretome. *Sci Signal* 2019; **12** [PMID: 31772123 DOI: 10.1126/scisignal.aaz0274]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com