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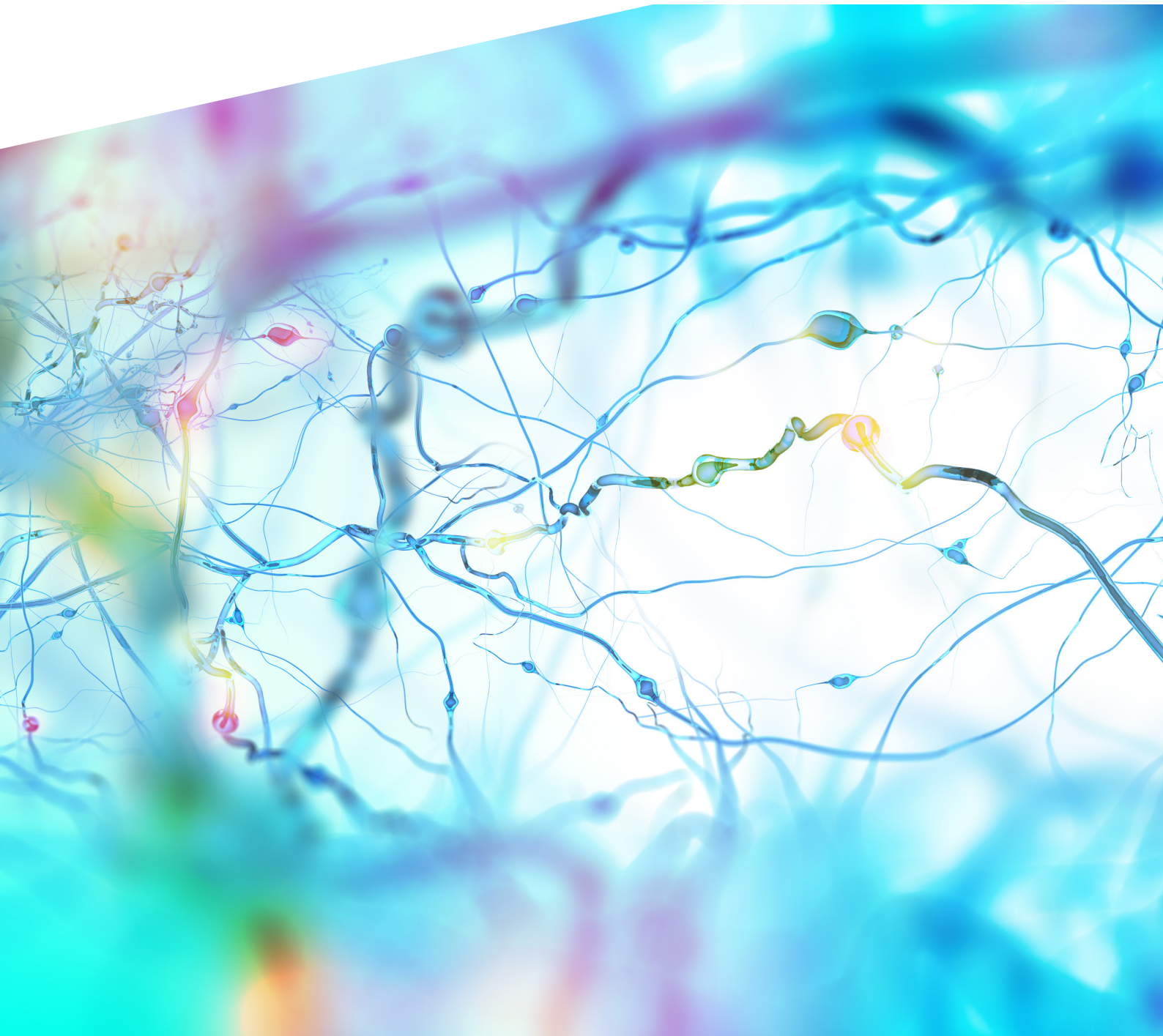

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Aims & Scope

The Ewha Medical Journal (Ewha Med J, http://www.e-emj.org), the official publication of Ewha Womans University College of Medicine and Ewha Medical Research Institute, is published quarterly a year, last day of January, April, July, and October. The first volume was published in March, 1978. It covers all fields of medical science including clinical research and basic medical science. The Journal aims to communicate new medical information between medical personnel and to help development of medicine and propagation of medical knowledges. All manuscripts should be creative, informative and helpful for diagnosis and treatment of the medical diseases and for communication of valuable information about all fields of medicine. Subscripted manuscripts should be written out according to the instructions for the Journal. Topics include original article, case report, images and solution, letter to the editor, invited review article and special issue in the respective field of medicine. The Ewha Medical Journal is indexed/tracked/covered by KoreaMed, KoMCI, KoreaMed Synapse, WPRIM, DOI/CrossRef, EMBASE and Google Scholar.

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Editorial Board

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Mission and Goals of the New Editor of the *Ewha Medical Journal*

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In July, I received a call from Dr. Eunhee Ha, the Dean of the College of Medicine at Ewha Womans University. She asked if I would consider becoming the editor-in-chief of the *Ewha Medical Journal* (EMJ), the college's official publication. I was taken aback by this offer, as I am set to retire from Hallym University next February. In Korea, it is traditional for retiring faculty members to step down from all official roles. Since 2005, I have been the editor of the *Journal of Educational Evaluation for Health Professions* (JEEHP) [1]. Juggling the editing responsibilities of two journals is no small task, but I accepted the offer. I have always been an avid reader of EMJ, and Dr. Ryung-Ah Lee, the previous editor (2013 to August 2023), is a close colleague of mine. During my term as the President of the Korean Association of Medical Journal Editors (KAMJE) from April 2020 to March 2023, she served as the Chair of the Committee for Planning and Administration of KAMJE. Her commitment to the role was greatly admired.

Furthermore, the Editorial Board members, Drs. Hae-Sun Chung and Hyungju Kwon, who also served with me on the KAMJE Committees, are renowned for their exceptional skills in editing academic journals. I look forward to collaborating with them. I am deeply grateful to Dean Dr. Ha for providing me with the opportunity to work alongside such outstanding editors.

What is the Mission of the New Editor?

I shall serve as the editor-in-chief from September 2023 to July 2025, succeeding Dr. Lee. My objective aligns with the goals of EMJ: *to publish the best research and information at the intersection of biomedical science, clinical practice, and medical education and to present this information in understandable, clinically useful formats that inform health care practice and improve patient outcomes. EMJ keeps healthcare professionals at the leading edge of medical knowledge, fosters broad understanding in their areas of interest, and provides a variety of engaging and innovative ways to learn*.

Goals for My 2-year Term

The following goals have been set for the next 2 years to accomplish the mission outlined above, considering EMJ's position in the international journal network.

First, it is imperative to recruit a sufficient number of manuscripts, aiming for a minimum of 40 annually. Despite the high quality of EMJ and its excellent editing, the number of publications has

stagnated recently, with 12 in 2020, 26 in 2021, and 28 in 2022. This plateau may be attributed to the journal's indexing status in international databases. However, EMJ has recently been indexed in the Emerging Sources Citation Index and Embase. It is worth noting, though, that many Korean universities do not regard these databases as top-tier.

Second, to address the issue of insufficient database indexing, I plan to continue working to add the journal to the Directory of Open Access Journals, MEDLINE, PubMed Central, and Scopus. My prior experience in advising journals on their inclusion in these international databases will be beneficial in this endeavor [2–4]. Additionally, I have successfully added JEEHP to these international databases [5].

Third, it will be necessary to take steps to distinguish this journal from other similar journals in this field. EMJ's scope is extensive, as the journal provides information for healthcare professionals, the general public, and medical students. However, the articles are primarily intended for physicians and medical scientists—and other general medicine journals in Korea already exist (Table 1).

Three of the seven general medicine journals are published by medical schools: Ewha Womans University, Sungkyunkwan University, and Yeungnam University. These institutions respectively publish the EMJ, *Precision and Future Medicine*, and *Journal of Yeungnam Medical Science*. Therefore, a credible rationale is needed for publishing EMJ, a journal associated with a specific medical school.

Fourth, we will work to satisfy the goals articulated in the journal's aims and scope by soliciting manuscripts from healthcare professionals beyond just physicians. We will also seek contributions from undergraduate students, graduate students, and residents. To further this policy, we will invite undergraduate and graduate students to join the editorial board. In Korea, there are nurses known as "community health practitioners" [6] who provide care for individuals in rural areas or islands. Only nurses who have undergone the necessary training are eligible to work in a community health center in Korea. The country has approximately 2,000 community health practitioners. These practitioners are authorized to prescribe a limited number of pre-approved medications, fewer than 90, as determined by the Ministry of Health and Welfare of the Korean government. Although their role is confined to specific areas and predetermined practices, they effectively perform the duties of physicians. EMJ will provide guidelines for their practice. Innovative learning methods fall within the scope of this journal, so education will be a recurring theme. The College of Medicine at Ewha University maintains connections and

Table 1. The list of journals from Korea indexed in the Web of Science Core Collection in the category of General & Internal Medicine [cited 2023 Oct 19]

Title	Scopus	PMC	JIF 2022	Quartile
Journal of Korean Medical Science	Yes	Yes	4.5	Q2
Yonsei Medical Journal	Yes	Yes	2.4	Q3
Korean Journal of Internal Medicine	Yes	Yes	2.4	Q3
Ewha Medical Journal	No	No	0.3	ESCI
Precision and Future Medicine	No	No	0.3	ESCI
Journal of the Korean Medical Association	Yes	No	0.3	ESCI
Journal of Yeungnam Medical Science	Yes	Yes	1.3*	ESCI

ESCI journals are not included in any quartiles.
PMC, PubMed Central; JIF, journal impact factor; ESCI, emerging sources citation index.
*This is not an official value, but an estimated value from the Web of Science Core Collection.

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collaborates with medical schools globally, and these partnerships will be featured prominently in EMJ.

Fifth, the editorial and publishing processes of the journal will incorporate Diversity, Equity, and Inclusivity (DEI) principles. As a non-profit educational institution, the publisher does not employ full-time staff for the journal, making it impossible to achieve DEI among employees. However, there will be a focus on promoting DEI among the editorial board, reviewers, and authors. EMJ will take into account equity in terms of geographical location and gender and will ensure that diverse voices are respected during the editing and publishing processes.

Sixth, we will diversify the types of publications. In addition to original articles, reviews, and case reports, we will include other more accessible formats such as comments, Korean reports, perspectives, and correspondence. These can be classified under the category of opinions.

Making suggestions is easy, but achieving the above six goals within 2 years is challenging. However, as the saying goes, a good start is half the battle. Dean Dr. Ha has pledged full budgetary support, which has allowed EMJ to transition to a diamond open access journal as of the October 2023 issue. For at least the next two years, there will be no publication fees or article processing charges levied on the authors. It's possible that we may not realize all our goals within the two-year period. However, the core of editing and publishing a non-profit journal lies in the joy of working collaboratively with our editorial board members and staff, all of whom volunteer their time and effort for the journal.

In This Issue

In this issue, we are publishing an invited opinion piece by Dr. Duck Sun Ahn, entitled "Healthcare Development Plan: Balancing Accessibility and Human Resources in Korea." As of October 2023, there is an ongoing debate regarding the number of new entrants to medical schools. When considering this issue, Dr. Ahn's opinion should be taken into account [7]. Determining the appropriate number of medical doctors is a complex issue. In Korea, medical doctors can continue to practice indefinitely, provided they complete their continuous medical education annually. In healthcare, supply can potentially create unlimited demand, which could lead to an increase in medical costs proportional to the number of practicing doctors.

We are also publishing a special issue on elbow pain. Dr. Youngbok Kim [8] states in his editorial that "this compilation of papers, encompassing a series of domestic epidemiological studies on elbow diseases, distinguishing factors for elbow pain, conservative and surgical treatments, and postoperative rehabilitation, is noteworthy as it provides a comprehensive overview of the understanding and treatment of elbow diseases." Big data analysis also revealed that the prevalence of diseases causing elbow pain was 114.21 per 100,000 for lateral epicondylitis, 32.82 for medial epicondylitis, 61.46 for elbow injury, dislocation, and sprain, and 39.15 for mononeuropathy of the upper limb [9]. The diagnosis, treatment, and rehabilitation of patients with elbow pain disorders will provide current and high-quality information for both specialists and general practitioners. The editorial board will continue to spotlight the most recent hot topics in Korean healthcare.

I wish health and happiness for the authors, reviewers, and readers of EMJ as they review or read the exciting and unique topics covered in EMJ.

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Conflict of Interest

Sun Huh has been an editor-in-chief of the *Ewha Medical Journal* since September 2023. However, he was not involved in the review process. No other potential conflict of interest relevant to this editorial was reported.

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Opinion

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Healthcare Development Plan: Balancing Accessibility and Human Resources in Korea

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The number of physicians per 1,000 people is very similar in South Korea (2.5), the United States (2.6), Japan (2.5), and Taiwan (2.1), with values all falling in the range from 2.1 to 2.6 [1,2]. However, due to vast differences in the geographical size among countries and the diverse nature of medical care and healthcare consumption culture, there is a significant disparity in patient waiting times between larger countries like the United States and smaller ones, such as South Korea or Taiwan. For instance, recent data from 2022 in the United States reveal that the average patient wait time for an appointment is approximately 26 days, marking an increase of 8% since 2017 and 24% since 2004 [3]. In contrast, such waiting times for primary care are considered unacceptable in Korean society.

If the waiting time for a primary care doctor's appointment in Korea exceeds one week, it would likely cause public outrage, potentially leading to calls for government change. In the United States, it is widely acknowledged that long wait times for doctor appointments are indicative of a physician shortage. Therefore, we can ask—does Korea's lack of an appointment backlog suggest an overabundance of doctors? The number of doctors per 1,000 people is, in fact, slightly higher in the United States than in Korea. Therefore, a clear scientific explanation is needed to understand how Korea's superior and swift access to care is achievable.

When discussing the shortage of doctors in Korea, we need to be more specific about the accessibility of healthcare in Korea. What are the drawbacks and sacrifices associated with a lack of promptness? A thorough and systematic study is needed to enhance accessibility in a country where the healthcare delivery system is still underdeveloped. One might hypothesize that a mandatory, low-cost medical reimbursement system, like the one in Korea, does not necessitate a well-defined healthcare delivery system. However, the crumbling of essential medical care, which underscores the limitations of rapid medical intervention, is increasingly evident. It is worth considering whether this issue can be addressed by increasing the number of medical schools or by establishing new ones.

A policy that fails to provide specific indicators for addressing the healthcare workforce issue, instead simply proposing increasing the overall number of physicians, would be highly unprofessional, oversimplified, and vague. Korea has not yet reached a consensus on the objectives and structure of its healthcare system. However, the policy of prioritizing low-cost coverage has become deeply embedded in our medical culture. Our strength lies in delivering affordable and efficient healthcare. The sustainability of the current healthcare provision, including the risk of essential medical services collapsing, remains to be determined.

The opposition parties and the Korean government consistently emphasize the need to enhance public healthcare services with a focus on equality. They view the establishment of medical schools as a critical strategy to achieve this objective. However, it is important to keep in mind that patients' freedom of choice is an inviolable principle, and there is a concern about losing votes in elections. While political parties and governments assert their commitment to strengthening the public oversight of healthcare provision, they do not exert control over healthcare consumption.

The "Framework Act on Health and Medical Service," enacted in 2000, requires the Minister of Health and Welfare of the Korean government to establish a healthcare development plan every 5 years. This plan is created after consultation with the heads of relevant central administrative agencies and deliberation by the Healthcare Policy Review Committee [4]. However, the government has not established a Healthcare Development Plan in the 23 years since the enactment of this law. The Second Public Healthcare Basic Plan (2021–2025), announced in June 2021, is based on the "Act on Public Healthcare," rather than being a Healthcare Development Plan as stipulated in the "Framework Act on Health and Medical Service." It emphasizes measures to enhance public health, with a focus on providing stable essential medical care in local communities and ensuring regular relief. However, it lacks specific details regarding various healthcare personnel [5].

The "Korean Healthcare Act" legally requires special mayors, metropolitan mayors, governors, special autonomous region governors, county governors, and mayor's office chiefs (referring to mayors of autonomous regions) to establish and implement local healthcare plans based on the finalized Healthcare Development Plan. This should be done with appropriate consideration of the actual situation of the local government, as prescribed by relevant laws and regulations [6]. However, the law creates an unworkable and impossible role for the government to fulfill. The lack of progress in national healthcare planning, apart from ensuring universal coverage in the shortest possible time, implementing low medical cost policies, and improving public awareness, reflects the private aspect of healthcare in Korea.

A country's healthcare policy must first establish a comprehensive dialogue on healthcare, and then assess the supply and demand for healthcare human resources based on clearly defined objectives and specific detailed plans. This process also necessitates the involvement and consensus of the professionals and hierarchical organizations tasked with healthcare provision. Healthcare policy is a complex and challenging issue that demands extensive collaboration. The time is now for the Korean government to formulate a cohesive short- and long-term plan, incorporating expert input, to guarantee the delivery of sustainable, top-tier healthcare services.

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Editorial

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When a Patient's Pain in the Elbow Turns into a Physician's Pain in the Neck

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Elbow pain-related diseases constitute a significant portion of musculoskeletal conditions, and their prevalence is steadily increasing from an epidemiological perspective [1]. In Korea, due to the rapid transition through industrialization and improved socioeconomic status, the patient and disease spectrum is broadening. This expansion encompasses a blend of occupational injuries, sports and leisure-related injuries, and degenerative diseases associated with an aging society [2]. Naturally, alongside efforts to clinically comprehend and manage these diseases, it is crucial to address and mitigate the escalating social and economic costs they incur [3]. In this issue of the journal, there is a collection of papers examining the epidemiology of common painful elbow conditions and providing a series of analyses from conservative treatment to surgical intervention and subsequent rehabilitation. These papers are anticipated to be a valuable resource for primary care physicians.

Indeed, our understanding of the anatomy and biomechanics of the elbow joint, as well as treatment modalities for the specific diseases that affect it, has lagged behind those of other major joints. While we are grateful that significant strides have been made in comprehending and treating elbow diseases in recent decades, we must acknowledge that there are still many challenges to overcome in comparison to other musculoskeletal fields.

The leading article in this collection offers the most recent and comprehensive analysis of the epidemiology of elbow joint diseases in Korea, utilizing insurance codes to provide a snapshot of trends within the domestic patient population. Korea's insurance code classification system, which has been computerized in a more detailed and consistent manner than in any other country and has been compiled over several decades, is particularly valuable for epidemiological analysis [4,5]. This is because the Korean insurance system requires doctors to specify diagnoses and treatments, as well as because the domestic population cohort is sufficiently large for nuanced research. However, in a busy clinical setting, data bias may occur as treatment often begins with a formal diagnosis equivalent to an impression, and a diagnosis favorable for billing is presented in line with changing billing regulations.

Moreover, as the aim of this collection of papers is to enhance the consistency of multidisciplinary primary physicians' understanding and treatment of elbow diseases, it is also necessary to consider differences in multidisciplinary diagnoses for the same disease. It is evident that epidemiological changes, including an increase in elbow patients and a diversity of diseases, are reflected in our clinical practice. The domestic socioeconomic situation, where patients are classified as a patient group as they actively seek treatment for previously overlooked symptoms, and

the unique situation in Korea, where doctors from various departments compete to provide musculoskeletal treatment, must also be taken into account [6].

When diagnosing elbow diseases, the location of pain and specific triggering situations are key distinguishing factors. However, in conditions like arthritis or calcific tendinitis, the pain location is not specific. Similarly, in cases of local nerve entrapment or proximal nerve compression disease, the pain location and lesion do not align. There is a tendency to diagnose elbow pain based solely on its location, which can introduce bias. For instance, oversimplifications such as "pain on the medial side must be medial epicondylitis and pain on the lateral side must be lateral epicondylitis" can lead to overlooking a more detailed approach to pain. In patients who report tenderness and exertional pain near the medial epicondyle, there are numerous possibilities, including calcific tendinitis, adventitious bursitis due to ulnar nerve dislocation, nerve entrapment such as anterior interosseous nerve syndrome, and medial collateral ligament damage or microfractures in sports injuries [7]. Contrary to a paper that described cubital tunnel syndrome as a cause of medial elbow pain, its primary symptom is not medial pain, but hand numbness and weakness. Therefore, a more comprehensive and insightful approach is necessary, bearing in mind that cases unrelated to the pain location are also possible.

Excluding tumors, infections, major fractures, and ligament injuries with significant joint instability, the majority of painful conditions around the elbow yield satisfactory results with conservative treatment in 80%–90% of cases [8]. Therefore, it is reasonable to manage most painful elbow conditions sufficiently with conservative measures, by reassuring and persuading the patient. Unlike weight-bearing joints, the correlation between radiographic findings and symptoms in elbow arthritis is not proportional, eliminating the need for early surgical intervention. Currently, in Korea, various biological agents based on regenerative medicine are available as conservative treatments for tendon enthesopathy [9–11]. However, it is important to note that there are skeptical and critical views regarding their efficacy and effectiveness. Local steroid injections have traditionally been used as a clinical tool for conservative treatment due to their rapid short-term effects [12,13]. However, repeated steroid injections into the tendon can increase the scale of any subsequent surgery and lead to unfavorable postoperative results [14,15].

If conservative treatment proves ineffective over a certain period, a surgical consultation may be advisable. In cases of nerve entrapment syndromes, such as cubital tunnel syndrome, decompression surgery could be beneficial before permanent anatomical and functional damage occurs [16]. Even in the case of calcific tendinitis, a benign condition, if pain persists indefinitely without resolution, early surgical removal of the calcific deposit might be beneficial [15]. Elbow surgery methodologies can be broadly categorized into arthroscopic surgery and open surgery. As neither method is definitively superior, the choice can be made based on the surgeon's preference, considering the condition and stage of the lesion. For end-stage joint disease with severe symptoms, replacement arthroplasty may be an option [17]. While elbow replacement surgery is currently yielding acceptable clinical results due to advancements in implant design and materials, it still presents more challenges compared to other joint replacement surgeries. Therefore, it should be considered as a last resort [18].

The elbow joint, which provides spatial configuration and support for hand function, must simultaneously perform the conflicting functions of stability and mobility. Biomechanically, the zone where both functions coexist is small. Consequently, post-surgery immobilization can easily lead to joint stiffness, while premature mobilization may result in instability before the major structures have fully healed [19]. Thus, the primary challenge in postoperative rehabilitation is to

restore the joint's range of motion while minimizing the risk of instability. Modern postoperative rehabilitation protocols for the elbow have been developed to be highly effective, taking into account the biomechanical characteristics of the elbow joint [20]. It is anticipated that these papers, which encapsulate the overarching principles and specific rehabilitation methods for each individual surgery, will serve as a valuable clinical guideline for physicians.

This compilation of papers, encompassing a series of domestic epidemiological studies on elbow diseases, distinguishing factors for elbow pain, conservative and surgical treatments, and postoperative rehabilitation, is noteworthy as it provides a comprehensive overview of the understanding and treatment of elbow diseases. We trust that the readers will appreciate that any perceived weaknesses or limitations are due to space constraints that prevent the publication of extensive content, with the anticipation that future papers will further elaborate on these topics.

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Epidemiology and Etiology of Elbow Pain Based on the Healthcare Bigdata Hub in Korea: A Longitudinal Observational Study

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Key Words
Elbow tendinopathy; Health expenditures; Prevalence; Sprains and strains; Republic of Korea

Objectives: This study investigated the epidemiological and etiological trends associated with elbow pain over the past decade in South Korea.

Methods: Nationwide health statistics data from 2011 to 2020 pertaining to elbow pain-related diseases and soft tissue damages were sourced from the Healthcare Bigdata Hub with disease codes M771 (lateral epicondylitis), M770 (medial epicondylitis), S53 (elbow injury, dislocation, sprain), and G56 (mononeuropathies of the upper limb). The study assessed the annual fluctuations in the total medical cost and the number of patients associated with these codes. Trends over time were characterized by evaluating the crude and age-standardized prevalence rates and the annual percentage change. Changes in the proportion of medical expenses based on age distribution were also investigated.

Results: A significant surge in medical costs was observed across all four codes. The M771, M770, and G56 codes experienced a pronounced increase in crude and age-standardized prevalence. Conversely, only S53 registered a significant drop in age-standardized prevalence. Moreover, within the total medical expenditures for the M771 code, the age bracket of 50 to 59 represented the largest proportion.

Conclusion: The data suggest that the average age of patients reporting elbow pain is rising. Given this shifting trend in South Korea's health statistics concerning elbow pain, there will be an increasing need for socioeconomic support, which will in turn necessitate improving health policies that address allocating medical expenses and resources for elbow pain.

Introduction

1. Background

The human elbow, an intricate fulcrum that can be considered a mechanical wonder, facilitates the primary point of articulation between the forearm and upper arm [1]. Its multifaceted role in the coordinated movements of the hand enables a diverse range of motions and functional activities [2]. This advanced functionality is attributed to its sophisticated structure, which comprises three unique articulations: the ulnotrochlear joint, which serves as a hinge; the proximal radioulnar joint, which enables rotation; and the radiocapitellar joint, which permits both hinge and rotational actions [3]. The synergistic functions of these joints provide the elbow with the ability to flex, extend, and perform the specialized movements of forearm pronation and supination.

Additionally, the distal humerus serves as a crucial attachment point for numerous muscle-tendon units, aiding in wrist and finger movements. The radial, median, and ulnar nerves, which are located within the soft confines of the elbow, carry out important functions but sometimes fall prey to various pathological conditions [4].

The elbow is predisposed to several disorders, notably epicondylitis, given its complex architecture. Often associated with specific sports, lateral epicondylitis is colloquially termed "tennis elbow," while medial epicondylitis is known as "golfer's elbow" [5]. Clinically, epicondylitis is characterized by pain focused on the epicondyle, which is intensified by resisted movements of the wrist muscles. Beyond the physical implications, this condition also carries significant socioeconomic consequences. These are manifested in lost workdays and prolonged periods of disability, leading to substantial economic burdens [6].

Chronic elbow pain is a significant concern for patients in clinical settings. Symptoms often reported by patients include swelling, pain, restricted mobility, stiffness, and neurological disturbances such as numbness [7]. The causes of chronic elbow pain are diverse, ranging from anomalies in bones, soft tissues, and nerves. Epicondylitis, which is due to tendinosis of the lateral or medial tendons, is the primary cause, affecting 1% to 3% of the population [8–11]. The development of conditions like epicondylitis is influenced by both occupational and recreational activities, underscoring the multifactorial nature of its etiology [5,6,12]. In addition to epicondylitis, other common pathologies associated with the elbow joint include nerve-related conditions such as cubital tunnel syndrome, radial tunnel syndrome, and pronator teres syndrome [7]. Traumatic injuries, including dislocations, ligament injuries, and fractures around the elbow joint, are also included [13].

In Korea, where most of the population is covered by National Health Insurance, strict protocols require all medical institutions to provide comprehensive patient data to the National Health Insurance Service. This data encompasses not only diagnostic details, such as the International Classification of Disease, 10th revision (ICD-10) codes, but also patient management strategies and economic implications. For example, in 2022, there were 660,767 patients diagnosed with lateral epicondylitis (M771) in Korea, with medical expenses amounting to 92,202,696 Korean won (KRW). Moreover, the financial burden has been steadily increasing each year, underscoring the seriousness of the situation [14].

2. Objectives

Given the increasing trends in medical demand and expenditures, a thorough analysis was conducted of the epidemiological and etiological trajectories of elbow pain. Utilizing a decade's worth of medical statistics from the Healthcare Bigdata Hub in Korea, this investigation offers a detailed understanding of elbow-related ailments, as informed by domestic medical claims.

Methods

1. Ethics statement

This study did not require IRB/IACUC approval since the data was achieved from the open data hub.

2. Study design

This was a longitudinal observational study based on public data.

3. Data sources/measurement

To investigate the epidemiological and etiological trends associated with elbow pain in Korea over the past decade, we sourced medical statistical data from the HIRA Bigdata Open portal spanning from 2011 to 2020 [14]. During this study period, we extracted codes for common elbow pain etiologies from the four-tier ICD codes for lateral and medial epicondylitis. Additionally, three-tier classification codes frequently associated with elbow pain and primary soft tissue injury codes were incorporated (Table 1). Specifically, these were: (1) lateral epicondylitis (M771); (2) medial epicondylitis (M770); (3) elbow injury, dislocation, sprain (S53); and (4) mononeuropathies of the upper limb (G56).

We derived annual trends in treatment costs and disease prevalence from medical statistical data for the selected four diagnostic classification codes. The annual treatment costs were computed based on the total expenses claimed for each diagnostic classification code throughout the year. We determined the annual number of patients using the period prevalence, which is defined as the percentage of the total population treated for the condition during a specific period. To analyze changes in trends, we utilized the concepts of crude prevalence rate and age-standardized prevalence rate. The crude prevalence rate was calculated as the patient ratio per 100,000 of the average annual population. The age-standardized prevalence rate used the 2010 South Korean population data, provided by the KOSIS National Statistics Portal (www.kosis.kr), as the standard population. We applied weights to this data to compare prevalence rates across different age structures using a direct standardization method.

We further segmented the data based on demographic attributes, categorizing medical usage trends by age. Given the lower incidence rate in individuals below 30 for elbow disorders, we grouped them together and defined the following age cohorts: under 40, 40–49, 50–59, 60–69, 70–79, and 80 and above.

We excluded data on fractures specific to the skeletal structure of the elbow and osteoarthritis diagnoses within this structure. Given the HIRA Bigdata Open portal classification limit (up to the third tier), ambiguous diagnostic codes that might not precisely represent clinical diagnoses, such as unspecified arthropathy or arthritis (M13 or M19), were omitted.

Table 1. Classification of the main ICD-10 codes associated with elbow pain

Disease classification	Subclassification	Comments
Lateral epicondylitis (M771)		
Medial epicondylitis (M770)		
Dislocation, sprain and strain of joints and ligaments of elbow (S53)	Dislocation of radial head (S53.0)	Pulled elbow
	Dislocation of elbow, unspecified (S53.1)	
	Traumatic rupture of radial collateral ligament (S53.2)	
	Traumatic rupture of ulnar collateral ligament (S53.3)	
	Sprain and strain of elbow (S53.4)	
Mononeuropathies of upper limb (G56)	Other lesions of median nerve (G56.1)	Pronator teres syndrome
	Lesion of ulnar nerve (G56.2)	Cubital tunnel syndrome
	Lesion of radial nerve (G56.3)	Radial tunnel syndrome

ICD-10, International Classification of Diseases, 10th revision.

To assess annual percentage changes (APCs) in prevalence over a decade, we employed joinpoint regression analysis (Joinpoint Regression Program ver.4.3.1.0; National Cancer Institute, Bethesda, MD, USA), utilizing a 95% confidence interval and setting the significance threshold at $P<0.05$. For each trend line, considering both the APC values and their statistical significance, the classifications were as follows: stable for $-0.5 \leq APC \leq 0.5$, with statistical non-significance. A non-significant change was defined as an $APC<-0.5$ or >0.5 with no statistical significance. An $APC>0$ with statistical significance was classified as indicating a rising trend. Likewise, an $APC<0$ with statistical significance was defined as a falling trend.

4. Statistical methods

All other statistical analyses were conducted using SPSS Statistics software (Version 24.0; IBM, Armonk, NY, USA), with a significance threshold set at $P<0.05$. Descriptive statistics were used to highlight the frequencies and growth rates of variables, while a simple correlation analysis was applied to the decade-long shift in cumulative treatment costs. Pearson correlation analysis was utilized to evaluate the relationships between continuous variables.

Results

1. Medical expenses

From 2011 to 2020, a total of 551,986,637 KRW was spent on treatment costs under the M771 code (lateral epicondylitis). In 2011, the total treatment cost was 35,447,254 KRW. This amount steadily rose to 78,518,749 KRW in 2020, representing an approximate increase of 122% compared to 2011 (Fig. 1). Conversely, the code defined as elbow injury, dislocation, sprain (S53) saw an increase of about 32% from 2011 to 2020, while the code for mononeuropathy of the upper limb (G56) saw an increase of 57%. The annual rate of increase in total treatment costs was statistically significant for all diseases ($P<0.001$).

2. Prevalence of diseases related to elbow pain

The annual patient counts, crude prevalence rates, and age-standardized prevalence rates for the four diagnostic codes related to elbow pain claimed over the past decade are summarized in Table 2. For lateral epicondylitis (M771), the crude prevalence rate gradually increased from approximately 969 cases per 100,000 in 2011 to 1,248 cases in 2020. There was a statistically significant increase from 2011 to 2018, with no statistically significant change observed after 2018 (Fig. 2A). The age-standardized prevalence rate also showed a significant increase from 2011 to 2018, with no notable changes observed after that (Fig. 2E). For medial epicondylitis (M770), the crude prevalence rate exhibited a significant increase from 2011 to 2017, followed by a non-significant change after 2017 (Fig. 2B). The age-standardized prevalence rate, similarly, showed a significant rise from 2011 to 2018 and a non-significant change after 2018 (Fig. 2F). Elbow injury, dislocation, sprain (S53) showed no significant change in crude prevalence throughout the study period (Fig. 2C), but its age-standardized prevalence consistently declined (Fig. 2G). For mononeuropathy of the upper limb (G56), the crude prevalence rate exhibited a significant increase from 2011 to 2018, followed by a non-significant change after 2018 (Fig. 2D). However, no significant change was found in the age-standardized prevalence rate (Fig. 2H).

Upon examining the demographics by age for the most significantly increasing condition, lateral epicondylitis (M771), it was revealed that in 2011, individuals aged 40–49 years accounted for approximately 37% of the treatment costs, while those aged 60–69 years represented

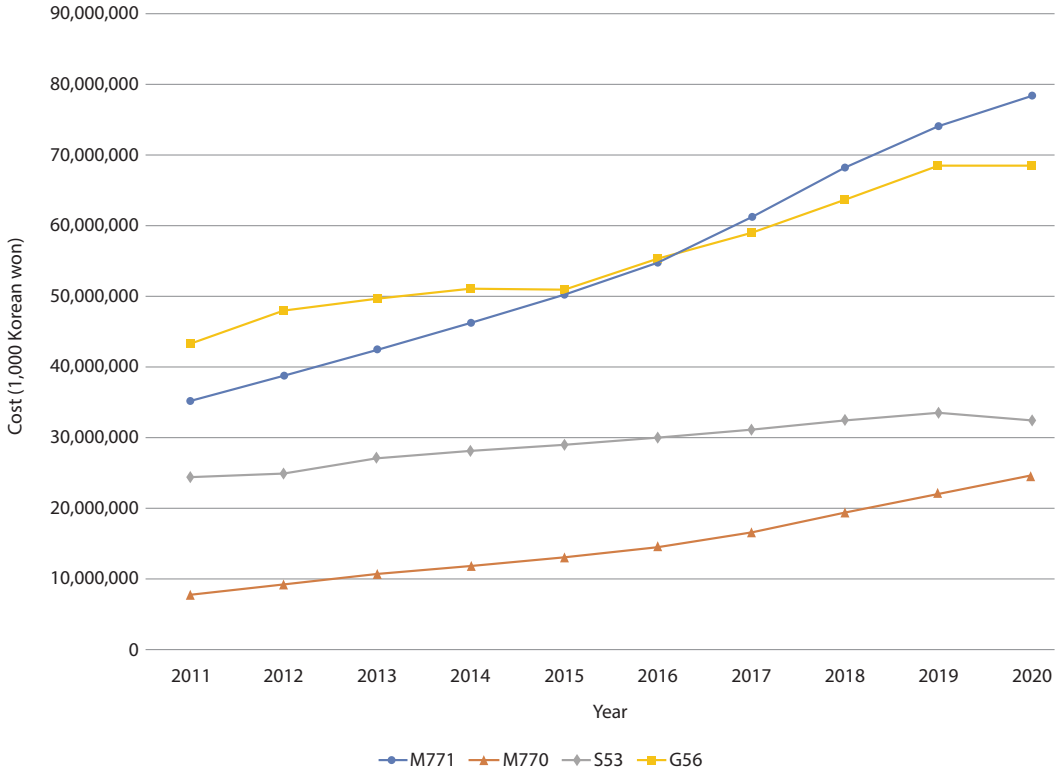

Fig. 1. Trends in the annual medical expenses (measured in 1,000 Korean won) for four elbow pain-related ICD-10 codes from 2011–2020 in Korea, as depicted by the authors. ICD-10, International Classification of Diseases, 10th revision.

about 12%. However, starting from 2012, the 50–59 age group became dominant, while the proportion of the 40–49 age group decreased and that of the 60–69 age group increased (Fig. 3). It is noteworthy that there were slight increases in the elderly demographics, with the percentage of the 70–79 age group rising from approximately 3% to 4%, and those aged 80 and above increasing from nearly 0% to 1%. The annual patient counts of lateral epicondylitis (M771) peaked in 2020, with 640,766 patients, making it the most common among elbow pain-related conditions. Over the past decade, there has been a significant increase in both the annual crude prevalence rate and the total treatment cost (Fig. 4), demonstrating a strong positive correlation between them ($r=0.944$, $P<0.001$).

Discussion

1. Key results

Based on the ICD-10 codes related to elbow pain, we analyzed the epidemiological trends of elbow pain in Korea over the past decade using data from the Healthcare Bigdata Hub in Korea. Excluding diagnoses related to fractures in the skeletal structure and osteoarthritis, it was observed that the annual total medical costs and the percentage change in the number of patients diagnosed with lateral epicondylitis (M771) showed the most significant increasing trend. Similarly, for medial epicondylitis (M770), the crude and age-standardized prevalence rates demonstrated statistically significant increases. However, both conditions showed non-significant trends from 2018 onward. In contrast, the age-standardized prevalence rate for elbow

Table 2. Number of patients and crude and age-standardized prevalence rate for the four main classification codes associated with elbow pain

Disease code	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
No. of patients										
M771	483,390	511,337	536,185	553,261	580,598	609,741	637,811	659,228	663,461	640,766
M770	109,225	121,141	130,428	138,852	147,458	160,989	171,644	181,872	190,606	189,509
S53	345,691	344,979	362,796	351,008	349,001	347,634	343,633	341,584	336,487	305,408
G56	200,321	219,814	227,589	230,293	230,867	239,721	247,695	246,689	243,928	229,781
Crude prevalence rate per 100,000 persons										
M771	969.11	1,015.66	1,060.51	1,089.89	1,139.51	1,192.93	1,244.98	1,285.02	1,292.35	1,247.86
M770	218.98	240.62	257.97	273.53	289.41	314.97	355.04	354.52	371.28	369.06
S53	693.05	685.23	717.57	691.46	684.96	680.13	670.76	665.84	655.44	594.77
G56	401.61	436.61	450.15	453.66	453.11	469.00	483.49	480.87	475.15	447.49
Age-standardized prevalence rate*										
M771	96.18	99.29	102.17	105.44	107.60	111.73	116.10	119.16	119.05	114.21
M770	21.66	23.40	24.66	26.26	26.98	29.04	30.66	32.15	33.34	32.82
S53	69.76	69.42	73.01	71.18	70.28	69.99	69.30	65.20	68.37	61.46
G56	39.95	42.22	42.75	43.30	41.88	42.90	43.87	43.10	42.02	39.15

* 2010 Standard population in South Korea as the control.

injury, dislocation, and sprain (S53) significantly decreased, while that of mononeuropathy of the upper limb (G56) significantly increased, becoming non-significant from 2018.

2. Interpretation

The COVID-19 pandemic, which began in 2019, is believed to have influenced the trends of various diseases after 2018. The COVID-19 pandemic seems to have not significantly impacted trauma patient hospital visits but might have influenced disease patients to endure pain and potentially delay hospital visits [15–18].

The changing demographic structure in Korea, combined with differences in the main diseases by age group, might have contributed to these findings [19]. Given the rapid aging of the Korean population, the proportion of people over 60 is increasing [20]. Thus, age, a critical factor related to elbow lesions, may be associated with the observed increase in prevalence. However, even after standardizing for age in this study, there remains a steady increase in prevalence, albeit less pronounced than the crude prevalence rate. Importantly, the significant upward trend in the crude prevalence rate suggests a growing number of patients, which implies a greater socioeconomic burden and heightened consumption of medical resources. This trend is further corroborated by the statistically significant and strong correlation observed between the annual increase in total medical costs and prevalence rate for lateral epicondylitis (M751) in 2020, the most common elbow pain-related diagnosis.

Another noteworthy observation of this study is the shift in the age distribution of total medical costs for elbow lesions over the past decade. In 2011, individuals in their 40s accounted for the highest proportion, but this proportion gradually decreased thereafter. In contrast, the proportion of costs incurred by individuals in their 50s and those in their 60s has increased since 2012. This trend is consistent with the age distribution of total medical costs for lateral epicondylitis (M771). The effect of COVID-19 seems to have temporarily stalled the increasing trend of patients

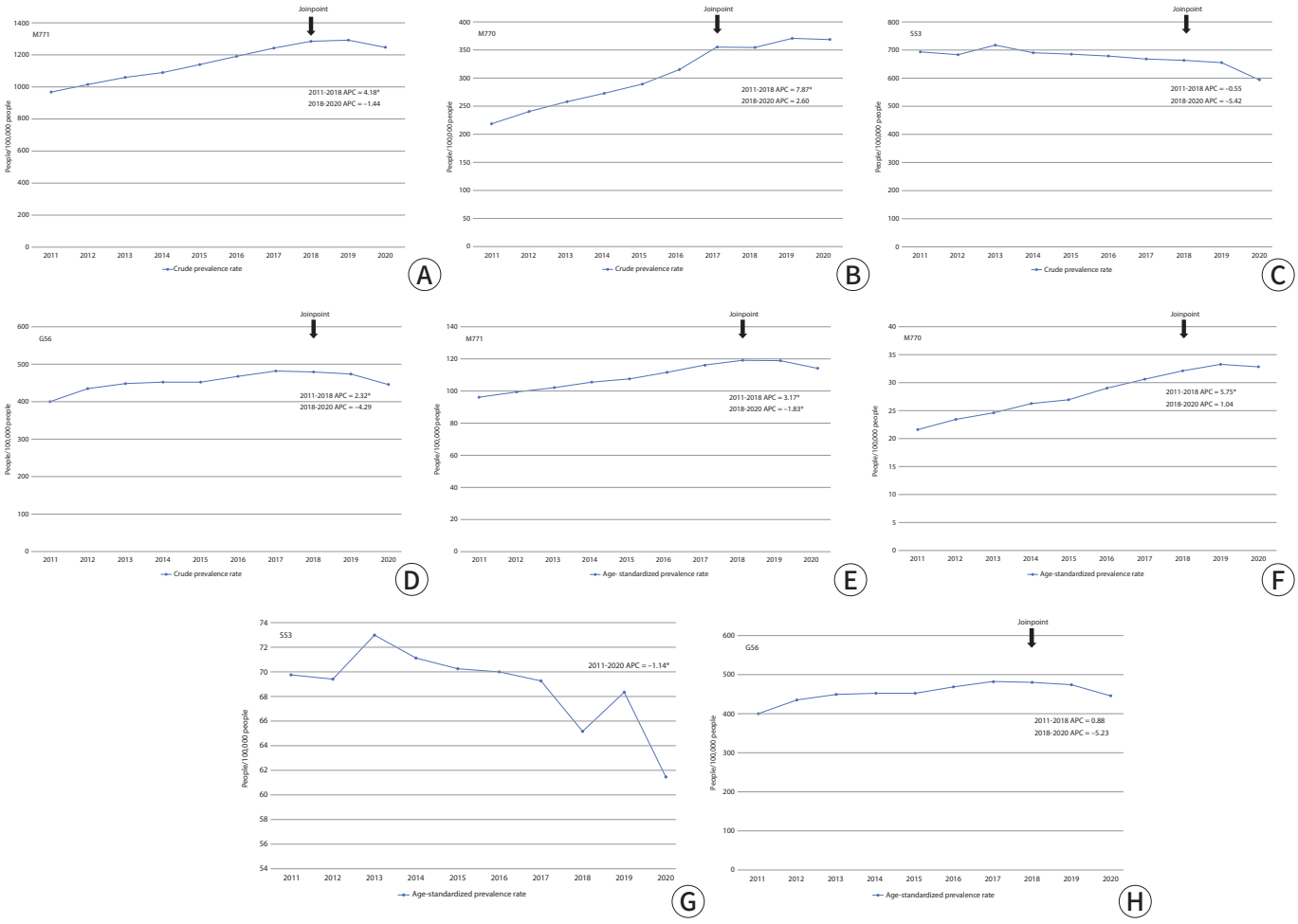

Fig. 2. Crude prevalence rates (A–D) and age-standardized prevalence rates (E–H) for lateral epicondylitis (M771); medial epicondylitis (M770); elbow injury, dislocation, sprain (S53); and mononeuropathies of the upper limb (G56) spanning the period 2011–2020 in Korea. APC, annual percentage change. * Indicates a value of P<0.05. Illustrated by the authors.

in 2019 and 2020 [21]. However, considering the overall decline in medical demand and inpatient treatment due to COVID-19, the trend would likely have continued to rise if the COVID-19 pandemic had not taken place.

3. Comparison with previous studies

The increasing trend in patient age aligns with domestic research on shoulder lesions. For instance, Jung et al. [22] conducted an epidemiological and etiological study on shoulder pain using health statistics data from the Healthcare Bigdata Hub in Korea. Their findings indicated that the age of patients experiencing shoulder pain is on the rise. In light of this observed trend, there is a pressing need for improved socioeconomic support and refinements in health policy, particularly in relation to the allocation of medical expenses and resources for managing elbow pain.

Our results align with those of prior studies, indicating a demographic aging trend in musculoskeletal disorders, especially concerning elbow pain. Given shifts in Korea's population over the past decade, there is a clear correlation with the nation's aging demographic structure.

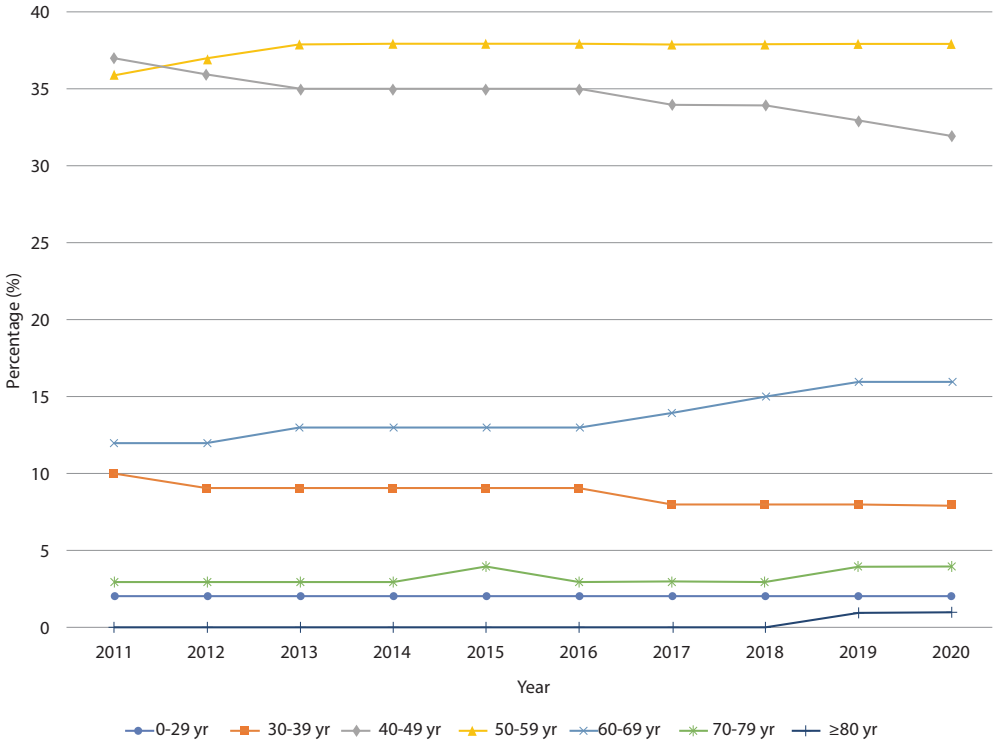

Fig. 3. Annual changes in medical expenses by age group for lateral epicondylitis (M771) between 2011 and 2020 in Korea. Illustrated by the authors.

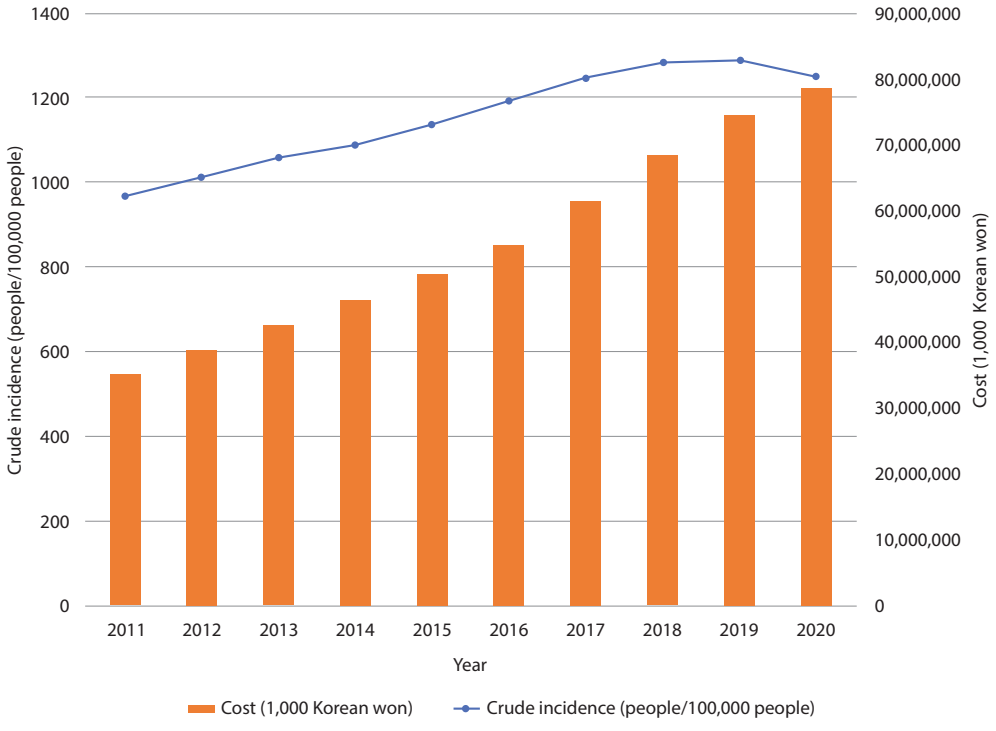

Fig. 4. Annual changes in both the total medical expenses (measured in 1,000 Korean won) and crude prevalence rate for lateral epicondylitis (M771) between 2011 and 2020 in Korea. Illustrated by the authors.

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As most elbow lesions are closely related to age, the prevalence of these lesions is anticipated to rise with population aging, leading to increases in medical expenses. Thus, elbow lesions have significant socioeconomic and healthcare implications. Factors like the aging population, diagnostic advances leading to more patient diagnoses, improved surgical techniques resulting in more frequent operations, and shifts in treatment indications and methods are all believed to have influenced the observed trends in age-related treatment costs. With the introduction of diverse injection therapies and conservative treatment approaches, along with newly incorporated therapeutic methodologies, there is a pressing need for in-depth research into evolving treatment modalities [8,23–25].

4. Limitations

This study has several limitations. First, the data were collected based solely on diagnostic codes rather than detailed clinical records. Consequently, it was challenging to determine the intensity, severity, and type of treatments, along with other specific clinical characteristics and aspects of disease progression. Nonetheless, this study is significant because it analyzed a large national sample obtained through the health insurance system to which most citizens are subscribed in order to understand epidemiological trends related to elbow pain. Second, issues such as plica syndrome, bursitis, or synovitis may not be accurately differentiated within the ICD-10 classification system. Sometimes, a single clinical diagnosis might be billed under different diagnostic codes depending on the medical professional's prescription.

Similarly, for conditions like elbow joint arthritis, one of the leading causes of elbow pain, the ICD-10 system does not allow differentiation between different joints. Moreover, accurate identification based solely on diagnostic codes is challenging when a patient has multiple possible diagnoses. For the G56 code, diagnoses are not restricted to the elbow; thus, this code aggregates elbow conditions together with wrist conditions, including median nerve, radial nerve, and ulnar nerve pathologies around the wrist joint. Additionally, elbow pain can be primary pain originating from the elbow or secondary pain due to another condition. Therefore, it is possible for the codes for elbow lesions to reflect mistaken or preliminary clinical diagnoses. This relates to the complexity of the elbow structure, its functional interconnectedness, and the ongoing evolution of medical concepts. Third, elbow conditions primarily originate in soft tissues. The diagnosis of these conditions mainly utilizes ultrasound or magnetic resonance imaging, and the use of various injections has expanded in recent years. Finally, there were limitations in the cost analysis for items prescribed as non-covered services. These items need to be included in future cost analyses.

Nonetheless, the primary aim of this study was to ascertain the epidemiological trends of diseases related to elbow pain. Over the past decade, the number of patients with elbow conditions and the total medical benefits have undoubtedly increased.

5. Conclusion

From 2011 to 2020, there were significant increasing trends in the total medical costs, prevalence, and age-standardized prevalence rate for lateral epicondylitis (M771). Additionally, the age group of 50–59 showed the highest expenditures for lateral epicondylitis, suggesting a trend of aging in elbow pain patients. Considering the demographic and aging trends in the Korea, along with the evolving health statistics related to elbow pain, there will likely be an increasing socioeconomic interest and need for health and medical countermeasures regarding the medical costs and allocation of medical resources for elbow pain.

Acknowledgements

Data used in this study can be extracted from the HIRA Big Data Open Portal available from: https://opendata.hira.or.kr/

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Methodology: Kim H, Jang T
Project Administration: Kim H
Writing – Original Draft: Kim H
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Ethics Approval and Consent to Participate

Not applicable.

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Review Article

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Differential Diagnosis of Elbow Pain

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Elbow pain; Diagnosis, differential; Anatomic location

Elbow pain is a common symptom encountered in clinical practice. Pathology can arise from any component of the joint, including the bone, tendons, ligament, bursa, or nerves. This paper discusses how elbow pain can be differentiated according to its anatomic location and presents the corresponding causes, diagnosis, and treatment options.

Introduction

The elbow is a complex joint with a wide range of motion and many functions. Its bony structure, composed of the humerus, radius, and ulna, and various muscles and ligaments work as a functional unit. One or multiple elbow joint components can cause pain and functional deficits; therefore, determining the underlying etiology of elbow pain can be difficult. Accordingly, this paper discusses the causes of common conditions that can lead to elbow pain and their respective diagnosis and treatment options.

Main Text

The location and quality of elbow pain can generally localize the injury to one of the four anatomic regions: anterior, medial, lateral, or posterior [1]. Table 1 presents the differential diagnosis of elbow pain by anatomic location [1].

1. Anterior elbow pain

1) Primary osteoarthritis

Osteoarthritis of the elbow joint, also known as degenerative or primary osteoarthritis, is distinct from secondary arthritis, which is caused by trauma or underlying disease. The incidence of elbow osteoarthritis is lower than that of knee joint osteoarthritis, a typical type of degenerative arthritis, and the pain is often less severe as the elbow is a non-weight bearing joint. However,

Table 1. Differential diagnosis of elbow pain based on anatomic location

Diagnosis	
Anterior	Medial
Anterior capsule strain Biceps tendinopathy Gout Intra-articular loose body Osteoarthritis Pronator syndrome Rheumatoid arthritis	Cubital tunnel syndrome Medial epicondylitis Medial collateral ligament injury Valgus extension overload syndrome
Lateral	Posterior
Lateral epicondylitis Osteochondral defect Plica Posterolateral rotatory instability Radial tunnel syndrome Posterior interosseous nerve syndrome	Olecranon bursitis Olecranon stress fracture Osteoarthritis Posterior impingement Triceps tendinopathy

Data from Kane et al. [1].

the elbow does bear a dynamic load due to gravity and muscle contraction during dynamic arm swing motion. This can lead to severe disabling symptoms such as pain, locking, and stiffness [2,3].

The elbow joint can be subdivided into the ulnohumeral joint, the radiocapitellar joint, and the proximal radioulnar joint. Arthritis mainly affects the radiocapitellar and ulnohumeral joints from an anatomical perspective. Cadaveric studies and biomechanical experiments have reported that the radiocapitellar joint bears a greater load, leading to more severe joint wear [4,5]. This can be attributed to the fact that the radiocapitellar joint—unlike the ulnohumeral joint, which only performs a hinge function—facilitates both hinge and rotational movements. This dual functionality increases the load on the articular cartilage.

The main pathology of degenerative arthritis involves degeneration of the articular cartilage. However, the lesions that lead to clinical symptoms are the formation of osteophytes around the joint and the contraction of the joint capsule. Osteophytes primarily occur in the apex of the coronoid process, the radial fossa, and the coronoid fossa on the anterior aspect, as well as in the apex of the olecranon and the olecranon fossa on the posterior aspect. It is also common for an osteophyte to fracture, forming a loose body. Osteoarthritis often involves posteromedial and anterior capsule contractures, which are significant contributors to the restriction of joint motion. A posteromedial capsule contracture can limit elbow flexion and compress the ulnar nerve, while an anterior capsule contracture can result in a flexion contracture of 10°–20°.

The main symptoms are pain and limited range of motion in the elbow joint, which gradually intensify as arthritis advances. Until the disease reaches its end-stage, pain typically manifests at the point of maximum extension (posterior pain) or flexion (anterior pain), and is often absent in the mid-range of motion. Pain during extension is a symptom triggered by the mechanical impingement of the olecranon apex and the olecranon fossa. In severe instances, this may hinder the ability to extend the arm in daily activities. Accompanied by ulnar neuropathy [6], progression of the condition may result in numbness of the fourth and fifth fingers, or even atrophy of the intrinsic finger muscles.

Plain radiographs and CT are helpful in the diagnosis. On lateral radiographs, anterior and posterior osteophytes and loose bodies can be observed. The joint space is generally preserved, except in instances of advanced arthritis. CT scans are particularly useful for preoperative

planning, as they allow for a more precise and straightforward observation of the location and size of osteophytes and loose bodies.

Conservative treatments for osteoarthritis of the elbow joint include NSAIDs, rest, lifestyle modification, physical therapy, and intra-articular steroid injection therapy. However, steroid injections should be used with caution due to the potential for systemic disorders and further soft tissue damage [7]. It is important to note that many patients' symptoms are related to occupational causes and often persist. If conservative treatments fail, surgical intervention is considered based on the patient's symptoms, functional needs, and the progression of the disease.

Representative surgical treatments for elbow joint osteoarthritis include arthroplasty and total elbow replacement. Arthroplasty is generally recommended for younger patients who experience pain only at the maximum range of extension and flexion, and do not report pain during mid-range joint motion. Open debridement is a conventional surgical approach. A notable example of this is the Outerbridge-Kashiwagi procedure, which involves a posterior approach to penetrate and enlarge the olecranon fossa and coronoid fossa, thereby expanding the space and eliminating bony impingement [8]. Ulnohumeral arthroplasty is a variation of this method, where the expansion of the olecranon fossa is performed concurrently with the removal of surrounding osteophytes and a capsulectomy. However, this method has limitations in identifying anterior structures and lesions in the ulnohumeral joint.

Total elbow replacement is a viable procedure for elderly patients suffering from severe osteoarthritis, but it is typically reserved for those with a limited range of motion. Generally, total elbow replacement for degenerative osteoarthritis is less common than for rheumatoid arthritis.

2) Gout

Gout is a condition characterized by the excessive production of monosodium urate, which is then deposited as crystals in joints or surrounding tissues, leading to inflammation. Acute gout primarily affects the first metatarsophalangeal joint, although it can also occur in the elbow joint. In fact, the elbow joint is affected in 20%–30% of all patients with this condition.

The primary complaint is often severe pain in a single joint, accompanied by swelling and redness around the joint. This necessitates differentiation from infectious diseases such as cellulitis, bursitis, and septic arthritis. Gout can be categorized into acute and chronic types, based on the nature of clinical manifestations. Acute gout is characterized by episodic symptoms in a single joint, which, over a period of intermittent symptoms, gradually progresses to chronic gout.

The diagnosis is confirmed when needle-shaped crystals, exhibiting negative birefringence, are observed under a polarizing microscope following joint fluid aspiration.

Acute gout is typically managed with conservative treatments such as immobilizing the affected joint with a splint, in conjunction with drug therapy. Common drug treatments involve the oral administration of colchicine, NSAIDs, and febuxostat, with steroids used sparingly. Surgical intervention may be considered when it is challenging to distinguish the condition from bacterial arthritis, or when the condition fails to respond to medical treatment. With the aid of an arthroscope, joint lesions can be readily observed, and accumulated urate and inflammatory synovium can be extracted. For chronic gout, it is advisable to implement ongoing drug treatment to regulate uric acid levels and prevent arthritis progression. Key medications include probenecid, which facilitates the excretion of uric acid, and allopurinol, which inhibits its production. These should be prescribed with consideration for the patient's kidney function and potential side effects.

2. Medial elbow pain

1) Medial epicondylitis

Medial epicondylitis, also known as golfer's elbow, is the predominant cause of medial elbow pain. However, it is relatively uncommon, with an incidence rate of approximately 0.5%, and it occurs 15%–20% as often as lateral epicondylitis. This condition occurs twice as frequently in males as it does in females.

The key areas implicated in medial epicondylitis are the medial conjoint tendon and its associated pronator teres and the origin of the flexor carpi radialis.

A standard physical examination for medial epicondylitis employs the golfer's elbow test. This test involves supinating the arm while the elbow is bent and the affected arm is clenched into a fist. Subsequently, the elbow and wrist joints are extended against resistance. This action may induce pain on the medial side of the elbow joint and the medial epicondyle. If pain is experienced, the test is considered positive.

Pain in the medial epicondyle could be attributed to structural damage to the ulnar nerve or ulnar collateral ligament. Therefore, it is crucial to evaluate these structures for any abnormalities prior to making a definitive diagnosis.

In 50% of patients with medial epicondylitis, symptoms of ulnar nerve involvement are also present, necessitating their differentiation. Conditions such as cervical or upper thoracic radiculopathy, or ulnar nerve compression, can produce similar symptoms. These neurogenic pains, often described as being pricked by several small needles or experiencing numbness, can serve as distinguishing factors in a patient's medical history. However, patients often struggle to accurately describe these sensations, which can lead to confusion. To differentiate cervical lesions, Spurling's test is required. In cases involving the posterior interosseous nerve or ulnar nerve, the area of entrapment and compression differs from the area of maximum tenderness in medial epicondylitis. If the Tinel sign is positive, this can provide a relatively clear distinction.

The treatment of epicondylitis can be divided into conservative and surgical approaches. The goal of these treatments is to reduce inflammation, distribute excessive load that is concentrated in one area by improving biomechanics, and ultimately regenerate tendons where tendinosis has occurred. Conservative treatment for epicondylitis boasts a success rate of approximately 90%. If epicondylitis remains unimproved after 3 to 6 months of treatment, it is considered refractory and surgical intervention may be indicated. Conservative treatment encompasses exercise therapy, physical therapy, drug therapy, bracing, extracorporeal shock wave therapy, percutaneous pie crusting of the tendon origin [9] polydeoxyribonucleotide injections [10], platelet-rich plasma (PRP) injections [11], autologous blood injections [12], and local corticosteroid injection therapy.

Various stretching methods serve as exercise therapy for the prevention and treatment of epicondylitis. For medial epicondylitis, maintaining a posture where the forearm is supinated, the wrist joint is extended, and the elbow joint is extended for 30 seconds to 1 minute proves effective. In the acute stage, a cold pack application and massage are followed by light stretching. As pain subsides, eccentric contraction exercises are then introduced.

Physical therapy encompasses techniques that utilize both superficial and deep heat. These methods are recognized as beneficial for managing acute or chronic refractory pain. However, the effectiveness of strong deep heat increases proportionally with the chronicity and refractoriness of the pain.

Injection therapy can be broadly categorized into trigger point injections, local steroid

injections, and PRP injections. Trigger point injection therapy, which involves injecting a local anesthetic into the palpated painful area, has long been in use. However, the results vary significantly depending on the operator, and it generally only provides short-term relief compared to other treatments. Local steroid injections are highly effective in the short term for treating refractory elbow pain. However, after 6 weeks, the therapeutic effect is typically less than that of other treatments, or the recurrence rate increases. Therefore, steroid injections should be used judiciously [13]. PRP injection therapy is designed to promote tissue healing and prevent the progression of tendinosis. Notably, it has been reported that various growth factors are concentrated at the injection site, which increases blood flow and promotes healing by attracting platelets to the damaged area.

Surgical treatment for medial epicondylitis should only be considered after ruling out diseases affecting other structures in the medial epicondyle region. It is typically reserved for patients who show no improvement after 3 to 6 months of non-surgical treatment. Furthermore, the presence of ulnar neuropathy also indicates the need for surgical intervention. Due to the potential risk of nerve damage, the primary approach to surgical treatment for medial epicondylitis is typically an open technique.

2) Medial collateral ligament injuries

Clinically, we often encounter medial collateral ligament injuries in individuals who are occupationally exposed to valgus overload, such as throwing athletes and gymnasts. From a biomechanical perspective, the stability of the elbow joint against valgus force is influenced by the degree of elbow joint flexion. Notably, the medial collateral ligament plays a crucial role in the flexion range of 20° to 120° [14].

Most patients with medial collateral ligament injuries report a gradual onset of pain in the medial elbow joint, a decrease in ball speed compared to previous performance, and difficulty in control [15]. Pain is most severe during the late cocking phase and early acceleration phase, with medial elbow pain followed by a "popping" sensation and medial collateral ligament rupture [15]. If mechanical symptoms such as elbow flexion contracture or catching are present, conditions like posteromedial impingement syndrome, radiocapitellar joint lesions, or an intra-articular loose body should be considered.

Generally, the elbow joint's range of motion is restricted in extension. If pain is present during terminal extension and is accompanied by a hard-end feeling, it may indicate posteromedial impingement syndrome. The carrying angle of the elbow joint is typically increased beyond the normal 11°–13°, often exceeding 15°. If tenderness is detected at the attachment site of the medial collateral ligament in the anteroinferior aspect of the medial epicondyle, it could suggest a medial collateral ligament injury. Similarly, if there is tenderness along the posteromedial side of the ulnohumeral joint and pain during terminal extension, posteromedial impingement syndrome should be considered.

On plain radiographs, it is essential to examine for bony avulsion or calcification of the medial collateral ligament, osteophyte of the olecranon, arthritic changes, and loose bodies. Calcification and olecranon osteophytes are the most frequently observed findings, appearing in more than 50% of cases [16]. A discrepancy of more than 0.5 mm compared to the unaffected side on the valgus stress view may suggest a complete or severe partial tear of the medial collateral ligament [17]. However, it has been noted that the medial joint gap is approximately 0.32 mm wider than the valgus stress test in the dominant arm of pitchers [18]. Therefore, caution is required, as many athletes exhibit valgus laxity without any specific symptoms. Currently, MRI

is acknowledged as an exceptional diagnostic tool for medial collateral ligament injuries, with its sensitivity increasing to 92% and specificity to 100% when combined with an intraarticular arthrogram [19]. Although it is possible to identify medial collateral ligament injuries through ultrasonography, the interpretation may vary depending on the expertise of the examiner.

In young athletes who have experienced a partial tear due to an acute injury, and who do not exhibit severe valgus instability, a systematic rehabilitation treatment that includes pronation-flexor strengthening exercises is recommended, provided symptoms improve after a minimum of 6 weeks of rest [20]. Steroid injections are not advised as they can potentially cause further damage to ligaments and tendons [21]. Surgical treatment may be an option for patients with chronic attritional tears that have not responded to at least 3 months of conservative treatment, as well as for pitching athletes who wish to return to their pre-injury exercise capacity in the event of carbuncle tears or highly partial tears [22]. Ensuring elbow stability in young throwing athletes is a crucial measure for preventing future injuries throughout their careers [23].

3. Lateral elbow pain

1) Lateral epicondylitis

Lateral epicondylitis, also known as tennis elbow, is characterized by tendinosis at the origin of the lateral epicondyle of the carpal joint extensors. This condition is one of the most common causes of elbow pain.

In cases of lateral epicondylitis, lesions are reported to occur 1 to 2 cm proximal to the attachment point of the extensor carpi radialis brevis (ECRB) tendon. However, lesions can also be found in the extensor digitorum communis, and are commonly known to occur in the proximal portion of the common extensor tendon.

Tenderness at the origin of the ECRB on the lateral epicondyle is typically present. Cozen's test, a standard physical examination, is conducted by passively flexing the wrist joint while the elbow joint is extended, or when the examiner strongly resists the patient's wrist extension. If this action induces pain, the test is considered positive.

Diagnoses that can be differentiated from lateral epicondylitis include radial canal entrapment syndrome, abnormal lesions within the lateral elbow joint, posterolateral instability of elbow, lateral triceps dislocation, lateral forearm cutaneous neuropathy, and radiculopathy caused by cervical arthritis.

In radial canal entrapment syndrome, the pain is typically more distal than that experienced in lateral epicondylitis. While Cozen's test may yield negative results, pain can be induced when resistance is applied during the extension of the thumb or index finger. To alleviate symptoms, the elbow joint can be bent at a 90° angle and the forearm placed in a neutral position. A splint can be used to secure this position, and movements such as supination or wrist extension against resistance can be performed. Generally, it has been reported that approximately 5% of cases involve both lateral epicondylitis and radial canal entrapment syndrome.

In cases of intra-articular lesions, such as an intra-articular loose body or radiocapitellar arthritis, the forearm is supinated, producing a painful sound at the end of extension. The point of maximum tenderness is typically located in the posterior part of the radiocapitellar joint, which helps distinguish it from lateral epicondylitis. Posterolateral instability may present similar symptoms, but it can be differentiated by the sensation of “giving way” or the presence of accompanying varus instability.

The treatment of lateral epicondylitis is similar to that of medial epicondylitis. This section

provides information specifically pertaining to lateral epicondylitis. For a broader understanding of lateral epicondylitis treatment, please refer to the section on medial epicondylitis treatment. Exercise therapy for lateral epicondylitis proves effective when a specific posture is maintained: the forearm is pronated, the wrist joint is flexed, and the elbow joint is extended. This position aids in lengthening the ECRB and extensor digitorum communis.

Surgical treatment for lateral epicondylitis is performed when there is no meaningful improvement even after about 6 to 9 months of non-surgical treatment. Surgical treatment for lateral epicondylitis is mainly performed through arthroscopic and open techniques.

2) Posterolateral rotatory instability

Posterolateral rotatory instability is a condition that arises when the ulna and the radial head rotate externally in unison, while the proximal radioulnar joint remains intact, leading to subluxation. This typically results from an injury to the lateral collateral ligament complex, which includes the lateral ulnar collateral ligament, radial collateral ligament, and annular ligament. This instability can also occur in the presence of a defect in the radial head or coronoid process.

In most patients, the symptoms are vague and there is almost no limitation of joint motion; thus, the diagnosis can be challenging unless it is suspected from the outset. A history of elbow dislocation, previous elbow joint surgery, and multiple steroid injections can be important clues to the diagnosis. Patients often complain of pain on the lateral side of the elbow joint, locking, catching, snapping, and instability, which most often occur around 40° of elbow flexion.

Screening tests for the stability of the lateral collateral ligament complex include the table-top relocation test [24] and the chair push-up test [25]. The table-top relocation test is performed by having the patient stand in front of a table, grasp the side edge, and execute a push-up with the forearm in a supinated position. When the elbow joint flexes to approximately 40°, the patient may experience pain and a sensation of elbow joint dislocation. The chair push-up test is considered positive if the patient shows hesitation in fully extending the arm or if subluxation occurs during extension. This is observed when the patient attempts to rise from a chair with the forearm supinated and arms spread wider than shoulder width.

The posterolateral pivot-shift test [26] is frequently utilized as a confirmatory test for posterolateral rotatory instability. During this test, the patient lies on their back with their arms extended overhead. The examiner, standing at the patient's head, flexes the patient's elbow joint while holding the upper arm with one hand and applying a valgus-supination force with the other, before slowly extending the elbow joint. Around 40° of flexion, the radial head subluxes posterolaterally, and a depression between the radial head and the capitellum can be palpated. However, confirming posterolateral rotatory instability in conscious patients using the posterolateral pivot-shift test is challenging. Most cases are initially suspected through other screening tests. Once surgical treatment is determined, posterolateral pivot-shift tests are typically performed under anesthesia in the operating room.

Most findings on plain radiographs are normal. However, in rare instances, a slightly widened humeral joint space or a posterior displacement of the radial head relative to the capitellum may be observed on lateral radiographs [27]. Although MRI is not essential for diagnosis, it is useful as a preoperative examination because it enables relatively accurate diagnoses in cases of severe injury to the lateral collateral ligament complex, and it can help differentiate other diseases that cause elbow joint pain.

While conservative treatments have been explored for posterolateral rotatory instability, they often prove unsuccessful, making surgical intervention the primary treatment option.

Conservative treatment may be considered when symptoms like pain or anxiety are mild. This could involve wearing an orthosis to limit forearm supination, elbow joint extension, and valgus force. Additionally, patient education to avoid actions or movements that induce pain, along with physical therapy that includes strengthening of the extensor muscles, may be attempted.

3) Osteochondritis dissecans

Osteochondritis dissecans of the elbow joint is a condition that often affects throwing athletes or gymnasts, and is one of the causes of lateral elbow joint pain [28]. This condition results from repetitive compression on the lateral side of the elbow joint, which damages the cartilage and subchondral bone of the radiocapitellar joint, leading to fragmentation and separation. It predominantly occurs in adolescent males and is frequently overlooked in diagnoses, which can lead to severe disability as they age.

The active radiocapitellar compression test serves as the provocative maneuver for the radiocapitellar joint. The test is deemed positive if it elicits pain in the elbow's lateral compartment when the patient rotates their forearm in both pronation and supination, while keeping their arm extended [29].

On plain radiographs, one can observe an irregular articular surface, local destructive lesions, or cystic changes of the capitellum, as well as a relative enlargement of the radial head in the late stages of the disease. Both ultrasonography and MRI play crucial roles in a prompt diagnosis.

The treatment method is determined based on the symptoms, radiologic findings, and the state of the bone fragment. If no loose body is present in the joint cavity, conservative treatments such as activity restriction, splinting, and NSAID administration may be implemented. Surgical intervention is considered when symptoms continue despite sufficient conservative treatment, or when osteochondral fragments are dislocated or detached.

4. Posterior elbow pain

1) Primary osteoarthritis

Refer to the section on primary osteoarthritis related to anterior elbow pain.

2) Olecranon bursitis

Olecranon bursitis is the most common type of superficial bursitis and is a common cause of posterior elbow pain and swelling [30]. This condition can also develop following an injury, due to crystal deposition such as gout, or as a consequence of systemic diseases such as rheumatoid arthritis, systemic lupus erythematosus, or uremia [31].

Olecranon bursitis can be categorized as either septic or aseptic. Patients with septic olecranon bursitis may report symptoms such as pain, swelling, and redness over the olecranon, and fever is observed in 20% to 86% of cases [32]. The diagnosis is confirmed by identifying the pathogen in the bursal fluid culture. Ultrasonography can be beneficial in detecting fluid retention in the early stages and in guiding needle aspiration. MRI is useful for distinguishing this condition from osteomyelitis or septic elbow arthritis. Septic olecranon bursitis can generally be effectively managed with antibiotics, and surgical treatment may be considered for cases that are resistant to other treatments.

Conversely, patients with aseptic olecranon bursitis may exhibit swelling over the olecranon, absent any signs of infection [31]. Aspiration of the bursa, while potentially leading to complications such as infection, is only undertaken when the diagnosis is unclear or to alleviate

symptoms in cases that are resistant to treatment [30].

3) Distal triceps tendon injuries

Distal triceps tendon injuries are very rare. In the early stages of such an injury, pain and swelling around the elbow joint often occur, complicating the process of making an accurate diagnosis. As time progresses, this injury can lead to a limited range of motion in the elbow joint or weakness in the extensor muscle [33]. Therefore, if this type of injury is suspected, a cautious approach is necessary. The most common cause of these injuries is the eccentric contraction of the triceps, which typically happens during a fall on an outstretched hand. This type of injury is particularly prevalent among males and soccer players.

A physical examination should assess the active extension of the elbow joint and inspect for any palpable defects in the proximal olecranon. The modified Campbell Thompson test is a useful diagnostic tool. In this test, the elbow joint is flexed to 90° in the prone position, with the forearm and hand relaxed. The examiner then compresses the triceps while the muscles are in a relaxed state. If the elbow joint extends, this indicates either normal function or incomplete damage. Conversely, a lack of movement in the elbow joint suggests a complete tear.

A plain radiograph should be used to check for any accompanying injuries or fractures. The flake sign, characterized by the observation of a small avulsion bone fragment on the posterior side of the olecranon, is useful for diagnosis [34]. A CT scan can verify the presence and location of small avulsion bone fragments and any other accompanying fractures. MRI is very useful for diagnosing a triceps tear, as well as confirming the location and extent of the damage.

Conservative treatment is an option for patients with a partial tear who do not have limitations on active extension, as well as for inactive elderly patients. In these cases, the elbow joint is stabilized using a brace or splint. Typically, pain subsides approximately 3 months post-injury, at which point all daily activities become feasible. However, if conservative treatment proves ineffective, or in the event of a complete rupture, operative treatment becomes necessary.

Conclusion

The elbow joint, with its wide range of motion, plays a crucial role in performing various movements in our daily lives. Consequently, elbow pain can significantly disrupt everyday activities. Given the diverse causes of elbow pain, it is essential to have a precise understanding of the structures that trigger this discomfort.

The patient's medical history plays a pivotal role in diagnosing elbow pain, as it aids in revealing the mechanism of injury. It also supplies crucial information necessary for achieving an accurate diagnosis through a comprehensive physical examination, supplemented by imaging studies. A systematic approach to assessing the characteristics, onset, and duration of pain, as well as associated symptoms, is essential for making a diagnosis.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Recent Nonoperative Treatment of Elbow Pain

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Elbow pain; Tennis elbow; Elbow tendinopathy; Cubital tunnel syndrome; Conservative treatment

Pain originating from the elbow can be due to issues affecting the joint itself or the structures surrounding it. These structures include the medial and lateral epicondyles, associated ligaments, the origins of wrist flexor and extensor muscles, the olecranon bursa, the distal biceps tendon, and the radial and ulnar nerves. Pain that appears to originate from a different location may actually be referred pain, potentially stemming from the neck (cervical radiculopathy) or the shoulder. Among complaints related to the elbow, lateral elbow pain is the most frequently reported. This pain could originate from the lateral epicondyle, the radiohumeral joint, or it could be referred pain from other areas. Medial elbow pain is the second most common complaint, often resulting from issues with the medial epicondyle or the ulnar nerve as it travels through the cubital tunnel. The biceps tendon is frequently the cause of anterior elbow pain. Patients who report swelling in the elbow are often experiencing olecranon bursitis. These conditions can often be effectively managed through conservative treatment. The aim of this article is to provide a structured approach to addressing patients with elbow pain, by detailing the common causes of such discomfort and exploring effective nonsurgical treatment options.

Introduction

Elbow pain can originate from various conditions that affect the joint itself, the surrounding soft tissues, or even from a different part of the body such as the neck, shoulder, or wrist [1]. Frequent culprits of pain include the joint and soft tissue structures like the attachment points of the epicondyles (both medial and lateral), the olecranon bursa, and the nearby radial, median, and ulnar nerves. The complex anatomy of the elbow joint, coupled with the wide array of potential causes, makes identifying the precise cause of elbow pain a challenging task [2–4]. Similar to addressing other musculoskeletal issues, the crucial steps in diagnosing elbow pain involve delving into the patient's history to understand the injury's mechanism and movements that worsen the pain, along with a focused physical examination. The patient's occupation and leisure activities can also provide valuable insights for the diagnosis. This article provides a systematic guide for approaching patients with elbow pain, by outlining the most typical sources of discomfort and exploring effective nonsurgical treatment options.

Main Text

1. Anatomy

The elbow joint is formed where the lower part of the humerus connects with the radial head

and ulna bones. Flexion and extension occur at the ulnohumeral joint and are driven by the biceps and triceps muscles, respectively. The normal range of motion is 0° (full extension) to 135° (full flexion).

Despite primarily being a hinge joint, the elbow possesses a unique capability to rotate the lower arm in pronation and supination. These distinct movements, combined with a wide array of dynamic forces during physical exertion, make the elbow and its structures susceptible to significant injuries, especially from repetitive actions. Rotation in pronation and supination takes place at the radiohumeral and proximal radioulnar connections within the elbow joint. The biceps muscle handles supination, while the pronator teres muscle is responsible for pronation. This enables the elbow to rotate between 0° and 180°. The elbow bears the weight generated by both gravity and muscle contractions during the dynamic motion of swinging the arm [5]. Understanding the anatomy and the forces involved in movement can assist in making diagnoses [6].

Several ligaments provide support to the elbow joint, with the ulnar collateral or medial group of ligaments being of particular clinical significance due to their contribution to valgus stability [7]. The anterior bundle of ulna collateral ligament, which runs from the medial humeral condyle to the coronoid process of the ulna, serves as the primary resistance against valgus stress. Another significant structure is the annular ligament, which is part of the lateral collateral ligament complex and plays a key role in stabilizing the proximal radioulnar joint. Due to its complex and exposed nature, the elbow can suffer severe fractures resulting from high-energy traumatic events, with disruptions to the joint's surface, damage to soft tissues, and injuries to nerves and blood vessels [8].

There are three main nerves around the elbow joint: the ulnar nerve, the median nerve, and the radial nerve. The ulnar nerve traverses a narrow space called the cubital tunnel, which is formed by the medial epicondyle, the olecranon, and a retinaculum (Osborne fascia) continuing distally with the arcuate ligament. The radial nerve does not pass through a specific tunnel or canal like the ulnar nerve. Instead, it courses through a groove in the humerus, which provides some protection to the nerve as it runs behind the humerus. The median nerve runs between the pronator teres and brachialis muscles, and it is sometimes difficult to distinguish from the muscles because of the compactness of the muscles and the minimal amount of fat [6].

The biceps brachii attaches to the radial tuberosity through a tendon that passes over the anterior aspect of the elbow joint and is mainly considered a strong elbow flexor muscle. The biceps tendon is a narrow tendon made up of the long and short bicipital heads, and it attaches to the posterior part of the radial tuberosity. Rotation of the radius along its longitudinal axis at the radiocapitellar joint can result in forearm supination [9].

The olecranon bursa is a subcutaneous sac sparsely lined by synovial cells, and normally no detectable fluid is present. It lies between the skin and a firm base that includes the triceps tendon and the back of the olecranon process. Due to its proximity to the skin and the support it receives from a firm base, it is susceptible to traumatic bursitis resulting from repetitive trauma, and septic bursitis, which is caused by skin bacterial infections. These conditions are relatively common [9].

2. Imaging

The initial evaluation of acute injuries often relies on plain radiography, which is particularly effective in revealing bone injuries, soft tissue swelling, and fluid accumulation within joints. Plain radiography also plays a role in assessing chronic conditions like enthesopathy, bone spurs,

and osteochondral diseases [10]. Many chronic elbow issues are diagnosed based on a clinical evaluation, and imaging can be employed to confirm the diagnosis before considering further steps or referrals. MRI is the favored imaging modality for patients with chronic elbow pain [11,12]. MRI excels at detecting abnormal conditions such as bone marrow edema, tendinopathy, nerve entrapment, and joint effusions. In instances where there is no effusion, magnetic resonance arthrography may be performed to identify ligament tears, osteochondral defects, or loose bodies [10,12].

Unlike MRI, CT plays a limited role in evaluating chronic elbow pain. However, it may outperform MRI in identifying soft tissue calcifications, such as myositis ossificans or intra-articular bodies. Musculoskeletal ultrasonography relies more on the operator's skill than MRI, yet it offers a cost-effective and dynamic assessment of commonly injured structures. The elbow is well suited for ultrasonographic evaluation because the majority of structures are superficial and it is possible to obtain long- and short-axis images of almost every anatomic structure [13]. When performing an ultrasonographic evaluation of the elbow joint, a careful investigation is required depending on the area. The distal biceps tendon, brachialis tendon, median nerve and anterior interosseous nerve should be evaluated anteriorly; the common extensor tendon origin, lateral collateral ligament, radial nerve and posterior interosseous nerve laterally; the common flexor tendon origin and medial collateral ligament medially; and the triceps tendon and ulnar nerve posteriorly [13]. Ultrasonography is less expensive than MRI and, when performed skillfully, exhibits a sensitivity of 64% to 82% in diagnosing medial and lateral elbow tendinopathy, in contrast to MRI's sensitivity of 90% to 100% [12].

Electrodiagnostic studies, including nerve conduction studies and electromyography, are beneficial for confirming the diagnosis of peripheral compressive neuropathy and ruling out conditions such as plexopathies and cervical radiculopathies. However, because it takes time for compressive or traction neuropathy to produce positive results in electrodiagnostic studies, there is a risk of false-negative results if testing is performed before symptoms have persisted for 6 to 8 weeks [10,14].

3. Etiology

Numerous common causes of elbow pain are related to the surrounding structures, such as epicondylitis (inflammation or degeneration of underlying tendons), olecranon bursitis, nerve entrapment, and referred pain. Conditions that affect the entire body (like rheumatoid arthritis) usually affect multiple joints and can be identified through a thorough assessment of a musculoskeletal history and physical examination. However, oligoarticular involvement can occur, as in seronegative spondyloarthritis.

Individuals with issues specifically related to the elbow typically present with complaints of pain (like in cases of epicondylitis or tendinopathy), swelling (as seen in olecranon bursitis), or a restriction in motion (such as after a joint injury).

4. Lateral elbow pain

Lateral elbow pain is a primary reason for medical consultations concerning non-traumatic elbow conditions. The most prevalent diagnosis is a tendon-related ailment known as lateral epicondylitis, commonly referred to as “tennis elbow.” Nonetheless, several pathological issues can resemble lateral epicondylitis, such as intra-articular plica, osteochondritis dissecans, radiocapitellar arthritis, or posterolateral rotatory instability. To differentiate these diseases, certain symptoms and diagnostic tests can be considered. For instance, patients with intra-

articular plica may report clicking sensations within the elbow joint, and imaging tests can confirm the presence of the plica. In cases of osteochondritis dissecans, imaging tests can identify loose fragments of bone or cartilage within the joint. For radiocapitellar arthritis, X-ray images may reveal arthritic changes such as joint space narrowing. Finally, patients with posterolateral rotatory instability may experience a sense of joint instability, and a stress test can be useful in these cases [15].

Each year, approximately 1% to 3% of the population experiences lateral epicondylitis, and despite its association with tennis, only a small fraction (5% to 10%) of tennis players actually develop this condition [16]. Most patients with lateral epicondylitis are in their 30s and 40s, and they typically develop lateral epicondylitis due to occupational factors rather than recreational pursuits [17]. The lateral side of the elbow is affected four to ten times more frequently than the medial side of the elbow [18]. The lateral epicondyle of the humerus serves as the shared origin for the active supinators of the forearm, including the extensor carpi radialis brevis. A physical examination reveals the most pronounced tenderness approximately 1 cm below the epicondyle, where the extensor carpi radialis brevis originates. Patients often experience pain and reduced strength when gripping against resistance, as well as during wrist supination and extension [18].

Nonoperative treatment is the primary approach for medial and lateral epicondylitis [2]. It has been suggested that a significant majority, ranging from 85% to 90%, of patients show a positive response to nonsurgical interventions [19]. However, some series have presented more modest outcomes, indicating that around 40% of patients with lateral epicondylitis still experience some lingering discomfort [20]. Moreover, there is a viewpoint suggesting that no treatment beyond addressing symptoms is necessary, given that this condition is typically benign and self-limiting, frequently accompanying middle age. A recent analysis of data from randomized controlled trials did not show any superiority of nonsurgical treatments over placebo. These studies investigated a variety of interventions, including injections of corticosteroids, platelet-rich plasma (PRP), autologous blood, hyaluronic acid, or glycosaminoglycan, as well as different therapies such as shock wave therapy, laser, ultrasound, iontophoresis, topical agents, and oral naproxen [21].

Physical therapy is classically the first-line treatment for lateral epicondylitis. Stretching exercises are among the most widely used, despite sparse published data on their efficacy [22]. A meta-analysis did not provide definitive conclusions about the use of stretching exercises [23]. Conversely, mobilization involving joint movements, Mill's manipulation, or regional mobilization may be beneficial [24].

For symptom relief, a fundamentally important approach is modifying one's activities to avoid activities that trigger symptoms. Studies have observed that tennis players who employ a two-handed backstroke have a lower likelihood of developing tennis elbow, likely due to altered biomechanics that dissipate forces upon ball contact [25]. Similarly, other equipment and technique adjustments can contribute to resolving symptoms.

A three-phase treatment approach has been proposed for epicondylitis. The initial phase involves modifying activities to prevent triggers and applying ice multiple times daily. NSAIDs might be used to alleviate any accompanying elbow synovitis. Nighttime splints and corticosteroid injections could be considered [26], and counterforce bracing can be employed during this phase to restrict muscle contractions. However, the effectiveness of these treatment options, including injections, bracing, therapy, and oral/topical medications, has been debated, and their efficacy remains uncertain [26,27].

The second phase entails commencing a rehabilitation regimen once acute symptoms have subsided, and painless motion in the wrist and elbow has been restored. This involves initiating a

program of isometric exercises and stretching, followed by the integration of resistive exercises and activities aimed at enhancing performance for sports or work-related tasks [26]. The third phase constitutes a maintenance period, encompassing adjustments to equipment and techniques for sports or work, along with ongoing conditioning to prevent symptom recurrence [26].

Various substances have been proposed as injections to treat lateral and medial epicondylitis. However, the evidence published to date is inconsistent and inconclusive, making it challenging to provide clear recommendations for injections as a treatment for lateral epicondylitis [21,28].

Botulinum toxin injections have been suggested for lateral epicondylitis, with some series demonstrating benefits, though not consistently across all cases. Muscle weakness is a possible side effect [29]. Autologous blood injections have also been proposed as potentially beneficial for treating epicondylitis [30]. PRP injections have been used, yielding mixed results—promising according to some studies, but less so in others [25–27]. Additionally, polydeoxyribonucleotide injections are a consideration, particularly since a combination of polydeoxyribonucleotide injections and exercises to strengthen the extensor muscles showed superior improvement in functional scores when compared to exercises alone or exercises combined with extracorporeal shock wave therapy (ESWT) [31].

A study focusing on tendinopathy cases found that both PRP and corticosteroid injections led to improvements in patient symptoms. The study concluded that PRP could serve as a safe and effective alternative to corticosteroids, even over extended periods, to lessen both local and systemic effects associated with corticosteroid injections [32,33]. This treatment strategy could be especially advantageous for patients with diabetes, as PRP injections have been shown to be well-tolerated and safe [34]. A recent case-control study also demonstrated that the combination of pie crusting and corticosteroid injections for lateral epicondylitis yielded superior results compared to corticosteroid injections alone [35].

5. Medial elbow pain

Medial elbow pain is the second most commonly reported elbow-related issue. It often originates from either the region near the medial epicondyle or the ulnar nerve as it passes through the cubital tunnel. Similar to lateral epicondylitis, pain associated with medial epicondylitis is highly localized and intensifies during activities that engage the wrist flexors and pronators, such as lifting or repetitive forearm and wrist movements. Pain originating from the ulnar nerve is indicated by sensations radiating into the ulnar side of the hand and accompanying sensory symptoms (and occasionally motor symptoms) in the fourth and fifth fingers.

Medial epicondylitis is notably less frequent than lateral epicondylitis and typically occurs in athletes or individuals who engage in activities requiring repetitive valgus stress, elbow flexion, and repetitive wrist flexion and pronation. It involves tendinopathy of the common flexor tendon, usually affecting the flexor carpi radialis and pronator teres tendons [1]. Patients often describe a gradual onset of pain at the medial elbow, sometimes accompanied by grip-strength weakness. The point of most intense tenderness typically is the insertion of the flexor-pronator mass, situated 5 to 10 mm distal and anterior to the medial epicondyle. The most sensitive sign during a physical examination is pain experienced when resisting pronation. It is also usually possible to replicate the pain with resisted wrist flexion [36].

The core approach to managing medial epicondylitis centers around conservative treatment. This involves using anti-inflammatory medications, splinting, and occasionally steroid injections to provide sustained relief for the majority of patients. Of note, steroid injections can be precisely

administered under ultrasound guidance.

ESWT may offer pain relief for certain patients. Stimulating the affected tendon with electrical impulses can promote angiogenesis, tendon healing, and provide short-term analgesia [37]. Lee et al. compared the outcome of ESWT or steroid injections in patients with medial or lateral epicondylitis. They reported worse clinical pain scores at 1 and 2 weeks with ESWT, but better patient satisfaction at 8 weeks [38]. However, another study reported favorable clinical results with ESWT in only 7 of 30 patients at 1-year follow-up, which was notably worse than the results from patients diagnosed with lateral epicondylitis who underwent similar treatment [39]. At this point, definitive recommendations exist for the use of ESWT for medial epicondylitis, including the treatment duration and stimulation protocol [40].

When noninvasive modalities achieve unsatisfactory results, a corticosteroid injection is often effective in reducing medial elbow pain. The corticosteroid is injected into the peritendinous and synovial tissues, rather than into the tendon itself [41]. Similar to oral anti-inflammatory medications, corticosteroids can reduce the surrounding synovitis and resultant pain [40]. A prospective study of steroid injections in 60 elbows diagnosed with medial epicondylitis reported an acute improvement in pain for 6 weeks after the injection but no difference at 3 months [42].

In the study examining the efficacy of PRP injections for lateral and medial epicondylitis, the treatment was found to be significantly effective, suggesting it could be a viable alternative to surgical intervention. Beyond its clinical efficacy in promoting structural healing, PRP has been associated with decreased narcotic usage, improved sleep, and a reduction in pain perception [43]. Consequently, it can be inferred that PRP injections are not only effective in restoring the structure and function of the lateral or medial epicondyles, but also in enhancing quality of life [44].

If nonoperative treatments do not yield satisfactory results, excising the affected tendon origin and reattaching it typically results in successful outcomes.

Cubital tunnel syndrome is a condition characterized by compression or traction of the ulnar nerve as it passes through the cubital tunnel in the inner elbow. It is the second most common compressive neuropathy affecting the upper limbs, following carpal tunnel syndrome [10]. Approximately 60% of patients with medial epicondylitis also experience compressive ulnar neuropathy [3]. These patients typically have recurrent pain in the medial elbow, often accompanied by numbness and tingling sensations along the ulnar side of the forearm and hand, extending to the ring and little fingers. If not addressed over an extended period, this condition can result in weakness in the hand's intrinsic muscles [3]. To rule out other compressive neuropathies, a comprehensive assessment of the upper limbs and cervical spine is necessary [17].

Conservative treatment should be the first approach when dealing with this syndrome, before considering surgical intervention. The severity of cubital tunnel syndrome can be categorized into three levels [45]. Mild dysfunction involves occasional paresthesia and subjective weakness. Moderate dysfunction presents with intermittent paresthesia and quantifiable weakness, while severe dysfunction is characterized by persistent paresthesia and measurable weakness. For patients with mild to moderate cubital tunnel syndrome, it is recommended to avoid prolonged elbow flexion during work and to use elbow extension splints during sleep. When applying the splint, care should be taken to prevent the forearm from being positioned in pronation, as this could potentially worsen the symptoms. To effectively limit elbow flexion while sleeping, towels or cushions can be secured around the elbow. The use of local steroid injections into the cubital tunnel is not widely supported due to their less favorable response [46,47]. A study examined

the effectiveness of steroid injections on 12 ulnar nerves by dividing patients into two groups: one that received treatment involving nighttime and occasional daytime splinting, and another that received the same splinting along with a local steroid injection. Mild symptoms were adequately addressed with splinting alone, and the inclusion of the steroid injection did not lead to any additional improvement [48]. Typically, conservative measures are pursued for a period of 3 months before surgical intervention is contemplated.

6. Anterior elbow pain

Pain in the anterior elbow often originates from the biceps tendon. Although distal biceps tendon ruptures are uncommon and make up only 3% of all tendon ruptures, distal biceps tendinopathy is more frequently encountered [49]. This condition follows a gradual pattern of anterior elbow pain, particularly during resisted flexion and supination movements of the forearm. Individuals with biceps tendinopathy may experience vague discomfort in the elbow's anterior region. Their medical history often includes repetitive elbow flexion coupled with forearm supination or pronation, as seen in activities like dumbbell curls. During a physical examination, a healthy biceps muscle belly should display a piston-like movement during passive supination and pronation of the forearm when the elbow is flexed at a 90° angle. The lack of this movement suggests a complete tear. Pain in the antecubital fossa is often recreated by resisted supination. To evaluate the tendon's continuity and changes in size, MRI or musculoskeletal ultrasonography can be utilized [50].

Surgery can sometimes be avoided by conservative management of partial or complete biceps ruptures; however, untreated complete distal biceps ruptures can result in an estimated loss of 40% to 60% of supination power and 30% of flexion power. Nevertheless, some patients may adapt well and even regain substantial strength during supination over time [51]. While functional challenges might endure, a study has reported that there could be a notable prevalence of lingering pain and weakness even after 4.5 years of follow-up after nonoperative treatment [52]. Conversely, other studies have shown that many patients adjust well, resulting in high rates of satisfactory outcomes and only a slight decrease in supination strength, as observed over a median follow-up period of 38 months [4]. Injection therapy around the distal biceps tendon can be considered. However, performing injection therapy with PRP or glucocorticoids around the distal biceps tendon and bicipitoradial bursa is complicated due to the lack of clear palpable markers, the complex anatomy of the distal biceps, and the close proximity of critical structures such as the brachial artery, median nerve, and posterior interosseous nerve [53].

7. Posterior elbow pain

Olecranon bursitis, the most common type of superficial bursitis, often results in posterior elbow pain and swelling [54]. This condition can present in two forms: septic or aseptic. Those suffering from septic olecranon bursitis typically experience pain, swelling, warmth, and redness over the olecranon, with approximately half also displaying symptoms of fever. Diagnosis is confirmed through an examination of the fluid within the bursa [55]. In contrast, aseptic olecranon bursitis may be associated with a history of minor elbow trauma, a non-tender mass over the olecranon without redness or warmth, limited range of motion, or absence of other infection-related symptoms [56]. Given the potential complications associated with bursal fluid aspiration, such as infection, this procedure should be reserved for instances when the diagnosis remains uncertain or when symptom relief is sought for persistent cases [54].

Aseptic olecranon bursitis may primarily concern the patient from a cosmetic perspective,

causing minimal to no discomfort, and it often resolves on its own. When the bursal swelling is neither tender nor excessively tense, management is symptomatic, involving the use of NSAIDs, compression, and precautions to prevent further injury. For acute hemorrhagic bursitis, aspirating the bursa, applying a compression dressing, and using ice can decrease the likelihood of developing chronic bursitis. In cases of aseptic olecranon bursitis with a significant, tense, and inflamed bursa, aspiration along with a steroid injection (after ruling out infection) has been shown to speed up symptom resolution. An alternative method involves aspirating the olecranon bursa and then injecting corticosteroids into the elbow joint, which has demonstrated favorable results with fewer complications [57]. After aspiration and steroid injection, employing a compression dressing and a brief period of limited movement could be beneficial. However, repeated steroid injections for aseptic olecranon bursitis have been linked to triceps rupture and should be avoided.

Managing septic bursitis involves the use of antibiotics targeted at penicillinase-producing *Staphylococcus* bacteria, along with splinting, warm soaks, and bursa drainage. The drainage can be accomplished via daily needle aspiration until the fluid is sterile [58]. Nevertheless, some cases might require an open incision and drainage, especially if the infection persists or becomes refractory [59].

Conclusion

Since conservative treatment is effective for numerous causes of elbow pain, it is crucial to administer adequate nonoperative treatment before contemplating surgical intervention.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Review Article

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The Recent Surgical Treatment of Elbow Pain

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Elbow; Tennis elbow; Elbow tendinopathy

The review article explores recent advances in the surgical treatment of elbow pain, a common ailment that can significantly impair daily functioning. With a surge in elbow-related conditions such as tennis elbow, osteoarthritis, and nerve compression disorders, the necessity for surgical approaches has become paramount. This article provides an overview of the cutting-edge procedures now available, including minimally invasive arthroscopic surgery. These modern methods have been shown to significantly reduce recovery times and improve overall patient outcomes. The combination of surgical management and targeted rehabilitation ensures a comprehensive and personalized treatment plan for patients with various elbow pathologies. This article aims to shed light on these recent surgical interventions and their potential for advancing the management of elbow pain, emphasizing the ongoing trend toward precision, efficiency, and patient-centered care.

Introduction

With recent trends toward global aging and the increase in the sports-playing population, there has been a rise in elbow pain due to degenerative elbow diseases and sports injuries [1,2]. Minor elbow injuries can often be managed with conservative treatment, but in cases of reduced joint range due to stiffness, persistent chronic pain, neurologic deficit and instability, surgical treatment is often necessary [3]. An accurate differential diagnosis is paramount, and surgical indications need to be considered, especially for chronic elbow pain [4–6].

Lateral Epicondylitis

Lateral epicondylitis, or tennis elbow, is a common overuse injury that can significantly impact a patient's quality of life. While conservative treatment is the first line of management, some individuals may require surgical intervention when non-surgical options fail to provide relief. The extensor carpi radialis brevis (ECRB) tendon is considered to be the main anatomic structure. It commonly occurs due to repetitive wrist and forearm motions, causing microtears in the tendon, leading to pain and tenderness on the outer aspect of the elbow. While most cases of lateral epicondylitis can be successfully managed with conservative treatments, such as rest, physical therapy, and anti-inflammatory medications, some patients may not respond adequately to non-surgical approaches.

1. Indications

Surgical intervention is typically considered when conservative treatment has failed to provide relief, and patients continue to experience debilitating symptoms that significantly impact their daily activities after appropriate non-surgical management for 3 months.

2. Surgical options and outcomes

Surgical options include arthroscopic ECRB release (Fig. 1), open release with or without ECRB repair and percutaneous tenotomy [7]. Both arthroscopic and open surgical procedures for lateral epicondylitis have shown satisfactory outcomes in relieving pain and restoring function. In the recent literature, the arthroscopic treatment of lateral epicondylitis has shown favorable results, with reduced postoperative pain and faster recovery compared to open procedures. Most patients experience significant improvement within several weeks after surgery, with full recovery taking several months. Rehabilitation, including physical therapy, stretching, and strengthening exercises, is essential for restoring elbow strength and range of motion (ROM).

The surgical approach should be chosen based on the severity of the condition, patient-specific factors, and the surgeon's expertise. A prompt diagnosis, appropriate surgical planning, and thorough rehabilitation are essential for achieving successful outcomes. Further research and long-term follow-up studies are necessary to optimize surgical techniques and improve patient satisfaction in the management of lateral epicondylitis.

3. Complications and potential risks

Due to the anatomical proximity of the ECRB tendon and the lateral collateral ligament (LCL) complex, care must be taken during surgery to avoid unnecessary damage to the LCL complex [8,9]. In cases of LCL complex insufficiency, which is often found as a concomitant lesion in patients with chronic recalcitrant tennis elbow, if instability is observed before surgery, it may be possible to perform LCL complex repair or reconstruction during surgery [10,11].

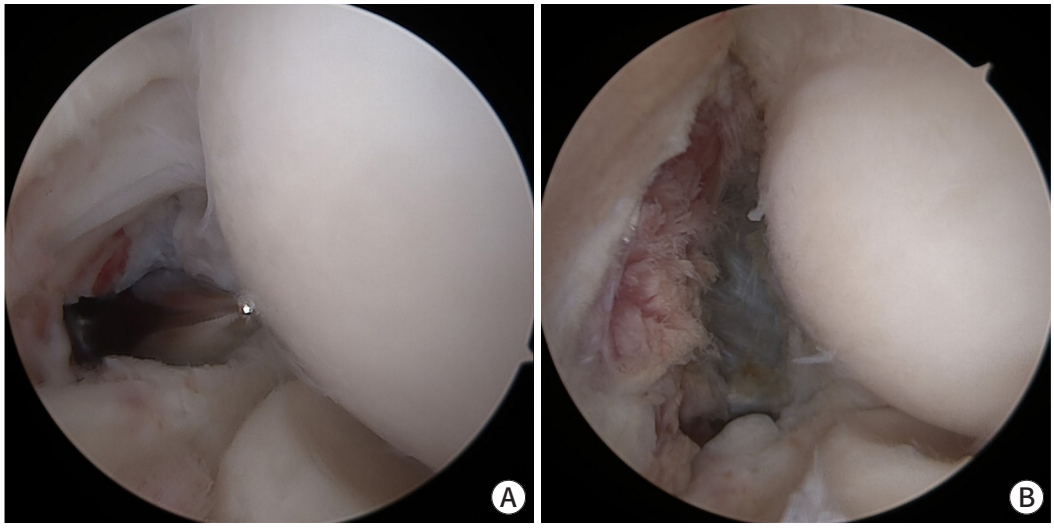

Fig. 1. Arthroscopic extensor carpi radialis brevis (ECRB) release. A lateral capsular tear due to significant ECRB common extensor group degeneration can be observed, which is a sign of chronic recalcitrant tennis elbow (A). ECRB release with preservation of the other extensor group of the extensor carpi radialis longus is possible using arthroscopic technique (B).

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Medial Epicondylitis

Medial epicondylitis, or golfer's elbow, is an inflammatory condition that affects the tendons of the forearm muscles, which are the wrist flexor and pronator, attached to the medial epicondyle of the elbow. The repetitive use of these muscles can lead to microtears and degeneration of the tendon, causing pain and tenderness on the inner aspect of the elbow. While most cases of medial epicondylitis respond well to conservative treatments, such as rest, physical therapy, and anti-inflammatory medications, surgical intervention may be necessary for patients who do not achieve satisfactory relief.

1. Indications

Surgical treatment is typically considered when relief is not achieved after more than 3 months of conservative treatment, and patients continue to experience significant pain and functional limitations. In rare cases, ulnar nerve symptoms may also be present, for which surgical management should be considered.

2. Surgical options and outcomes

As with lateral epicondylitis, both open and arthroscopic procedures for medial epicondylitis have shown favorable outcomes in relieving pain and restoring function. Arthroscopic procedures can have technical dependency due to limited visualization from the lateral viewing portal [12]. The main aim is to release the flexor tendon with the pronator group of the elbow. The surgical technique includes cortical bone resection and lengthening using pie crusting technique after release of the flexor tendon group (Fig. 2). Most patients experience significant improvement within several weeks after surgery, with full recovery taking several months.

3. Complications and potential risks

Due to the close anatomical proximity to the ulnar nerve, there is always the possibility of

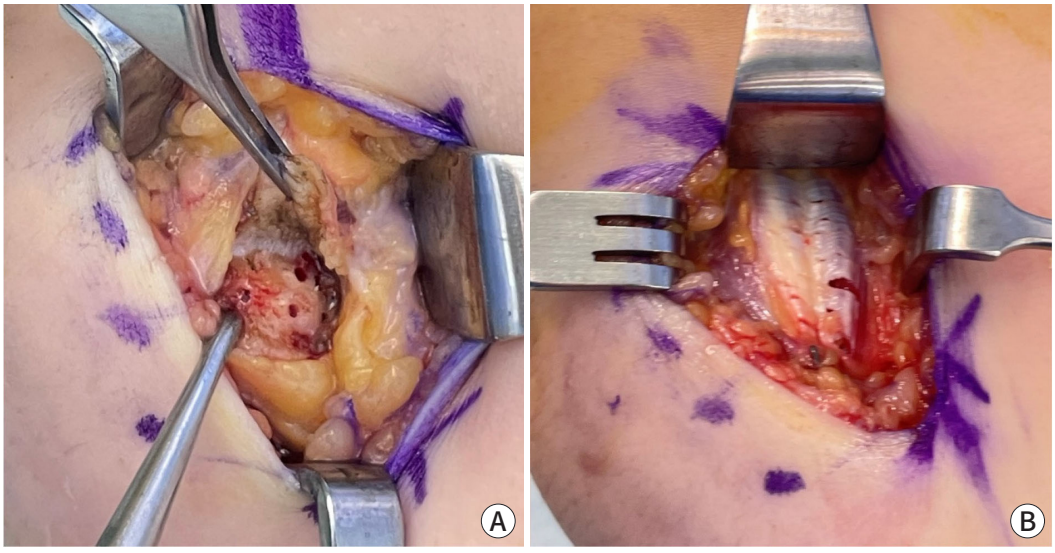

Fig. 2. Open flexor tendon release and repair with lengthening for surgical treatment of medial epicondylitis. The pathologic target anatomy was reflected and debridement using curettage of the bone-tendon interface was performed (A). The reflected flexor and pronator group was repaired using transosseous fixation (B).

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nerve damage; therefore, it is essential to routinely check the course of the nerve during surgery. During incision surgery, the course is verified, and decompression is performed as needed if symptoms of pressure on the spinal nerve are suspected. During the release, care should also be taken to avoid damaging the ulnar collateral ligament [13].

Pathologic Plica Syndrome

Elbow plica syndrome is a condition in which the synovial folds within the elbow joint become inflamed and hypertrophic, leading to painful symptoms and functional impairment [14]. When conservative treatment fails to provide relief, surgical intervention is often necessary [15]. Two common surgical approaches for elbow plica excision are open surgery and arthroscopic plica excision. This section compares these two techniques to help orthopedic surgeons make informed decisions regarding the optimal surgical approach for patients with elbow plica syndrome [16].

1. Indications

Surgical excision of pathologic plica is typically considered when the elbow plica is large and fibrotic, which could cause plica snapping or be associated with other intra-articular pathologies. This allows a more extensive view of the joint and facilitates concurrent management of any coexisting conditions [16].

2. Surgical options and outcomes

Both open surgery and arthroscopic plica excision are effective treatment options for elbow plica syndrome, each with its advantages and disadvantages [17]. Open surgery allows more direct visualization of the antero-lateral plica and any additional abnormalities, potentially enabling improved resolution of symptoms. Patients typically experience immediate relief from preoperative symptoms, with progressive improvement over several weeks. Arthroscopic plica excision is preferred for both anterolateral and posterolateral plica with significant intra-articular pathologies. This is a minimally invasive procedure that enables better preservation of the surrounding tissues (Fig. 3). Arthroscopic plica excision reduces surgical trauma, leading to a quicker recovery and less postoperative pain.

The choice of surgical approach should be based on the size and extent of the plica, the presence of concomitant intra-articular pathologies, surgeon expertise, and patient-specific factors. A thorough evaluation and informed decision-making process will lead to successful outcomes and improved patient satisfaction. Further research and comparative studies are warranted to refine surgical techniques and improve patient outcomes in the surgical treatment of elbow plica syndrome.

3. Complications and potential risk

The pathologic plica is primarily located around the radial head, extending from the front to the back. In particular, when excising the front plica, one must be fully aware of the course of the radial nerve to prevent injury to the radial nerve during surgery [18].

Elbow Osteoarthritis

Elbow arthritis is a progressive degenerative condition that affects the articular surfaces of the

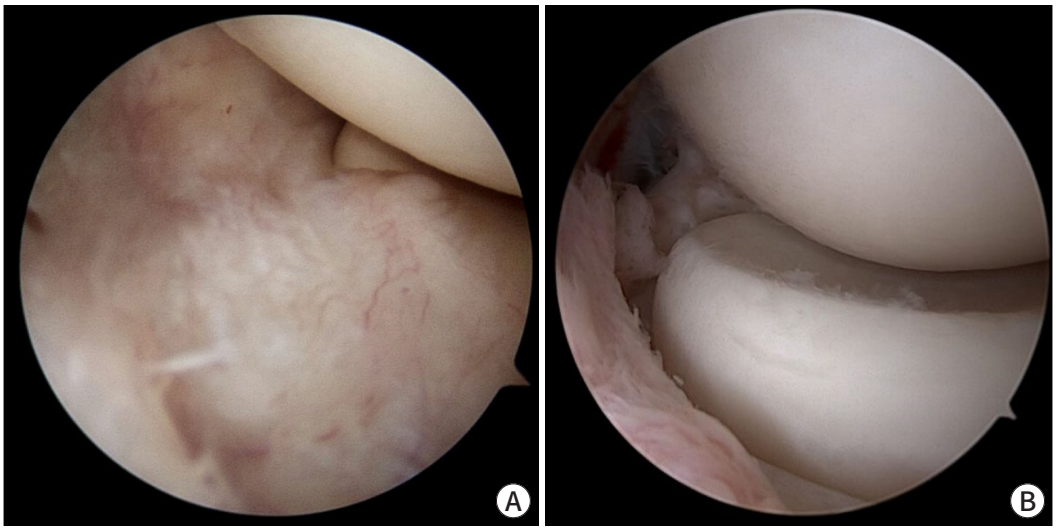

Fig. 3. Pathologic inflamed plica (A). After arthroscopic resection of the pathologic plica (B).

elbow joint, leading to pain, swelling, and limited joint mobility. It can result from various causes, including age-related wear and tear, post-traumatic injuries, or inflammatory conditions such as rheumatoid arthritis. While conservative treatments, such as pain management, physical therapy, and activity modification are commonly employed in early-stage arthritis, surgical intervention becomes necessary when non-surgical measures fail to provide adequate relief.

1. Clinical manifestation

Patients with osteoarthritis often experience their first symptoms around the age of 50, and this illness disproportionately affects men, with a male-to-female ratio of 4:1. Osteoarthritis is more typically found in the dominant extremity. Patients with elbow arthritis commonly complain of pain, weakness, and loss of motion.

- Loss of motion: The functional ROM required for daily living activities is 100° (30° of extension to 130° of flexion) and a 100° arc of forearm rotation (50° of pronation to 50° of supination). The main pathologic mechanisms causing motion loss include capsular contracture and osteophytes in the fossa, as well as processes of the olecranon and coronoid.

- Impingement discomfort (endpoint pain): Patients frequently experience pain at the end of motion in flexion and extension. Radiologic findings show that the three-dimensional matching of shape in the olecranon and coronoid fossa and process has been destroyed, with point contact leading to osteophyte growth. The concentration of contact force at the place of contact could be an explanation, although the cause of impinging discomfort remains unknown.

- Discomfort at rest or in the mid-arc: Some patients report discomfort in the mid-arc of motion or even at rest. This sort of discomfort is caused by cartilage erosion or destruction, which is common in severe elbow arthritis. If the discomfort is modest or inconsistent, using elbow mobility with axial loading as a provocative test may be beneficial.

2. Radiologic assessment

Because the most common symptoms of elbow osteoarthritis include resting discomfort, mid-arc pain from joint cartilage breakdown, endpoint pain, and reduced ROM from spurs and loose bodies, a staging system or classification for elbow arthritis should incorporate symptom-related

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variables to guide treatment. The Broberg and Morrey classification and the Hastings and Rettig classification have been used for qualitative staging to identify illness severity. [19] The Broberg and Morrey classification is based on osteophyte formation and narrowing of the joint space. The Hastings and Rettig system is based on the presence of subluxation and radiocapitellar joint involvement.

3. System of staging based on CT

A CT-based staging technique, or Kwak's classification, quantifies spurs in the fossa by assessing the involved depth on sagittal CT slices [20]. An "involved fossa" is defined as more than 50% involvement of the fossa. "Joint space narrowing" is defined as the presence of a gap of more than 1 mm in the ulnohumeral joint in more than 50% of the joint space in the reference section. A lack of involved fossa with intact joint space is defined as grade 0, a uni-compartmentally involved fossa with an intact ulnohumeral joint space is defined as grade 2, and joint space narrowing regardless of the state of the fossa is defined as grade 3 (Fig. 4). CT-based staging is more therapeutically practical and reproducible than prior plain radiograph-based staging techniques.

4. Indications and contraindications

The most common reason for arthroscopic osteocapsular arthroplasty (OCA) is functional loss of elbow motion and impingement pain caused by osteophytes and capsular tightness [21]. The rationale for surgery is uncomfortable impingement or functional impairment due to the necessity for terminal elbow extension in patients with a functional arc of motion, which is defined as flexion from 30° to 130° preoperatively. This indication does not apply to every

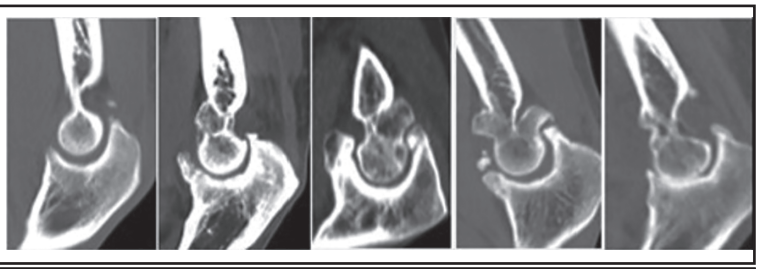
	Stage 0	Stage I (uni-fossa)		Stage II (bi-fossa)	Stage III
		IA	IP		
Fossa involvement	None	Anterior	Posterior	Both	Any
Joint involvement	Intact				Narrowing
CT image					
Definition					
Involved fossa	More than 50% osteophyte in the fossa				
Joint narrowing	Less than 1 mm in more than 50% of the articular space				

Fig. 4. Summary of the CT-based classification for primary elbow osteoarthritis. More than 50% involvement of the fossa is defined as an "involved fossa." "Joint space narrowing" is defined as the presence of a gap of more than 1 mm in the ulnohumeral joint in more than 50% of the joint space on the reference section. Grade 0: no involved fossa with intact joint space. Grade 1: uni-compartmentally involved fossa with an intact joint space. Grade 2: bi-compartmentally involved fossa with an intact joint space. Grade 3: joint space narrowing regardless of the state of the fossa.

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patient. Although most people may go about their daily lives with a functional arc of motion in their elbow, young and high-demand patients (often athletes) cannot tolerate smaller degrees of contraction. Low radiologic grades with apparent symptoms (e.g., impingement discomfort and mechanical symptoms of loose bodies) can also be evaluated. Arthroscopy can be used to treat less severe contractures in these patients.

End-stage elbow osteoarthritis can be considered a relative contraindication because it is associated with poor clinical and radiologic outcomes. However, even for advanced elbow osteoarthritis, elbow debridement or OCA is still an option as a palliative treatment for patients who refuse total elbow arthroplasty (TEA) or are not good candidates for TEA due to infection. Significant anatomic deformity is a contraindication. Depending on the surgeon's experience, prior submuscular transposition of the ulnar nerve may be a selective contraindication. Contraindications do not include ulnar nerve dislocation or prior subcutaneous transposition, unsuccessful prior contracture release, or significant scarring from skin grafts or flaps.

5. Surgical options and outcomes

Open elbow debridement, a procedure that involves removing the diseased or damaged tissue and smoothing out the remaining joint surfaces by eliminating osteophytes, the adhesive capsule, and loose bodies, has been a traditional approach to treating elbow osteoarthritis. It is generally recommended for severe osteoarthritis that needs severe adhesiolysis, and the elbow requires ulnar nerve management.

The arthroscopic approach has emerged as an appealing alternative for addressing both mechanical impingements caused by osteophytes and soft tissue contracture as less invasive surgical techniques have advanced (Fig. 5). The advantages of arthroscopic OCA include little surgical damage, which encourages faster rehabilitation and minimizes the likelihood of capsular contractures by lowering the morbidity associated with a long incision and joint exposure.

Both arthroscopic and open surgical techniques have shown positive outcomes in treating elbow arthritis [21–23]. With positive clinical outcomes for pain alleviation and ROM recovery, open debridement has been extensively performed and recommended by many qualified surgeons. It has been proposed that whatever functional restoration or symptom reduction that

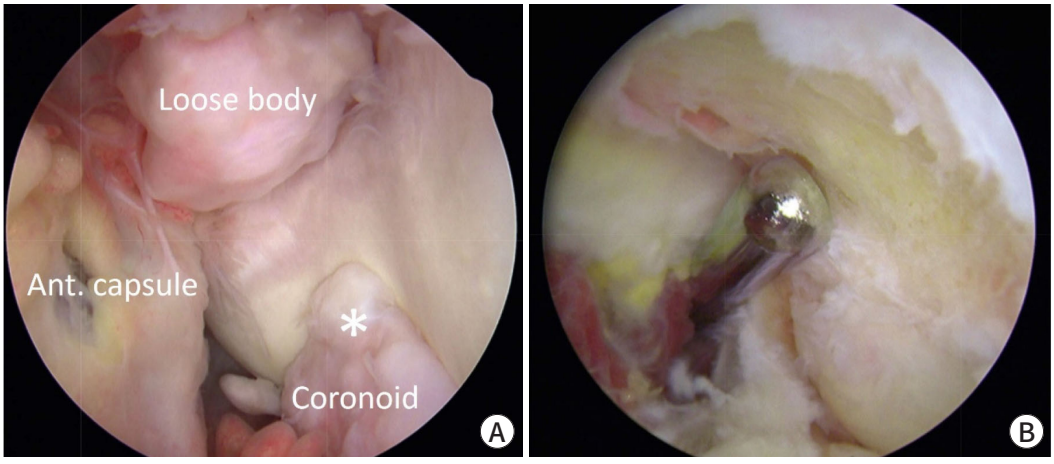

Fig. 5. Arthroscopic osteocapsular arthroplasty. Loose body in the coronoid fossa; the asterisk (*) denotes an osteophyte in the coronoid process (A). Clearance in the olecranon fossa and process with anterior capsulectomy (B).

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can be obtained through open surgery can be fully attained through arthroscopy. A recent study also found that arthroscopic OCA had comparable clinical outcomes, reaching the significant conclusion that neither technique can ensure excellent outcomes in patients with advanced osteoarthritis. Kim et al. found in a comprehensive analysis that both open and arthroscopic OCA enhanced ROM and clinical ratings, but that open debridement had higher complication and reoperation rates than arthroscopic OCA. However, arthroscopic OCA is more technically difficult than open surgery, and training and knowledge of the procedure are required to avoid neurovascular damage.

6. Complications and potential risks

After restoring elbow motion, delayed-onset ulnar neuritis (DOUN) may arise. DOUN has been observed to occur in 11% of cases following elbow arthroscopic contracture release [24]. The three clinical presenting patterns are rapidly progressive, non-progressive, and slowly progressive [25]. The most prevalent pattern that necessitates an urgent reoperation for nerve management is the rapidly progressing pattern, which is characterized by increased discomfort in the cubital tunnel, progressive loss of elbow motion, and neuropathy. If ulnar nerve transposition is delayed for more than 2 weeks following surgery, there is no complete return of neurological function. Preoperative hypertrophic ossification, preoperative neurological complaints, and the preoperative arc of motion are all connected with an elevated risk of DOUN. Before treatment, we advocate for restricted open ulnar nerve decompression while maintaining a high index of suspicion and avoiding end-range stretching if it generates symptoms such as ulnar neuritis or discomfort around the cubital tunnel.

7. Total elbow arthroplasty as a surgical option for end-stage elbow osteoarthritis

TEA was initially created to treat advanced rheumatoid arthritis, but its indications have since been expanded to include unfixable comminuted fractures, post-traumatic arthritis, and primary osteoarthritis [26,27]. Because TEA is seldom performed, most surgeons have less experience with it than with hip and knee arthroplasty, and limited long-term outcome data are available. To avoid making unnecessary errors, surgeons must learn about this surgery by carefully examining previous literature [28–30].

Osteochondritis Dissecans

Osteochondritis dissecans (OCD) of the capitellum is an articular cartilage and subchondral bone disorder that primarily affects juvenile gymnasts and overhead athletes such as baseball and tennis players [31]. This disease is thought to be caused by recurrent loading at the comparatively weakly vascularized capitellum. Stable lesions may produce pain during and after physical exercise in the early stages. Advanced (unstable) lesions, in which the cartilage has separated, and loose bodies have formed, can cause considerable pain, loss of motion, and locking of the elbow joint, eventually leading to the termination of athletic activity. Rest, analgesics, and physical therapy are advised for early-stage lesions in skeletally immature patients, whereas surgical treatment is recommended for advanced symptomatic lesions.

1. Indications

Arthroscopic treatment is generally recommended for stable OCD lesions that have not progressed to severe cartilage damage or loose body formation. This technique is less invasive

and allows better visualization and treatment of early-stage lesions. Open surgery is considered for more advanced OCD lesions, particularly those with loose bodies or extensive cartilage damage that may not be amenable to arthroscopic treatment.

2. Surgical options and outcomes

Surgical intervention plays a vital role in managing elbow OCD when conservative treatments are insufficient. Both arthroscopic and open surgical techniques have shown positive outcomes in treating this condition, with each approach having its specific indications and advantages.

Arthroscopic debridement and microfracture for advanced capitellar OCD have favorable clinical outcomes in terms of pain, function, ROM, and comorbidities, particularly in patients with an open growth plate, loose body removal, and shorter duration of symptoms. However, given that only 62% of our patients returned to their major sport, a more active strategy may be required for high-level athletes who want to return to their pre-injury level [32]. Open surgical procedures for elbow OCD can also be effective in cases with more significant cartilage damage and loose bodies. Patients may experience a more prolonged recovery compared to arthroscopic surgery, and rehabilitation is crucial for regaining elbow function. Long-term outcome studies are needed to show whether the improved clinical outcomes of arthroscopic debridement and microfracture are sustained.

The choice of surgical technique should be based on lesion stability, cartilage damage extent, patient age, activity level, and surgeon experience. Early diagnosis and appropriate surgical management can lead to successful outcomes and the preservation of elbow function for patients with OCD. Further research and long-term follow-up studies are necessary to optimize treatment strategies and enhance patient satisfaction in the surgical treatment of elbow OCD.

Nerve Entrapment Syndrome

1. Radial tunnel syndrome

Elbow radial tunnel syndrome is a nerve entrapment disorder that involves the compression or irritation of the radial nerve within the radial tunnel, situated beneath the supinator muscle [33]. The condition of irritation or compression of posterior interosseous nerve can lead to persistent forearm pain and sensory disturbances along the dorsal aspect of the hand [34,35]. When conservative treatments, such as rest, physical therapy, and anti-inflammatory medications, fail to alleviate symptoms, surgical intervention may be necessary. Surgical decompression is considered when conservative measures have been ineffective, and the patient experiences persistent pain, functional limitations, or progressive neurological deficits [36]. The procedure aims to relieve the pressure on the compressed radial nerve within the radial tunnel. Surgical decompression of the radial nerve in the radial tunnel has shown promising results, with most patients experiencing a reduction in pain and improved function. Sensory disturbances and weakness tend to improve gradually after surgery [37].

2. Cubital tunnel syndrome

Elbow cubital tunnel syndrome is a neurological condition characterized by the compression of the ulnar nerve as it travels through the cubital tunnel, which is located on the medial aspect of the elbow [38]. Entrapment can lead to various symptoms, including pain, tingling (paresthesia), weakness, and numbness in the hand and forearm (Fig. 6). When conservative treatments, such as activity modification, splinting, and anti-inflammatory medications, fail to alleviate symptoms,

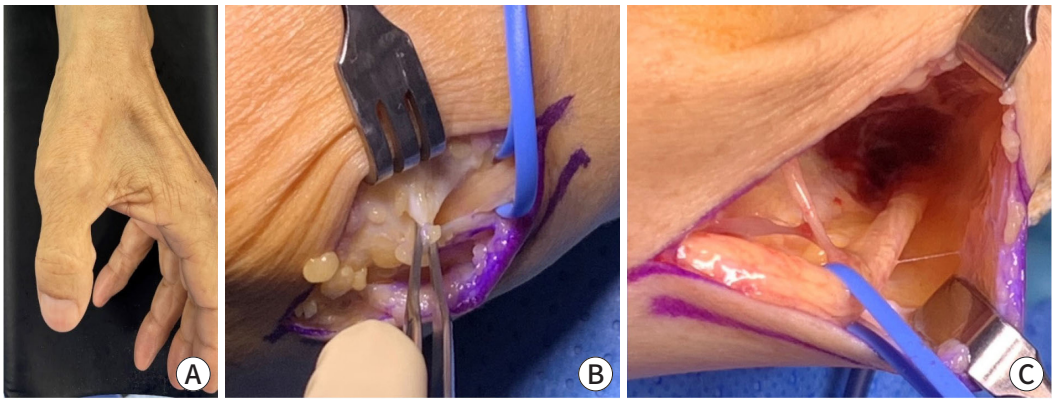

Fig. 6. Ulnar nerve compression due to the two thick heads of the flexor carpi ulnaris tendon (B). The ulnar nerve was freely decompressed all the way around the cubital tunnel (C).

surgical intervention may be necessary. This section explores the various surgical options for elbow cubital tunnel syndrome, assisting orthopedic surgeons in making informed decisions regarding the management of this condition.

Surgical options include ulnar nerve transposition, medial spondylectomy, or simple decompression. The chosen method depends on the severity, anatomical considerations, and the surgeon's preference and experience. Postoperative care, involving physical therapy and close monitoring, is essential to ensure nerve recovery and functional restoration. A comprehensive review of both surgical techniques and postoperative care strategies reveals a generally favorable prognosis with a low complication rate. Tingling, weakness, and numbness tend to improve gradually after surgery depending on disease severity and disease period [39]. Successful surgical outcomes rely on a prompt diagnosis, accurate localization of the entrapment site, and meticulous surgical technique. Careful patient selection and thorough preoperative evaluation are essential to achieve favorable results and minimize potential complications.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Informed consent for publication of the images was obtained from the patient.

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Review Article

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Postoperative Rehabilitation of Elbow Pain

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Elbow pain; Postoperative care; Rehabilitation

The elbow joint, with its intricate anatomy, plays a pivotal role in the upper limb's functional movements. Common surgical indications include epicondylitis, osteoarthritis, tendon tears, and neuropathies. Irrespective of the nature of surgery, appropriate postoperative rehabilitation is essential to enhance recovery, optimize functional outcomes, and minimize complications. Protective measures for the elbow vary based on the surgical procedure is performed. Extended postoperative immobilization is generally not advised. Temporary splints may be utilized to protect the soft tissues in the immediate aftermath of surgery, with patients advised to intermittently remove them to facilitate elbow movement. To increase mobility while ensuring the safety of repaired tendons or ligaments, articulated dynamic braces are recommended. This review delivers clinically useful recommendations specific to various surgical procedures, designed to be user-friendly even for non-specialists in orthopaedic surgery.

Introduction

The elbow joint is a complex structure, comprised of two distinct joints: the ulno-trochlear joint and the radio-capitellar joint. The ulno-trochlear joint functions as a hinge, while the radio-capitellar joint operates as a limited ball-and-socket joint. As a result, the elbow joint is capable of two types of motion: flexion/extension and supination/pronation. Furthermore, the elbow joint is encased by a joint capsule and ligaments, which include the lateral ulnar collateral ligament and radial collateral ligament in the lateral compartment, and the medial collateral ligament in the medial compartment. The joint is also surrounded by muscles, such as the extensor/flexor, biceps tendon, and triceps, as well as joint fluid. Pathologies of these complex anatomical structures can potentially induce elbow joint pain (Fig. 1) [1–3].

While most elbow pathologies can be effectively addressed with various conservative treatments, patients experiencing persistent pain or compromised function may require surgical intervention. Common causes of elbow joint pain that necessitate surgery include epicondylitis (medial and lateral), osteoarthritis (degenerative/post-traumatic), biceps/triceps tears, and neuropathy (ulnar/radial) [4–9]. Additionally, it is challenging for surgeons to achieve satisfactory clinical outcomes for fractures near the elbow joint. Although most patients who undergo surgery for the aforementioned causes have acceptable results, there are potential complications, such as stiffness, residual pain, decreased function, and exacerbated neuropathy [10–13]. These complications can be minimized—and the need for additional surgery could potentially be eliminated—if patients receive appropriate postoperative rehabilitation based on correct

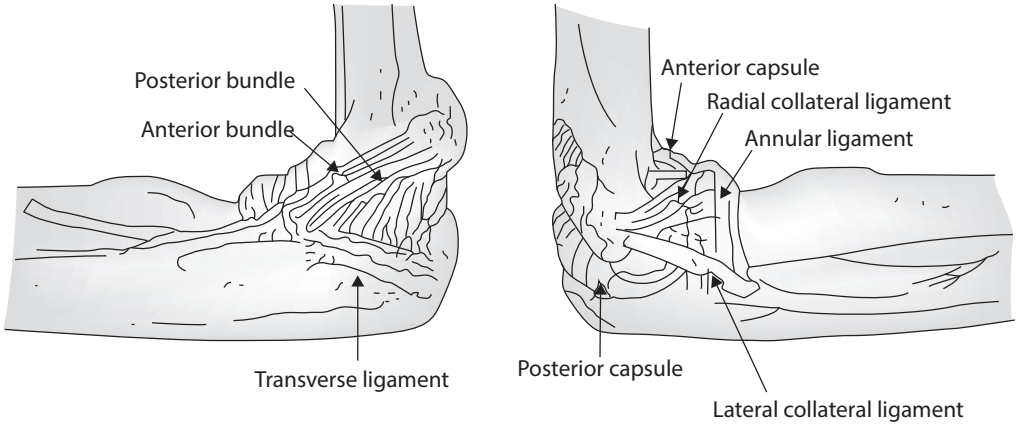

Fig. 1. Anatomy of the elbow joint.

principles.

Therefore, we reviewed previous studies on postoperative rehabilitation for various pathologies or surgical procedures of the elbow joint. We discuss the principles of postoperative rehabilitation for the elbow joint, drawing from recently published articles. We hope to provide suggestions that will be accessible and useful to clinicians, even those with limited experience in orthopaedic surgery.

General Principles

The objective of elbow rehabilitation is to restore optimal function without pain, while taking into account the patient's anatomical and physiological limitations. To achieve successful rehabilitation, practitioners should adhere to the following guiding principles: 1) make a comprehensive and accurate diagnosis, 2) manage and alleviate pain and swelling, 3) start gentle motion exercises early on, 4) reestablish neuromuscular stability around the elbow, 5) consider the entire kinetic sequence when approaching elbow rehabilitation, and 6) assist the patient in returning to their preoperative level, whether that involves sports or simply everyday tasks [14].

The general principles of elbow fracture management are as follows [15,16]:

- Week 1–2: Protect and stabilize the wound by decreasing swelling. A gentle passive range of motion can be allowed under a clinician's guidance. During this period, hand and shoulder motion is recommended.
- After 2 weeks: If the wound is stable, the stitches can be removed. If not, stitch removal can be delayed until 3 weeks.
- Weeks 2–6: Conduct physical therapy to improve the range of motion with assisted active and passive motion exercises.
- Week 6: Increase the intensity of range of motion exercises, using active motion exercises.

Rehabilitation after Common Elbow Surgery Procedures

1. Lateral and medial epicondylitis

Lateral epicondylitis, also known as "tennis elbow," is an overuse injury that affects the wrist extensor muscles. These muscles include the extensor carpi radialis brevis, extensor digitorum

communis, and extensor carpi radialis longus, and the injury occurs at their insertion on the lateral epicondyle. Medial epicondylitis, also referred to as "golf elbow," is characterized by chronic tendinosis of the flexor-pronator musculature at its insertion on the medial epicondyle of the humerus, resulting from overuse or repetitive stress. Surgical treatment is considered after other conservative treatments have been tried. These treatments include medication with NSAIDs, physical therapies, strengthening exercises for the extensor/flexor muscles with counterforce braces, injection therapy (which may include steroids, autologous blood, polydeoxyribonucleotide, or platelet-rich plasma), and extracorporeal shockwave therapy [17–23]. Open, percutaneous, or arthroscopic approaches to tendinopathy, involving release and debridement, have shown excellent outcomes in resolving chronic, recalcitrant elbow pain and functional disability [17,24]. However, returning to work and restoring the normal range of motion in the elbow joint, as well as grip strength, can only be achieved following essential postoperative rehabilitation. This rehabilitation should involve active physical therapy, including eccentric strengthening exercises.

The general principles for postoperative rehabilitation in lateral and medial epicondylitis are identical. These often involve periods of protection, active physical therapies, and strategies to restore the full range of motion and strength in the elbow. Rehabilitation following a ligament repair typically necessitates a longer protection period, often requiring the use of a removable static splint for up to 2 weeks (Fig. 2). For managing postoperative swelling and pain, icing, elevation, and compression can be utilized. NSAIDs or other prescribed pain medications may also be recommended. After 2 weeks, controlled mobilization and isometric strengthening exercises are progressively introduced. Clinicians should encourage patients to mobilize the affected elbow side, which includes flexion and extension in the forearm's neutral position. Depending on the surgeon's guidelines, gentle passive and active assisted range of motion exercises can commence. Gradual progression of these exercises helps restore flexibility and prevent joint stiffness. Additionally, isometric exercises, where the muscle contracts without moving the joint, can begin. These are followed by isotonic exercises, which involve joint

Fig. 2. Removable static splint.

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movement. At this point, patients can start light daily activities, ensuring no pain is elicited. Six weeks post-surgery, functional exercises and eccentric strengthening exercises, where the muscle lengthens under tension (like slowly releasing a weight), can be particularly effective for tendinopathies and can be initiated. Physiotherapy is prescribed if any residual stiffness in the elbow is noticed. Depending on the patient's goals, specific exercises mimicking daily or sporting activities can be started. Physical therapists may also use ultrasound, electrical stimulation, or laser therapy to promote healing and reduce pain. Full recovery to sports or work is typically expected between three to six months [24,25].

During the recovery process, a counterforce brace treatment just distal to the elbow and a cockup wrist splint can be recommended to reduce the load at the operative site (Fig. 3). The wrist splint is required to protect the extensor carpi radialis brevis, which inserts at the base of the third metacarpal bone (Fig. 4). Rehabilitation following debridement usually involves a shorter protection period, with an earlier introduction of mobilization exercises to prevent stiffness and adhesions. Recovery from open surgery often requires longer immobilization to ensure wound healing and to minimize stress on the repaired or treated structures (Fig. 5). Physical therapy, initially focusing on gentle range of motion exercises, is crucial. For arthroscopic surgery, which involves smaller incisions and minimal soft tissue disruption, faster rehabilitation is often permitted. Patients may initiate range of motion exercises sooner, and strengthening exercises may be introduced earlier than after open surgery.

2. Primary osteoarthritis

Since the elbow joint is not weight-bearing, osteoarthritis is not as common as in other joints. However, the elbow bears the load created by gravity and muscle contracture in dynamic swing movements [26]. For this reason, degenerative arthritis frequently develops in individuals who engage in heavy manual labor, rely on crutches, or are overhead-throwing athletes [27]. Recently, surgical procedures such as open or arthroscopic osteo-capsular arthroplasty have been commonly performed to alleviate primary symptoms associated with osteoarthritis. These symptoms include pain at the terminal range of motion, mechanical symptoms (such as impingement, locking, and crepitus), and stiffness [28]. The procedures involve steps such as capsular release, synovectomy, and the removal of osteophytes and loose bodies, all aimed at reducing pain and increasing range of motion [29].

The clinical outcomes after surgical treatment for osteoarthritis are largely influenced by post-

Fig. 3. Wrist brace.

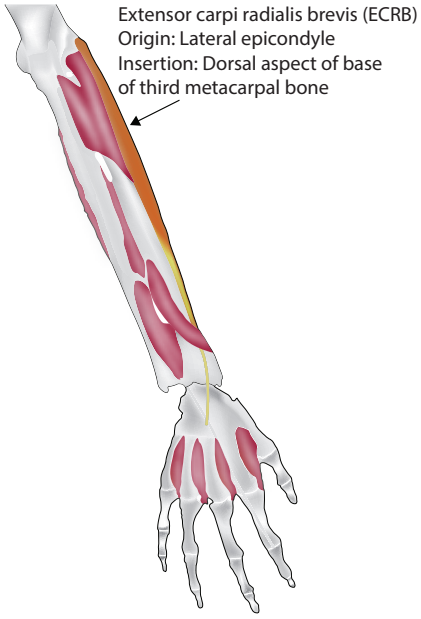

Fig. 4. Extensor carpi radialis brevis anatomy.

Fig. 5. Hinged articulated brace for protection from valgus/varus stress. It can control the angle of flexion/extension, depending on the rehabilitation stage.

operative management. One of the primary objectives of these treatments is to regain the range of motion, ideally achieving a functional range of motion of 30°–130° in extension-flexion and 50° in pronation-supination. Initially, a soft compressive dressing is applied after the surgical procedures. This dressing is replaced with a simpler one on the first postoperative day, and patients are taught to perform active assisted range of motion exercises with help from the contralateral

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hand (Fig. 6). Upon discharge, patients are encouraged to move their elbows within a comfortable range and are instructed to continue practicing range of motion exercises at home for a period of 3 months. Nighttime splinting is recommended during the first 3–4 weeks post-surgery. The home rehabilitation regimen involves completing full extension and flexion exercises ten times consecutively, with a 10-second pause between each repetition, six times daily [29,30]. Telehealth and YouTube have proven to be valuable educational resources for rehabilitation, with patients often expressing satisfaction with their usefulness. Telehealth, in particular, offers a platform for real-time interaction between patients and healthcare professionals, facilitating guided exercise demonstrations, immediate feedback, and personalized adjustments to rehabilitation plans. Conversely, YouTube provides a wealth of video tutorials and demonstrations related to rehabilitation exercises. These videos typically include step-by-step instructions, common pitfalls to avoid, and variations to accommodate different levels of mobility and strength. Given their detailed guidance and accessibility, both telehealth and YouTube are highly recommended as effective tools to support and enhance the home rehabilitation process [31,32].

In cases where traditional treatments or other joint-preserving procedures fail to yield positive results, and individuals continue to suffer from symptoms such as pain during specific ranges of motion, discomfort during flexion and extension, and persistent pain even at rest or during the night, total elbow arthroplasty (TEA) may be considered. However, before deciding on this surgical intervention, it is crucial for individuals to understand and consent to the activity limitations that come with a TEA. Following the procedure, standard postoperative care for TEA is implemented. The operated arm is typically immobilized using a splint for a few days to a week,

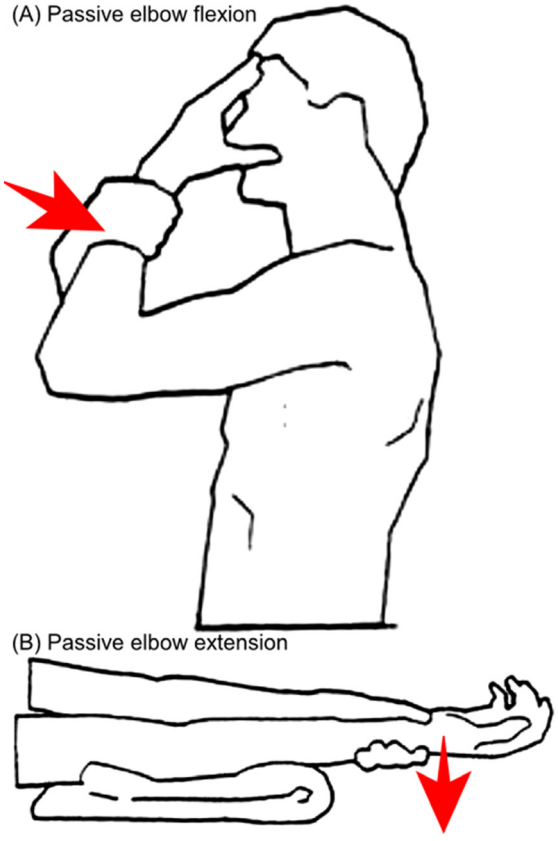

Fig. 6. Self-conducted range of motion exercises. (A) Passive elbow flexion, (B) passive elbow extension.

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depending on the condition of the extensor mechanism and the surrounding tissues. When the arm is not in the splint, periodic active or passive elbow movements are encouraged. By the end of six weeks, the use of the removable splint is typically discontinued. After surgery, patients are generally advised to avoid repetitively lifting anything over 1 kg and to limit lifting anything over 5 kg to rare occasions [33–35].

3. Cubital tunnel syndrome

Cubital tunnel syndrome is the second most common type of peripheral neuropathy in the upper extremity [36]. Chronic ulnar nerve neuropathy may lead to a loss of sensation, muscle weakness or atrophy, and joint contractures. While non-surgical management may be indicated for mild cases of cubital tunnel syndrome, surgical intervention is typically pursued for more advanced cases. Numerous types of procedures are available, including *in situ* decompression and or ulnar nerve anterior transposition, which can be submuscular, intramuscular, or subcutaneous.

Postoperative care and rehabilitation can vary based on the surgical method used. For *in situ* decompression, a bandage is used for protection for at least 2 days. The patient is permitted to move their elbow immediately. For patients who undergo ulnar nerve anterior transposition, additional protection may be necessary. This often involves the use of a removable splint at night for the first 2 weeks. The initial phase, which lasts 7–10 days, requires patients to refrain from elbow range of motion activities, particularly full extension. During this time, a posterior splint is continuously applied for protection. Simultaneously, therapeutic exercises focus on shoulder stretching, and range of motion exercises are customized for the wrist, hand, and fingers. However, it is crucial for patients to avoid any resistance exercises involving the elbow or wrist.

As the patient transitions into the second phase, which lasts from the end of the first week to four weeks after surgery, they begin full elbow flexion exercises. These are supplemented by a gradual increase towards full extension. The splint, which was previously essential, is now removed at the surgeon's discretion, usually during post-operative check-ups. At this point, no bracing is advised. Techniques such as applying heat before exercises and ice after exercises are also incorporated into the rehabilitation process. From weeks 4 to 6, patients are urged to achieve full elbow range of motion. If they have difficulty reaching full extension, passive counter-pressure techniques can be used to assist. No bracing is utilized during this phase. Additionally, emphasis is placed on wrist and forearm strengthening exercises, which are resistance-based. After the 6-week mark, rehabilitation is characterized by a return to full, pain-free elbow movement. Therapeutic exercises transition to more advanced strengthening routines. As patients regain strength and confidence, training specific to their sport is introduced. Activities such as throwing and hitting are gradually incorporated, in line with the individual's recovery rate. The ultimate goal is to ensure patients can safely and confidently resume their full range of activities as their post-operative condition allows.

4. Biceps tendon tear

Distal biceps tendon ruptures can result in diminished elbow flexion strength and forearm supination ability [37]. These ruptures, often caused by a strong eccentric contraction of the muscle [38], are relatively uncommon, with an annual incidence rate ranging from 1.2 to 9.6 per 100,000 individuals (Fig. 7) [39,40]. They are observed more frequently in middle-aged men [41]. Choosing not to undergo surgery can result in a decline in the power of both elbow and forearm movements [37]. Therefore, the preferred treatment for a ruptured distal biceps

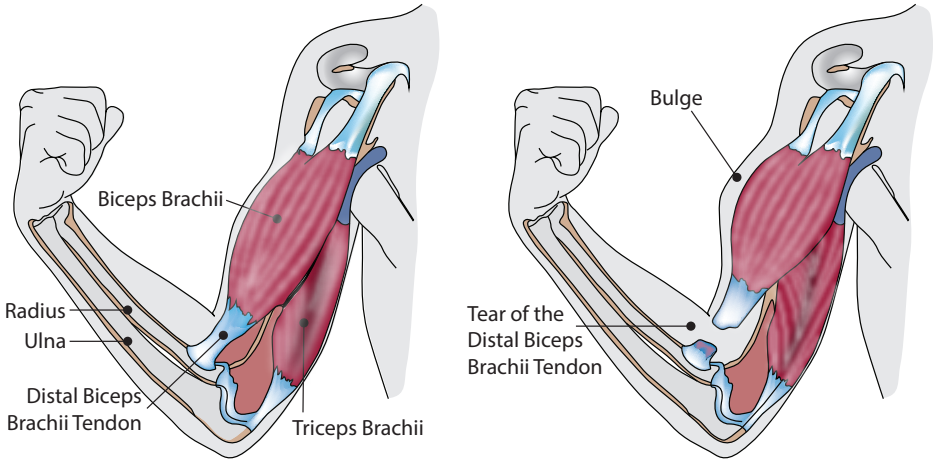

Fig. 7. Biceps tendon anatomy and tear pathology.

tendon is typically surgical repair. Post-operative procedures, including immobilization and the commencement of passive and active movements, are determined by the surgeon's specific guidelines. The primary goal of rehabilitation is to improve patient functionality and enable a successful return to their prior activities [42].

During the immediate postoperative period following biceps tendon repair, the focus of rehabilitation is on alleviating post-surgical pain and swelling, preserving the integrity of the surgical repair, and fostering optimal tissue healing. In the first week, patients are advised to avoid any elbow movement and to refrain from placing weight on the repaired limb. A posterior splint is used to provide necessary protection, particularly during this critical healing phase. By the second week, patients transition to progressive exercises, with an emphasis on controlled range of motion activities. These activities gradually shift from passive to more active movements. As patients move into the intermediate phase (2–6 weeks), they participate in targeted exercises designed to improve mobility. These exercises include shoulder and wrist activities, all while adhering to weight-bearing restrictions. The late postoperative phase, which spans from weeks 7 to 10, marks an advanced stage in the rehabilitation process. The objectives during this period are to consolidate the surgical repair and fine-tune scapulothoracic mechanics. Weight-bearing on the elbow is introduced in the eighth week and is progressively increased. Combined motion exercises become a crucial part of the regimen, with composite activities such as forearm planking and quadruped progressions being introduced. Efforts are also made to strengthen the scapulothoracic region, using exercises like wall slides and seated retractions [15,42].

Rehabilitation Strategies after Elbow Arthroscopy

Elbow arthroscopy offers several advantages when treating conditions such as lateral epicondylitis and elbow osteoarthritis. This procedure allows for direct visualization of intra-joint components through minimal incisions, thereby reducing scarring, inflammation, wound complications, and the risk of heterotopic ossification (HO). These advantages lead to less postoperative discomfort and expedite rehabilitation, facilitating a faster return to daily activities

and sports [43]. A hallmark of the arthroscopic technique, particularly relevant to conditions like lateral epicondylitis, is the immediate commencement of rehabilitation, often on the day of surgery or the following day. This is subject to individual post-surgical responses, including factors such as anesthesia-induced nausea or personal pain thresholds. Patients can benefit from edema control techniques, which include rest, ice, compression, and elevation, or the use of compression garments and cold compresses [43]. Active range of motion exercises, crucial for managing conditions like elbow osteoarthritis, are initiated with the primary dressing still in place on the day of surgery. By the next day, this dressing can be removed, allowing for an increase in range of motion exercises based on the patient's comfort levels. In the case of lateral epicondylitis, post-debridement stretching exercises for the forearm muscles are implemented [44], and putty exercises are introduced early for minor grip strengthening and edema reduction [45]. This proactive approach contrasts with the more conservative postoperative care seen in open elbow procedures, where the arm might be immobilized for up to 2 weeks in a brace or post-surgery cast, usually maintaining the elbow in a 90° flexed position.

Postoperative Rehabilitation Strategies for Elbow Trauma Surgery

Trauma to the elbow joint can range from simple dislocations to more complex injuries such as fractures of the radial head/neck, proximal ulna (olecranon), distal humerus, and fracture dislocations like the terrible triad. Managing traumatic elbow injuries can be relatively challenging due to the joint's complex anatomy and the typically complicated nature of the injury, which can involve the bony structure, ligaments, nerves, and soft tissue. Common complications include post-traumatic stiffness, HO, arthritis, nerve injury, and soft tissue-related issues such as infection [46]. Therefore, while the postoperative rehabilitation program should be tailored to each patient, one of the key objectives in rehabilitating elbow trauma-related surgery is the prevention of stiffness [47]. Prolonged immobilization is a risk factor for developing stiffness, while early mobilization can facilitate quicker recovery and return to work without jeopardizing the stability of the fixation. However, since ligament injuries are common in traumatic elbow injuries, ligament repair or reconstruction is often necessary. To prevent re-rupture or instability of the repaired side, protection from varus/valgus stress should be provided through a hinged brace. This brace can control the angle of flexion/extension to avoid stressing the valgus/varus direction (Fig. 3). Additionally, HO can cause stiffness. To prevent the development of HO, the use of NSAIDs should be considered postoperatively.

Conclusion

The complex anatomy and functionality of the elbow make postoperative rehabilitation essential for optimal recovery. Tailored rehabilitation programs, designed according to the specific pathology or procedure, can lead to improved functional outcomes, fewer complications, and a faster return to daily activities following surgery. The fundamental principles of rehabilitation encompass accurate diagnosis, management of pain and swelling, early initiation of motion exercises, and the maintenance of neuromuscular stability. Adopting a patient-centric approach, which understands and caters to individual needs and preferences, and incorporates modern technology such as telehealth and YouTube for educational purposes, can further enhance postoperative care. Future research should aim to refine rehabilitation protocols in

order to minimize complications and facilitate even quicker recovery trajectories.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Review Article

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Protective Effects of Statins against Alzheimer Disease

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Key Words
Alzheimer disease; Hydroxymethylglutaryl-CoA reductase inhibitor; Neuroinflammatory diseases; Oxidative stress

Alzheimer disease (AD) is a common neurodegenerative disorder, characterized by memory impairment, dementia, and diminished cognitive function. This disease affects more than 20 million people worldwide. Amyloid beta (Aβ) plaques and neurofibrillary tangles (NFTs) are important pathological markers of AD. Multiple studies have indicated a potential association between elevated cholesterol levels and increased risk of AD, suggesting that lowering the cholesterol level could be a viable strategy for AD treatment or prevention. Statins, potent inhibitors of cholesterol synthesis, are widely used in clinical practice to decrease the plasma levels of LDL cholesterol in patients with hyperlipidemia. Statins are known to play a neuroprotective role in limiting Aβ pathology through cholesterol-lowering therapies. In addition to Aβ plaques and neurofibrillary tangles, the brains of AD patients exhibit signs of oxidative stress, neuroinflammatory responses, and synaptic disruption. Consequently, compounds with antioxidant, anti-inflammatory, and/or neuroprotective properties could be beneficial components of AD treatment strategies. In addition to lowering LDL cholesterol, statins have demonstrated therapeutic efficacy in various forms, including antioxidant, anti-inflammatory, and neuroprotective effects. These properties of statins are potential mechanisms underlying their beneficial effects in treating neurodegenerative diseases. Therefore, this review was conducted to provide an overview of the protective effects of statins against AD.

Introduction

Dementia is a progressive neurodegenerative disease that not only profoundly impairs the health and well-being of patients, but also poses a major public health problem. Alzheimer disease (AD) is a common neurodegenerative disorder characterized by a gradual deterioration in cognitive performance, particularly in the memory domain, which impacts the daily functioning and life of the individual. The prevalence of AD increases with age, doubling every 5 years from the age of 60 years [1]. This disease is marked by compromised cognitive function, often associated with a significant reduction in brain volume [2]. Another characteristic of the disease is the presence of amyloid beta (Aβ) plaques in the brain, which result from the deposition of a specific substance in the cerebral cortex. The pathogenesis of AD is commonly linked with the

accumulation and aggregation of Aβ and the hyperphosphorylation of tau proteins, leading to neurofibrillary tangles (NFTs) and synaptic disruption [3].

Cognitive and memory impairment in AD is linked to neuroinflammation, oxidative stress (OS), synaptic disruption, and lipid dysregulation [4]. Clinical studies have shown that statin therapy can improve cognitive functions in patients with AD. Additionally, the use of these compounds has been found to reduce the risk of dementia in adulthood. Statins are effective inhibitors of cholesterol synthesis, primarily through the inhibition of HMG-CoA reductase (HMGCR). Statins are known to exert pleiotropic effects, including antioxidant, anti-inflammatory, and neuroprotective impacts, across multiple biological pathways [5]. These properties of statins may underlie their beneficial effects in various pathological conditions, such as AD. These effects will be discussed in detail in this review article.

Statins

Statins are primarily used in the treatment of hypercholesterolemia. These drugs inhibit HMGCR, the rate-limiting enzyme in cholesterol synthesis, which regulates the conversion of HMG-CoA to mevalonic acid. Beyond their cholesterol-reducing effects, statins also lead to the depletion of downstream isoprenoid products of this pathway, including isopentenyl pyrophosphate, farnesyl pyrophosphate, and geranylgeranyl pyrophosphate. This depletion induces changes to small GTPases, such as Ras proteins [6]. These products serve as the primary lipid attachments for the post-translational modification of various proteins, including heterotrimeric G proteins and small GTP-binding proteins of the Ras, Rho, Rap, and Rab GTPase families, as shown in Fig. 1 [7].

Statins can be categorized into two groups based on their method of production. The first group comprises natural or fungal-derived statins, including mevastatin, lovastatin, pravastatin, and simvastatin. The second group consists of synthetic statins, such as fluvastatin, atorvastatin, cerivastatin, pitavastatin, and rosuvastatin [8]. Statins can also be classified by their solubility into lipophilic and hydrophilic statins. Lovastatin, simvastatin, atorvastatin, and fluvastatin fall under the lipophilic category, while pravastatin and rosuvastatin are classified as hydrophilic (Table 1). The various properties of statins should be considered when utilizing them as effective treatments for brain diseases. Notably, for a drug to impact the brain, it must be able to cross the blood-brain barrier (BBB). Among the statins, lovastatin and simvastatin are the most frequently used in brain research [9].

Lipophilic statins exhibit a greater impact on neurodegenerative diseases and dementia than hydrophilic statins [10]. A study by Pan et al. demonstrated that lipophilic statins were more effective in reducing the risk of AD [11]. However, another study indicated that lipophilic statins were associated with a higher risk of AD compared to hydrophilic statins [12]. These results can be attributed to the superior capacity of lipophilic statins to passively cross the BBB and easily interact with various tissues, including the CNS, adipose tissue, and muscle [13]. In other research, hydrophilic statins have been reported to decrease the risk of AD more strongly (by 28%) than lipophilic statins (16%). In general, hydrophilic statins require a carrier to enter tissues other than the liver [13].

Pathogenesis of Alzheimer Disease

The key agents involved in the pathogenesis of AD have garnered considerable attention, yet

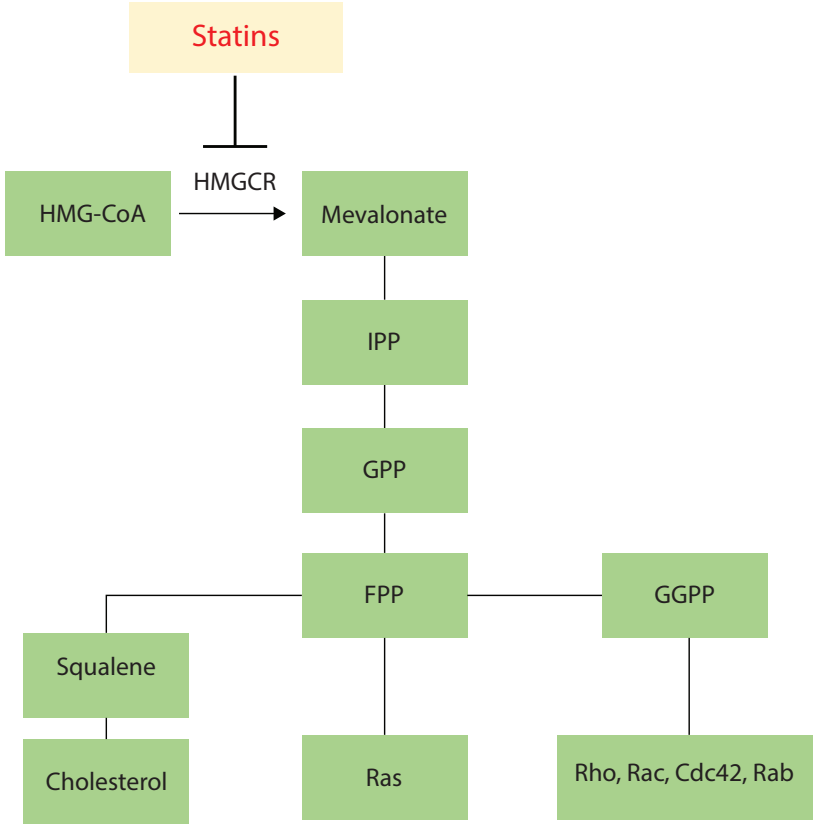

Fig. 1. Synthesis of endogenous cholesterol. The HMGCR enzyme controls the rate of the mevalonate pathway and facilitates the conversion of HMG-CoA to mevalonate. Statins can significantly inhibit this enzyme. HMGCR, HMG-CoA reductase; IPP, isopentenyl pyrophosphate; GPP, geranyl pyrophosphate; FPP, farnesyl pyrophosphate; GGPP, geranylgeranyl pyrophosphate.

Table 1. Classification of statins

	Simvastatin	Pitavastatin	Lovastatin	Fluvastatin	Rosuvastatin	Pravastatin	Atorvastatin
Type	Natural	Synthetic	Natural	Synthetic	Synthetic	Natural	Synthetic
Solubility	Lipophilic	Lipophilic	Lipophilic	Lipophilic	Hydrophilic	Hydrophilic	Lipophilic
BBB permeability	High	Low	High	Low	Low	Low	Low
Half-life (hours)	1–2	12	2	4.7	19	1–2	14

BBB, blood-brain barrier.

the mechanisms of this disorder remain incompletely defined and continue to be questioned. A prevailing theory is the amyloid cascade hypothesis, which proposes that Aβ peptides act as a trigger for subsequent events that lead to AD [14]. AD is marked by the presence of Aβ plaques and NFTs. Aβ peptides spontaneously aggregate into soluble oligomers, fibrils, and senile plaques; these subsequently cause oxidative damage, activation of microglial and astrocytic cells, and changes in kinase/phosphatase activity, ultimately culminating in neuronal cell death [15]. Aβ peptides may also induce tau phosphorylation, which results in the destabilization of microtubules, impaired axonal transport, and eventual neuronal death [16].

Given the evidence that tau hyperphosphorylation can induce neuron death, it is widely recognized that tau-oriented therapeutic strategies could be effective for AD and other disorders characterized by tauopathies [17].

Conversely, it has been determined that Aβ indirectly contributes to neurotoxicity by stimulating microglia to secrete inflammatory substances such as cytokines. Furthermore, an increasing body of evidence suggests that Aβ plaques are associated with local synapse loss and synaptic disruption [18].

Generally, the memory impairment and dementia observed in AD are associated with the accumulation of Aβ. This accumulation triggers neuroinflammation, increases OS, induces synaptic dysfunction, and promotes tau protein hyperphosphorylation (Fig. 2).

Dysregulation of Lipid Homeostasis and Alzheimer Disease

Evidence from various studies suggests that dysregulation in lipid metabolism homeostasis within the CNS significantly increases the risk of developing AD. Indeed, the concept that maintaining cholesterol homeostasis could offer new potential therapeutic strategies to inhibit or delay the progression of AD is gaining traction [19]. A prior study indicated that midlife cholesterol levels were elevated in individuals exhibiting mild memory loss or dementia [20]. Similarly, high cholesterol levels at midlife have been found to significantly heighten the risk of late-life dementia [21]. Additionally, aging is a key risk factor for developing some forms of dementia, such as AD. In humans, aging is associated with increases in plasma concentrations of triglycerides, cholesterol, and LDL. High cholesterol levels are associated with an elevated risk of memory loss and AD. This implies that the risk of developing neurodegenerative diseases such as dementia and AD is dramatically increased in older adults [22].

Cholesterol levels in the cortical gray matter of the brains of patients with AD have been found to be elevated by 19% to 34% [23]. A diet high in cholesterol can approximately double the levels of Aβ in the hippocampus, leading to damage to the BBB [24]. Dysregulation of lipid homeostasis may elevate Aβ levels by influencing the cleavage of amyloid precursor protein (APP), a primary risk factor associated with the pathogenesis of AD [25].

A substantial body of research on the potential link between high cholesterol levels and increased AD risk suggests that reducing cholesterol levels could be an effective strategy for the treatment or prevention of AD. A growing amount of evidence suggests that chronic treatment

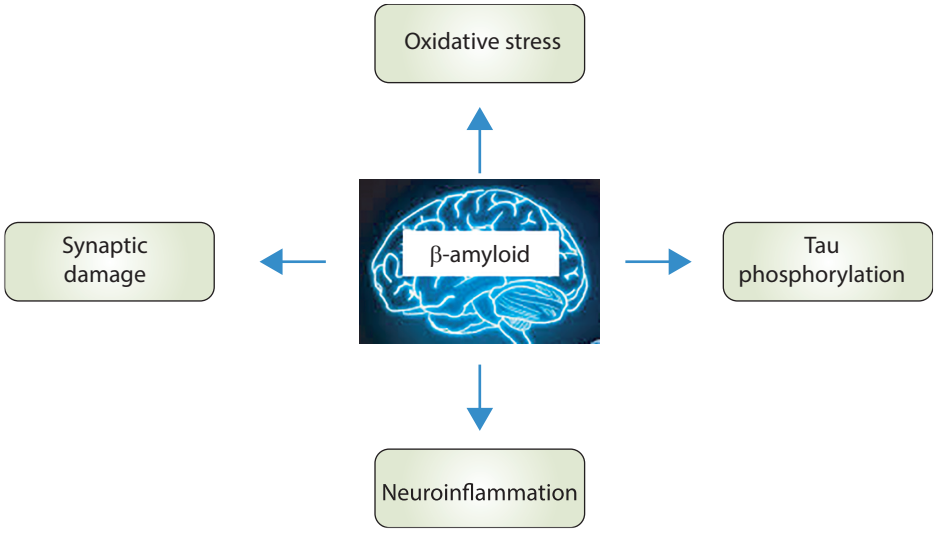

Fig. 2. Dysfunctions associated with β-amyloid.

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with statins, as HMGCR inhibitors, reduces the risk of developing AD. Statins can reduce the formation of Aβ by lowering cholesterol levels. Initial results supporting the favorable effects of statins in AD have been obtained from two studies; the findings indicated that these drugs were associated with up to a 70% reduction in AD incidence [26,27]. Supporting the previous notion that statins can have beneficial impacts on neurocognitive disorders, a study by Wolozin et al. found that lovastatin and pravastatin were associated with a reduced risk of AD development [28]. Additionally, the capacity of statins to combat AD may stem from the prevention of protein isoprenylation [29]. Aβ, the primary component of senile plaques in AD, is a product derived from APP. The knockout of Rho family protein activity reduces levels of APP C-terminal fragments by enhancing lysosome-dependent degradation. A previous study indicated that statins may reduce Aβ formation by inhibiting proteins of the Rho and Rab families, suggesting a mechanism of statin action in AD [30]. This research proposes an additional potential mechanism by which statins can mitigate AD pathogenesis, via the inhibition of protein isoprenylation.

Protective Effects of Statins

1. Attenuation of oxidative stress

The accumulation of high levels of free radicals, defined as OS, is hazardous. This accumulation may result from either excessive production or insufficient removal of radicals. The removal process can occur through several potential mechanisms and is typically carried out by an antioxidant compound. These compounds are molecules that substantially delay or prevent the oxidation of an oxidizable substrate. Antioxidant mechanisms include the scavenging of free radicals, the quenching of sources of free radicals, and the regeneration of endogenous antioxidants [31].

The reactive oxygen species (ROS) family of compounds includes the partially reduced oxygen species $O_2^{\bullet -}$, H_2O_2, and HO•. These free radicals are generally defined as oxygen-containing chemicals that possess reactive properties. An increased level of ROS within a biological system can interact with fundamental biological macromolecules such as DNA, RNA, lipids, and proteins. The brain is particularly vulnerable to oxidative damage induced by OS, given its substantial consumption of dioxygen and its high lipid content [32].

OS manifests early in the progression of AD, reinforcing its potential role in the pathogenesis of this disease, particularly in relation to the presence of Aβ. In fact, elevated levels of Aβ correlate with an increase in oxidation compounds derived from proteins, lipids, and nucleic acids in the hippocampus and cerebral cortex [33].

Research has established that Aβ impairs mitochondrial redox activity and increases the production of ROS. Various studies provide evidence that Aβ-induced OS results in the apoptotic death of neuronal cells, a process that can be inhibited by antioxidants [34]. These data imply that ROS could serve as a crucial mediator of Aβ-induced neuronal cell death in the progression of AD.

The proposed association between OS and elevated AD risk suggests that antioxidant compounds could be a suitable treatment for AD. The antioxidant properties of statins are recognized as an inherent characteristic of these drugs, first documented *in vitro* [35]. In an investigation of the antioxidant activity of statins, Franzoni et al. found that all of these compounds exhibited antioxidant effects, but they varied in potency and the types of free radicals most effectively scavenged [36]. More specifically, research has indicated that fluvastatin demonstrates the greatest anti-peroxyl radical antioxidant effect, while simvastatin

shows the highest anti-hydroxyl radical activity [37]. Thus, the antioxidant effects of statins may vary depending on the targeted substrate.

The accumulation of Aβ in the brain is a crucial pathogenic event in AD. Among the various mechanisms proposed to explain the neurotoxicity of Aβ deposits, one suggests that Aβ indirectly causes neurotoxicity by activating microglia to produce ROS. Nicotinamide adenine dinucleotide phosphate oxidase (NOX) is a key contributor to oxidative damage and processes. Increased NOX activity is known to lead to the development of various diseases by producing excess ROS and establishing OS conditions [38]. Consequently, inhibiting this enzyme could be a promising therapeutic strategy for the treatment of various diseases. Aβ engages with microglia, activating these cells and causing the overproduction of $O_2^{\cdot-}$ by NOX. This $O_2^{\cdot-}$ is then converted into H_2O_2 and ultimately to $^{\cdot}OH$ in the Fenton reaction. Aβ peptides induce mitochondrial dysfunction and OS through the activation of NOX [39]. Statins are well-known to prevent the toxic effects of oxidative conditions by suppressing the activation of the NOX pathway [40]. Specially, Rac plays a key role in the activation of NOX and the subsequent production of ROS [41]. Interestingly, statins inhibit Rac activity and effectively prevent protein interaction and NOX production, ultimately reducing ROS generation.

Additionally, research has demonstrated that statins upregulate the activity of antioxidant enzymes such as glutathione peroxidase, catalase, and superoxide dismutase, which eliminate ROS while generating oxygen and water [42]. A pathway involving nuclear factor erythroid 2-related factor 2 (Nrf2), a key transcription factor, can regulate the expression of certain genes. The protein products of these genes contribute to the detoxification and elimination of ROS through conjugative reactions and by increasing cellular antioxidant capacity. Furthermore, Nrf2 is a crucial factor in regulating the expression of endogenous antioxidants, including heme oxygenase-1 (HO-1). The Nrf2/HO-1 signaling pathway is reportedly instrumental in cellular responses under oxidative conditions [43]. Nrf2 elevates the expression levels of genes related to antioxidant enzymes and promotes the synthesis of these enzymes in astrocytes. Notably, antioxidant enzymes produced in astrocytes are transported to neuronal cells, providing a protective effect against OS [44]. Statins have been found to influence the Nrf2/HO-1 signaling pathway, thereby safeguarding cells against the destructive effects of ROS [45]. Habeos et al. reported that statins could augment the DNA-binding activity of Nrf2, leading to the expression of its target genes, including HO-1 and glutathione peroxidase, and protecting cells from ROS toxicity [46]. Increased lipid peroxidation is a common risk factor for AD, as it diminishes membrane integrity and alters the permeability of various ions in the plasma membrane. Studies have shown that statins can scavenge ROS and markedly reduce lipid peroxidation [47,48].

Overall, the beneficial effects of statins against oxidative damage are indisputable and have been confirmed in multiple neuropathological conditions, ranging from brain injuries to AD. Statins reduce OS by stimulating the Nrf2/HO-1 pathway and inhibiting the NOX pathway (Fig. 3).

2. Attenuation of neuroinflammation

Inflammation is a response that occurs in reaction to injury, trauma, or infection affecting cells and tissues. A substantial body of evidence in the literature details the biochemical connection between the brain and the immune system. Inflammation occurring within the brain is identified as neuroinflammation. Microglia and astrocytes, two key components of the brain's immune system, play pivotal roles in the process of neuroinflammation [49].

Inflammation is a primary contributor to the development of neurological disorders, as evidenced by the heightened expression of inflammatory factors in the CNS. Findings from

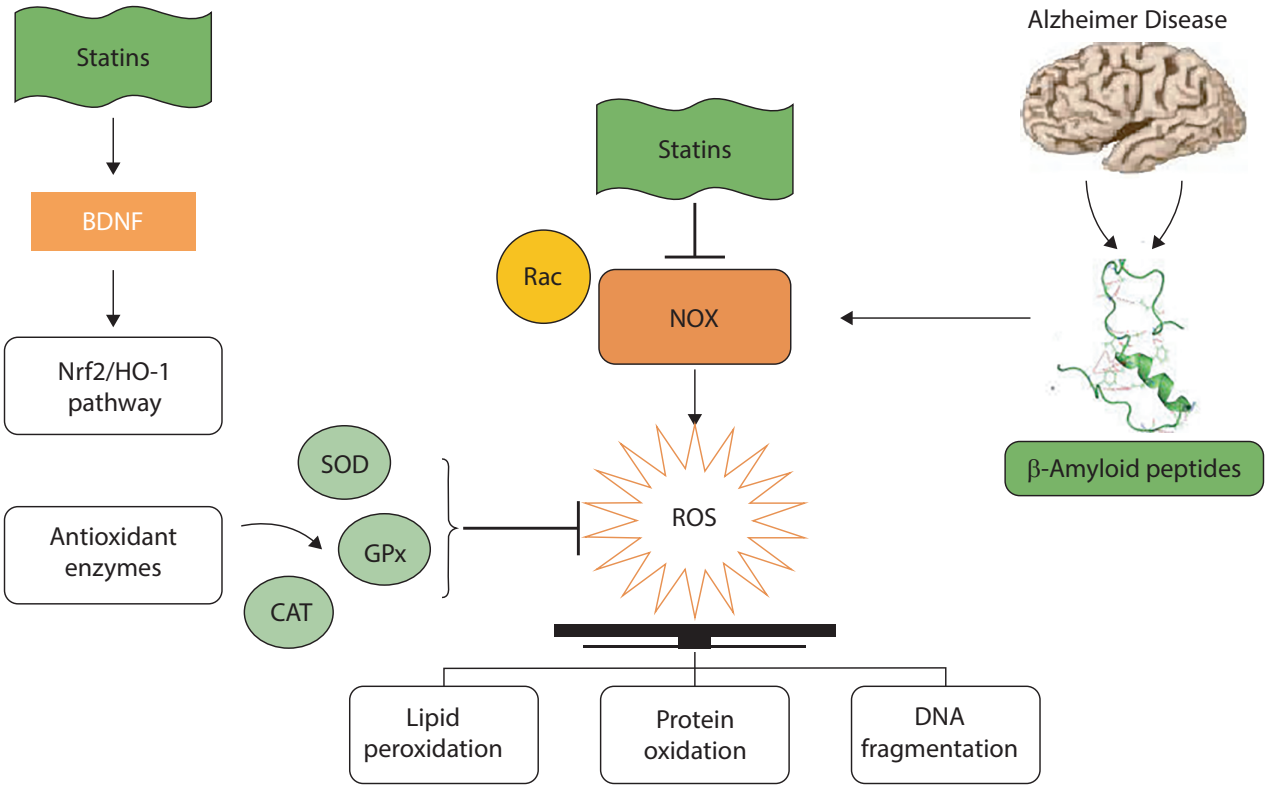

Fig. 3. Statins reduce oxidative stress in Alzheimer disease. The β-amyloid peptide increases the production of ROS by activating NOX. The Nrf2/HO-1 signaling pathway promotes expression of genes related to antioxidant enzymes and enhances antioxidant enzyme synthesis. Statins function as potent antioxidant compounds by activating the Nrf2/HO-1 pathway and inhibiting the NOX pathway. ROS, reactive oxygen species; NOX, nicotinamide adenine dinucleotide phosphate oxidase; Nrf2, nuclear factor erythroid 2-related factor 2; HO-1, heme oxygenase-1; BDNF, brain-derived neurotrophic factor; SOD, superoxide dismutase; GPx, glutathione peroxidase; CAT, catalase.

the 1980s indicate that immune-related factors are present near Aβ plaques [50]. It is now established that the release of cytokines and the broad activation of associated receptors in the brains of patients with AD lead to neuroinflammation [51]. However, some studies have demonstrated that a persistent immune response in the CNS is linked to neurodegeneration and can also induce and exacerbate Aβ pathologies [52]. Furthermore, inflammation may mediate a connection between early Aβ pathology and the subsequent development of NFTs [53].

Activation of microglial cells triggers the generation and release of proinflammatory cytokines. These cytokines stimulate neighboring astrocytes to further produce Aβ oligomers, which may stimulate neuronal cell death by intensifying inflammation [51]. In AD, the accumulation of intraneuronal Aβ, which forms senile plaques, instigates neuroinflammation through microglial activation. This process results in neurodegeneration and ultimately escalates neuronal death in the hippocampus. Given the clear link between statin administration and the reduction of inflammatory responses in AD, decreased neuroinflammation could be proposed as a key mechanism for the neuroprotective effects of statins. In AD, a reduction in Aβ formation has been associated with decreased neuroinflammatory responses [54]. One study demonstrated that atorvastatin prevents Aβ-induced microglial activation, which marks the initial phase of neuroinflammation [55].

The activation of microglia results in the release of several inflammatory factors, including TNF-α, IL-1β, and IL-6. These factors can exacerbate the pathogenesis of neurodegenerative

disorders by establishing an inflammatory microenvironment. The secretion of TNF-α and IL-6, both proinflammatory mediators, promotes neuronal apoptosis [56]. IL-6 is primarily synthesized in neuroglia, and it triggers the accumulation of inflammatory cells and the increased production of ROS during inflammation; furthermore, it collaborates with TNF-α to induce calcium overload and cell apoptosis [57]. Consequently, TNF-α is considered an effective target for the treatment of inflammatory diseases. A connection between statins and TNF-α production has been established. Previous research has indicated that statins can reduce the production of TNF-α and interferon gamma [58]. Lindberg et al. found that microglial cultures exposed to statins (specifically, atorvastatin and simvastatin) demonstrated a decrease in IL-6 levels [59]. Separately, Inoue et al. suggested that the cytokine inhibitory effects of statins on the capacity of IL-6 to promote inflammation may be linked to interference with the phosphorylation of the transcription factor STAT3 [60].

Beyond TNF-α and IL-6, the nuclear transcription factor kappa B (NF-κB) plays an important role in pathological processes and the generation of pro-inflammatory cytokines. NF-κB is instrumental in activating and advancing key events in AD, such as CNS dysfunction and neuroinflammation. Encouraging research has been published on the modulation of NF-κB activation within the CNS, which subsequently attenuates the processes that trigger neural degeneration [61].

As reported by Hilgendorff et al., all statins including atorvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin, and simvastatin inhibit NF-κB activity in monocytes. Despite this common property among statins, notable differences exist in the degree of inhibition provided. The potency of the statins, ranked from highest to lowest, is as follows: cerivastatin, atorvastatin, simvastatin, pravastatin, lovastatin, and fluvastatin. These differences are also reflected at the transcriptional level and the protein level of NF-κB–regulated tissue factor expression [62]. In a separate study conducted by Hernandez-Presa et al., treatment with simvastatin in a rabbit model of atherosclerosis yielded a decrease in the activity of the transcription factor NF-κB [63].

In the context of neuroinflammation, NF-κB regulates several genes, including TNF-α, IL-1β, and IL-6, through the nuclear translocation of transcription factors [64]. Monica et al. conducted a study to investigate the impact of statins on NF-κB activity, which is known to induce the messenger RNA expression of chemokines. Their findings suggest that statins can reduce inflammation by inhibiting both NF-kB activity and chemokine gene expression [65].

The enzyme cyclooxygenase (COX) has been documented to be important for the synthesis of prostaglandins, which are potent inducers of inflammation. Certain treatments have demonstrated positive effects in inhibiting neuroinflammation associated with disease progression through the inhibition of COX. Research has also indicated that the expression of COX-2 is primarily regulated by NF-κB [66]. Given that several studies affirm the role of NF-κB in COX-2 expression, inhibiting NF-κB can suppress COX-2 expression. Atorvastatin has been shown to mitigate inflammation by reducing the activity of NF-κB, in turn decreasing the expression of the pro-inflammatory enzyme COX-2 [63]. Ramalho et al. reported that the inactivation of NF-κB can inhibit the expression and synthesis of certain pro-inflammatory agents, including IL-6, TNF-α, and COX-2, as well as prostaglandin E_2 synthesis [67]. Therefore, based on the studies conducted, the inflammatory response appears to be an important characteristic of the pathogenesis of AD. Aβ stimulates inflammatory responses by activating NF-κB, which subsequently produces cytokines such as IL-1β, IL-6, TNF-α, and COX-2 [65]. Thus, inhibiting the production of these factors could be a potential therapeutic strategy for AD. Indeed, statins have been shown to prevent Aβ-induced microglial activation, an initial phase in neuroinflammation (Fig. 4).

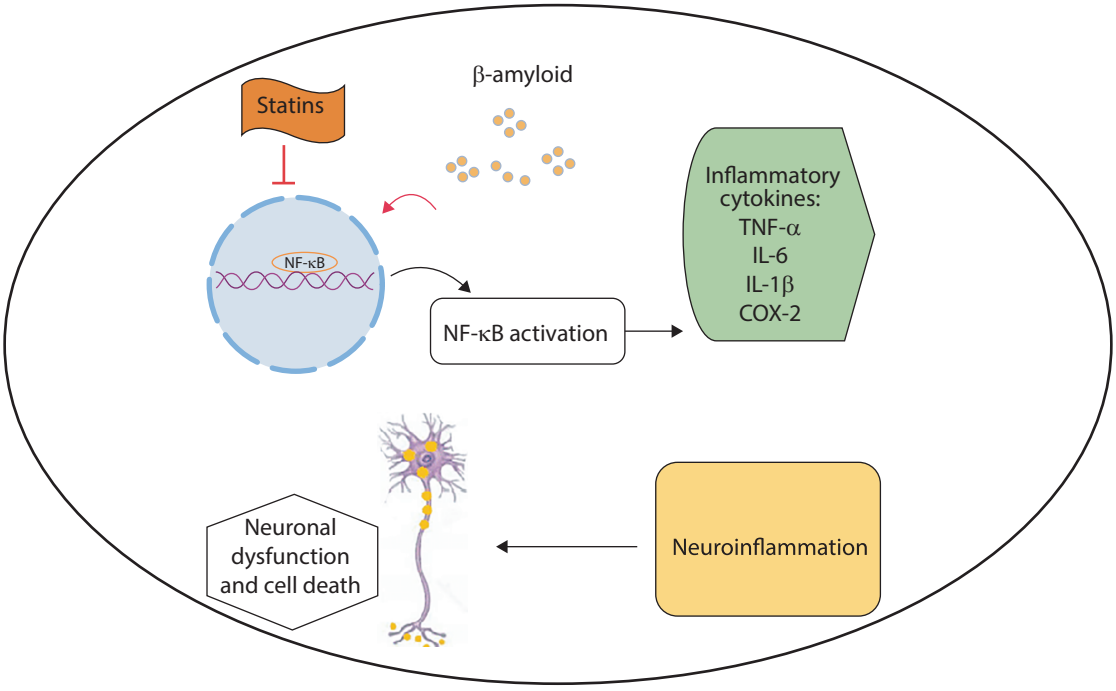

Fig. 4. Statins reduce neuroinflammation in Alzheimer disease. β-amyloid exerts neurotoxic effects by activating NF-κB, which in turn produces toxic inflammatory mediators, including cytokines. By decreasing NF-κB activity, statins lead to decreases in pro-inflammatory cytokines such as IL-1β, IL-6, TNF-α and COX-2. NF-κB, nuclear transcription factor kappa B; COX-2, cyclooxygenase 2.

3. Decreased synaptic damage and loss

Long-term potentiation (LTP), a form of synaptic plasticity, has been identified as the primary mechanism involved in the plasticity related to learning and memory [68]. Two recognized types of LTP occur in different regions of the mammalian nervous system. The first type relies on the activation of the N-methyl-D-aspartate receptor (NMDAR), while the second type, which has been less extensively studied, is NMDAR-independent. The most prevalent form of LTP involves the activation of the glutamate ionotropic NMDAR, which is highly permeable to calcium ions [69].

Early functional and structural synaptic loss in AD correlates with the severity of the disease. Multiple studies have revealed the mediating role of Aβ in the key mechanism involved in LTP impairment [70,71]. In the initial stages, Aβ oligomers induce reversible synaptic alterations that largely mirror those involved in normal action-dependent synaptic plasticity and dendritic pruning during development in the adult brain. However, in the later stages of the disease, tau-related neuropathology triggers irreversible changes [72]. Research from animal models suggests that Aβ interacts with tau to induce synaptic degeneration [17]. One important finding is that Aβ inhibits the induction of LTP in the hippocampus, specifically in the CA1 and DG areas [70,73]. Chen et al. reported that Aβ particularly impacts both presynaptic and postsynaptic neurons, reducing the NMDA peak amplitude [71]. Previous studies have indicated that statins can reduce Aβ levels in the CNS [74,75]. Moreover, atorvastatin has been confirmed to decrease Aβ by reducing APP, β-secretase, and OS in clinical models of dementia [76,77]. Simvastatin has also been reported to enhance vascular activity in the brain, decrease neuroglia activation, and reduce the number of dystrophic neurites induced by Aβ plaques [78].

Research supports the involvement of the Rho/Akt/cAMP response element-binding protein (CREB) pathway in the enhancement of LTP and memory induced by statins. This indicates

that statins promote the upregulation of the memory-related genes encoding c-Fos and Egr-1. The transcription of these genes takes place downstream of CREB activation [79]. Experiments conducted on the hippocampal CA1 region have shown that statins can enhance LTP by inducing Akt phosphorylation [80]. Besides directly inhibiting the production of mevalonate, statins influence synaptic plasticity and memory function through mechanisms that are independent of the mevalonate pathway. As ligands for peroxisome proliferator-activated receptor alpha, statins increase the transcription of CREB, thereby inducing the expression of neurotrophic factors such as brain-derived neurotrophic factor and neurotrophin-3 [81] (Fig. 5).

Glycogen synthase kinase 3 (GSK3) is a crucial enzyme in glycogen metabolism, with two isoforms: GSK-3α and GSK-3β. Research has shown that GSK-3β is associated with synaptic dysfunction and memory disruption. The activation of this enzyme results in a deficiency in LTP and an induction of long-term depression through its impact on NMDA receptors [82]. GSK-3β activity has been shown to lead to tau hyperphosphorylation, which can intensify neurodegeneration, synaptic dysfunction, and neuronal death in the hippocampus [83]. In other words, Aβ triggers abnormal activation of GSK-3β, resulting in the loss of dendritic spines and changes in spine morphology, which can contribute to neuronal loss in AD [84]. Interestingly, statins have been found to decrease the activity of GSK-3β, which is responsible for tau protein phosphorylation. As reported by Salins et al., statins lower the production of senile plaques by reducing the activity of GSK-3β, ultimately protecting neurons from the toxicity caused by Aβ [85].

AD and dementia strongly impact cholinergic neurons, which play an important role in memory function. Two types of receptors for acetylcholine (ACh) include nicotinic receptors (nAChRs) and muscarinic receptors (mAChRs). The selective loss of α7 nAChRs in the brains of patients with AD suggests a connection between this nAChR subtype and the pathophysiology of the disease [86]. In general, two potential strategies are used to address the cholinergic system dysfunction observed in patients with AD and dementia. One strategy involves the use of

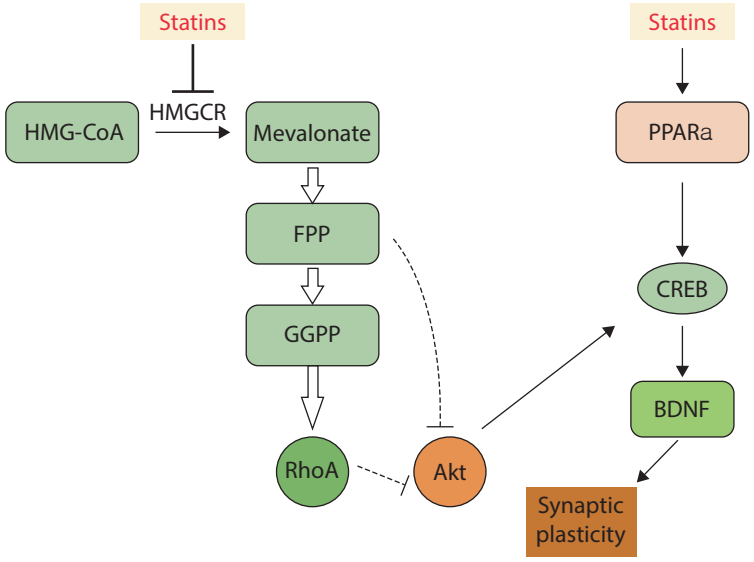

Fig. 5. Statins can regulate synaptic plasticity via impacts on neurotrophic factors such as BDNF. Through both MVA pathway-dependent and pathway-independent mechanisms, statins can stimulate the activation of CREB signaling molecular pathways. HMGCR, HMG-CoA reductase; FPP, farnesyl pyrophosphate; GGPP, geranylgeranyl pyrophosphate; PPARα, peroxisome proliferator-activated receptor α; CREB, cAMP response element-binding protein; BDNF, brain-derived neurotrophic factor; MVA, mevalonate.

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acetylcholinesterase inhibitors, which prevent the breakdown or hydrolysis of ACh, thereby increasing its levels in the CNS [87]. The second strategy proposes the activation of nAChRs and mAChRs to restore cholinergic function in patients with AD [88]. Zhao et al. reported that lovastatin can significantly increase the activity of choline acetyltransferase in the cortex and hippocampus [89]. In contrast, simvastatin reduces acetylcholinesterase activity in the frontal cortex of rats, which may consequently increase the levels of ACh in the synaptic cleft and alleviate the cholinergic dysfunction in AD [90]. GSK3 has also been established to decrease ACh synthesis, a process associated with the cholinergic deficiency in AD [91]. Interestingly, it has been previously noted that statins can decrease the activity of GSK-3β [85].

Overall, studies indicate that the activation of GSK-3β, followed by tau hyperphosphorylation, CREB inhibition, and cholinergic system deficiency, contribute to neuronal loss in patients with AD. Statins appear capable of enhancing synaptic plasticity by inhibiting the activation of GSK-3 β (Fig. 6).

Conclusion

AD is a devastating age-related neurodegenerative disease with a rapidly increasing prevalence. In addition to Aβ and NFT plaques, the brains of patients with AD exhibit signs of a persistent oxidative state, neuroinflammatory response, and synaptic disruption. Aβ stimulates microglial proliferation and triggers the release of ROS due to NOX activation. Extensive research suggests that the role of NOX in the development of various diseases, through excessive

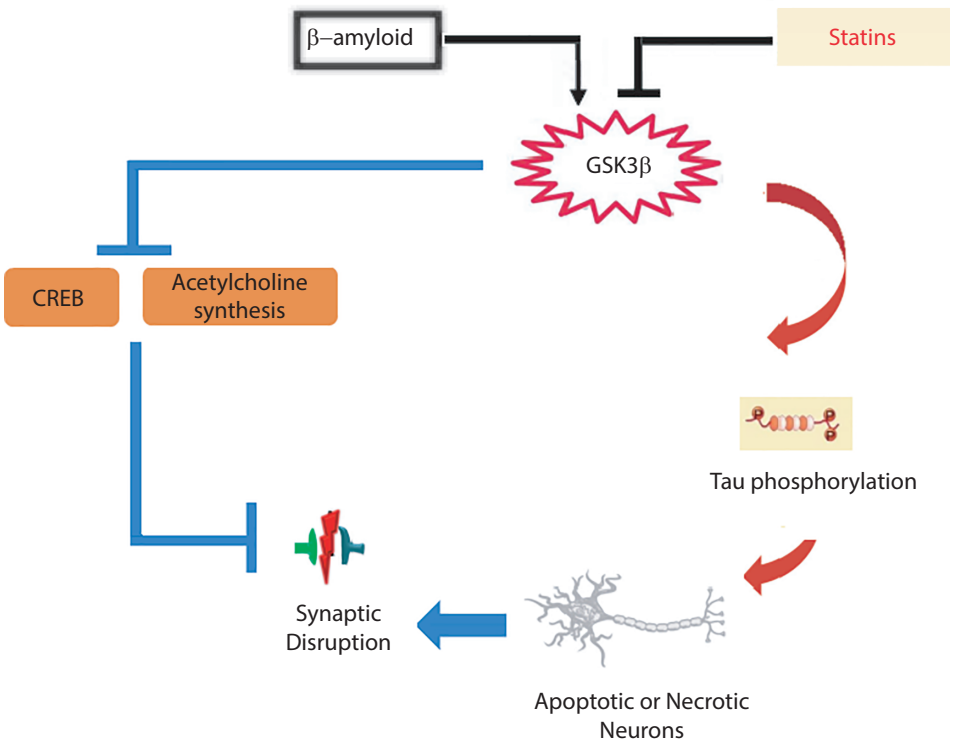

Fig. 6. Roles of GSK-3β in synaptic disruption. GSK-3β activation and subsequent tau hyperphosphorylation, CREB inhibition, and cholinergic system deficiency are involved in synaptic disruption. Statins can enhance synaptic plasticity by inhibiting GSK-3β activation. GSK-3β, glycogen synthase kinase 3 beta; CREB, cAMP response element-binding protein.

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production of ROS and establishment of an OS condition, implies that the inhibition of this enzyme by statins is responsible for statin-induced antioxidant effects. Additionally, statins exert antioxidant effects through the stimulation of the brain-derived neurotrophic factor/Nrf2 pathway and the subsequent reduction in intracellular ROS via the preservation and enhancement of endogenous antioxidants. Neuroinflammation is another key factor involved in the progression of AD, as evidenced by the increased release of inflammatory factors in the CNS. In AD, the interaction of Aβ fibrils with microglial cells leads to the activation of NF-κB, which in turn promotes the release of inflammatory cytokines including IL-1β, IL-6, TNF-α, and COX-2. Statins can reduce neuroinflammation by inhibiting NF-κB transcription factor activity and subsequently suppressing the release of inflammatory cytokines. According to the findings, early functional and structural synaptic loss in AD correlates with the severity of the disease. An aberrant increase in GSK-3β activity, induced by Aβ in the CNS, results in the loss of dendritic spines, morphological changes of spines, and neuronal loss. GSK-3β activation and subsequent tau hyperphosphorylation, CREB inhibition, and cholinergic system deficiency are implicated in synaptic disruption in AD patients. Statins appear to improve synaptic plasticity through the inhibition of GSK-3β activation. Given that statins exhibit several beneficial properties, including neuroprotective, anti-inflammatory, and antioxidant effects, they may be effective in treating neurological diseases.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Ethics Approval and Consent to Participate

Not applicable.

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Review Article

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Diagnosis and Management of Osteoporosis in Children and Adolescents

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Recent advances in medicine have led to an increase in the number of children and adolescents treated for various chronic diseases and cancer. Increasingly sophisticated genetic analysis techniques have also clarified some genetic factors that contribute to bone fragility. Osteoporosis, characterized by reduced bone mass and skeletal fragility, can result from primary or secondary causes that originate in childhood and adolescence, which are critical periods for bone mineral acquisition. It is essential to identify children and adolescents at risk of fractures due to osteoporosis, and early intervention is crucial. Conservative management strategies, such as treating underlying diseases, replacing deficient hormones, providing nutritional support to meet calcium and vitamin D requirements, and encouraging regular physical activity, should be prioritized. Pharmacological treatment should be initiated in a timely manner following a comprehensive bone health examination. Intravenous pamidronate therapy has been safely and effectively administered to children and adolescents, although long-term follow-up is necessary. Further investigation is needed regarding bone fragility fractures of unknown etiology and the application of new medications for pediatric use.

Introduction

Osteoporosis is a disorder characterized by a decrease in bone mass and changes in bone tissue micro-architecture, leading to skeletal fragility and an increased risk of fractures [1]. Historically, osteoporosis was considered an adult disease. However, it is now understood to have roots in childhood and adolescence, as these are the periods when bone mass and architecture are accumulated. The total bone mass reaches its peak a few years after the long bone epiphyses have fused. This maximum bone mass an individual can achieve is referred to as peak bone mass (PBM). A significant portion of PBM is determined by unmodifiable genetic factors [2]. However, other factors such as hormones, immobility, nutrition, pubertal timing, increased cytokines, and certain medications can also impact bone health. Therefore, chronic illnesses and specific osteotoxic treatments during childhood and adolescence can affect PBM accrual, leading to low bone mineral density (BMD). Low BMD during these formative years can increase the risk of fractures in youth, potentially leading to osteoporosis and fractures in adulthood. The incidence of fractures in children and adolescents is on the rise, with fractures resulting from a combination of intrinsic and extrinsic factors [3]. As such, it is crucial to assess bone health and adopt preventive measures early in children and adolescents at risk for low BMD. This article reviews the diagnosis,

causes, and management of osteoporosis in children and adolescents, with the aim of applying this knowledge to the clinical field for the evaluation and treatment of pediatric osteoporosis.

Definition and Diagnosis of Osteoporosis in Children and Adolescents

The World Health Organization defines osteopenia and osteoporosis based on T-scores, which are used to compare a patient's BMD with the maximum BMD of young adults. This comparison is only applicable to postmenopausal women. Some definitions categorize a Z-score of less than −1.0 as osteopenia and less than −2.5 as osteoporosis. The International Society for Clinical Densitometry (ISCD) recommends the term "low BMD for chronological age" when the BMD Z-score is lower than −2.0 [4]. The diagnosis of osteoporosis in children and adolescents should not be made solely based on bone densitometry (dual-energy X-ray absorptiometry [DXA]) [5]. The presence of one or more vertebral compression fractures without local disease or high-energy trauma indicates osteoporosis [6]. In the absence of a vertebral compression fracture, osteoporosis is defined by the presence of both a clinically significant fracture and a BMD Z-score of less than or equal to −2.0 [6]. Three or more long bone fractures are considered clinically significant (or two or more long bone fractures if the patient is under 10 years old) [6]. The ISCD definition aims to prevent the overdiagnosis and overtreatment of osteoporosis in young individuals who do not have skeletal fragility. However, waiting for a second or third fracture could unnecessarily delay treatment in children and adolescents with bone fragility, potentially leading to permanent disability [7]. In addition, a BMD Z-score>−2.0 does not preclude the possibility of skeletal fragility or increased fracture risk, as is also noted in the ISCD guidance [6]. Therefore, children and adolescents with risk factors for low BMD require a comprehensive bone health evaluation, which could lead to an accurate diagnosis of osteoporosis and identify the cause of bone fragility [7]. DXA is part of a comprehensive skeletal health examination in children and adolescents [6]. Although lumbar BMD and whole-body (total body minus head) BMD measurements are commonly performed in children, the 2019 ISCD guideline recommends using the proximal femur, lateral distal femur, and radius as skeletal sites for BMD measurement in children who need additional information, or in whom spine or whole-body DXA cannot be performed, if reference data are available [6]. Interpreting and reporting DXA results in children and adolescents should be done with caution. Appropriate reference data should be established, and BMD results should be adjusted in children with short stature or growth delay. The clinical utility of these measurements may be limited in very young children due to a lack of reference data for those under 5 years old. A few Korean pediatric reference BMD data sets have been published. BMD increases with age, reaching a plateau at 17–20 years in females and 20–23 years in males [8–10].

High-resolution peripheral quantitative computed tomography (pQCT) is a novel imaging method to evaluate BMD. pQCT at the radius and tibia can provide information about bone and muscle geometry, as well as volumetric cortical and trabecular BMD [11]. The potential diagnostic value and clinical applicability of pQCT for evaluating pediatric bone health warrant further investigation.

In cases of low BMD, a lateral thoracolumbar radiograph is recommended for detecting vertebral fractures. Lateral spine radiographs should be regularly performed in children and adolescents with persistent risk factors [12]. Asymptomatic vertebral fractures can sometimes be detected in patients with prolonged glucocorticoid (GC) treatment, progressive myopathy,

or immobility [12]. Specifically, children and adolescents with reduced mobility due to cerebral palsy or myopathy should receive a lateral spine X-ray examination at 6–8 years of age [13]. The bone condition of patients chronically treated with GCs requires careful follow-up, including a lateral spine X-ray before the initiation of GCs and regularly during treatment. Follow-up lateral spine X-rays are recommended according to the patient's risk factors, with a follow-up period ranging from 6 months to 2 years [14].

Physical examination and laboratory findings can provide us with clues to distinguish between various diseases that cause osteoporosis. The following clinical presentations may suggest congenital bone fragility: skin laxity, blue sclerae, abnormal dentition, easy bruising, a dysmorphic face, joint hypermobility, and wormian bones. In such instances, inheritable osteoporosis may be identified through molecular analysis. Genetic analysis has also revealed disease-causing variants of osteogenesis imperfecta (OI) associated genes in individuals who have a significant history of fractures but no extraskeletal symptoms [15]. Conversely, there have been instances of fragility fractures with unknown causes and mechanisms, despite negative genetic testing results. This highlights the need for further research into monogenic and polygenic determinants of skeletal strength. Hormonal studies should be conducted to diagnose or exclude hormone-deficient states. Bone turnover markers such as type 1 procollagen, carboxy-terminal telopeptides, alkaline phosphatase, and osteocalcin can be useful in monitoring medical therapy [16].

Causes of Osteoporosis in Children and Adolescents

Numerous factors can influence bone mineral deposition and the formation of bone mass. Certain genetic diseases can lead to inherent bone vulnerability and an increased risk of fractures, a condition known as primary osteoporosis. OI, Ehlers-Danlos syndrome, Marfan syndrome, cleidocranial dysplasia, osteoporosis-pseudoglioma syndrome, and fibrous dysplasia are all well-documented genetic diseases associated with bone fragility. Among these, OI is a rare inherited disorder characterized by bone fragility, which is caused by defects in the biosynthesis of type 1 collagen [17]. The clinical manifestations of OI can range from subclinical to lethal, and may include low bone mass, skeletal deformities, hypermobile joints, short stature, blue sclera, dentinogenesis imperfecta, and hearing loss. Consequently, OI is classified into several types based on these clinical features. The most common mutations associated with all types of OI are found in the *COL1A1* and *COL1A2* genes [18]. Apart from these genetic diseases, idiopathic juvenile osteoporosis can also present with symptoms such as bone pain, bone deformities, fractures, and low bone mass, all of which stem from an unknown cause. A diagnosis of idiopathic juvenile osteoporosis is made after other potential diseases have been ruled out.

Secondary osteoporosis develops due to chronic illness or treatments affecting bone formation, resorption, or bone matrix mineralization. The incidence of pediatric secondary osteoporosis is increasing as a consequence of improvements in the survival rates of chronic diseases, including cancer. Low BMD could be caused by hormone deficiencies or excess, malnutrition, immobilization, chronic inflammation, and medication associated with underlying diseases.

Table 1 summarizes various causes of secondary osteoporosis. Sex hormones influence the growth and maintenance of bone, consequently impacting PBM [19]. Therefore, the risk of fractures increases in several clinical conditions associated with hypogonadism, including delayed puberty, premature ovarian failure, hyperprolactinemia, Turner syndrome, Klinefelter syndrome, and hypogonadism induced by cancer treatment. Bone formation and resorption

Table 1. Causes of secondary osteoporosis

Neuromuscular disorders	Cerebral palsy
	Duchenne muscular dystrophy
	Progressive myopathy
Endocrine disorders	Delayed puberty
	Hypogonadism
	Growth hormone deficiency
	Hyperthyroidism
	Hyperparathyroidism
	Cushing disease
	Vitamin D metabolism disorder
Hematologic disorders	Leukemia/Lymphoma
	Hemoglobinopathy
Gastrointestinal disorders	Inflammatory bowel disease
	Celiac disease
	Malabsorption
	Chronic liver disease
	Milk intolerance
Renal disorders	Chronic renal failure
	Nephrotic syndrome
Connective tissue disorders	Systemic lupus erythematosus
	Juvenile idiopathic arthritis
	Juvenile dermatomyositis
Inborn errors of metabolism	Glycogen storage disease
	Galactosemia
	Gaucher disease
Others	Immobilization
	Anorexia nervosa
	Glucocorticoids
	Chemotherapeutic agents
	Immune suppressants
	Anticonvulsants
	Anticoagulant
	Radiation therapy

Adapted from Galindo-Zavala et al. [14] with CC-BY.

are also affected by growth hormone deficiency and thyroid disorders, leading to secondary osteoporosis. Hyperparathyroidism, which can result from parathyroid adenoma, chronic renal failure, disorders related to vitamin D metabolism, and multiple endocrine neoplasms, can enhance bone resorption by stimulating the receptor activator of nuclear factor kappa B ligand (RANKL) and reducing osteoprotegerin (OPG) levels due to an excess of parathyroid hormone [20]. In addition to endocrinologic disorders, neuromuscular, gastrointestinal, and renal disorders can also contribute to the development of secondary osteoporosis (Table 1). Childhood

cancer survivors often have low BMD due to the cancer itself, the effects of chemotherapy and radiotherapy, accompanying hormonal deficiencies, and poor nutritional status [21]. GC treatment is necessary for children and adolescents with certain chronic diseases, including cancer. Excessive GCs, whether iatrogenic or not, can directly or indirectly inhibit bone formation while increasing bone resorption [22]. Direct effects include upregulation of PPAR-γR2, increased sclerostin expression, and an increased RANKL/OPG ratio. Secondary hypogonadism, reduced calcium resorption, and decreased insulin-like growth factor-1 production can indirectly affect bone remodeling [22]. Therefore, patients receiving GC treatment for more than three months require special attention. A higher cumulative dose and longer duration of GC treatment are risk factors for low lumbar BMD in pediatric patients with chronic diseases [23].

Management of Osteoporosis in Children and Adolescents

It is essential to identify children or adolescents who are at risk for osteoporosis based on the abovementioned causes. Early diagnosis and management are critical for preventing recurrent fractures and permanent bone deformities. A developing skeleton has more potential for recovery and reshaping because growing bones continuously elongate, widen, and strengthen. Thus, the diagnosis of osteoporosis in children and adolescents does not automatically necessitate pharmacologic therapy. A comprehensive bone health examination should assess whether risk factors are transient and whether there remains growth potential. In cases of secondary osteoporosis, treatment of the underlying disease and cessation of osteotoxic medication are prioritized. Hormonal deficiencies should be diagnosed as early as possible and adequately managed [24,25]. Although conservative management is preferred in children and adolescents, pharmacological therapy should be considered in patients with recurrent lone bone fractures or vertebral fractures [7].

1. Conservative measures

The Committee on Pediatric Bone Health of the Korean Society of Pediatric Endocrinology has published clinical practice guidelines for optimizing bone health [26]. These guidelines recommend calcium and vitamin D supplementation, lifestyle changes, and regular physical activity for children and adolescents with chronic diseases to help prevent osteoporosis. Additionally, maintaining a healthy body composition and ensuring adequate hormonal status are also advised for optimal bone health.

Calcium and vitamin D supplementation improves BMD, particularly in children and adolescents with a low-calcium diet or decreased vitamin D concentration [27,28]. Calcium-rich foods are preferred over calcium tablets or powder. The recommended daily calcium requirements range from 500 mg to 1,000 mg according to age [26]. The 25-OH-vitamin D level should be maintained above 20 ng/mL (50 nmol/L) [29]. Vitamin D must be prescribed for patients with chronic diseases with vitamin D levels below 20 ng/mL. In individuals with low BMD (Z-score≤–2.0), vitamin D supplementation should be considered when vitamin D levels are below 30 ng/mL (75 nmol/L) [14]. However, meta-analyses of vitamin D supplementation have shown no effects on BMD or fracture risk when the baseline 25-OH-vitamin D level is >16 ng/mL (40 nmol/L) [30]. The maintenance dose of vitamin D is 400 IU for children below 1 year old and 600 IU for children over 1 year old. Calcium and vitamin D should be provided to all children and adolescents taking GCs, particularly when treatment lasts over 3 months. Healthy dietary supplements that contain appropriate calories, proteins, and vegetables or fruits containing

vitamins and minerals are also helpful for maintaining bone health [26].

Regular physical activity may enhance bone quality and strength, as the mechanical forces exerted on the bone aid in bone remodeling [31,32]. Weight-bearing exercises, including running, jogging, jumping, and resistance training, can boost bone mineral acquisition in children, especially during early puberty [31]. However, excessive exercise may also heighten the risk of fractures, underscoring the need for careful monitoring and control of activity intensity. For optimal bone health maintenance, a sedentary lifestyle should be avoided. Furthermore, an extremely lean physique can impact PBM accrual in adolescents, indicating the importance of maintaining an appropriate body weight [33].

2. Drug therapy

Bisphosphonates are the most frequently used medications for treating osteoporosis. These are synthetic analogs of pyrophosphate that inhibit osteoclastic function and decrease bone remodeling. Bisphosphonates are commonly prescribed to individuals with primary osteoporosis, such as OI. Current research indicates that oral or intravenous bisphosphonates can enhance BMD and decrease the frequency of fractures in both children and adults with OI [34,35]. Bisphosphonate therapy has proven to be effective and safe for both secondary and primary pediatric osteoporosis [36]. Bisphosphonates can significantly improve BMD in conditions of bone fragility related to disuse, such as cerebral palsy [37]. Intravenous bisphosphonate therapy can alleviate back pain and improve the vertebral height ratio when used to treat painful vertebral fractures in Duchenne muscular dystrophy [38]. Furthermore, bisphosphonates are well tolerated in childhood cancer survivors with low BMD [21].

Several bisphosphonates exist, each with varying potency and dosage (Table 2). Oral bisphosphonates are typically considered for mild cases or those without vertebral fractures [39]. However, the efficacy and safety of oral bisphosphonates in children have not been well studied. If oral bisphosphonates are contraindicated or vertebral fractures are present, an intravenous bisphosphonate should be used [14]. Intravenous pamidronate (3-amino-1-hydroxypropylidene-bisphosphonate) is primarily used in children and adolescents, and can be administered to children under 2 years of age. The dosage, interval, and duration of pamidronate may vary based on the center's or clinician's experience (Table 2). Zoledronic acid (ZA), a highly potent third-generation intravenous bisphosphonate, is increasingly being used in children and adolescents [40]. Recent studies have shown that ZA significantly improved BMD in children and adolescents

Table 2. Bisphosphonates used in pediatric patients

Drug	Administration	Dose	Potency
Pamidronate (second generation)	Intravenous (in 200–250 mL saline in 3–4 hours)	0.5–1 mg/kg/day, 2–3 consecutive days every 2–4 months 9–11.5 mg/kg/year Maximum: 60 mg/dose	100
Alendronate (second generation)	Oral	1–2 mg/kg/week <40 kg: 5 mg/day or 35 mg/week >40 kg: 10 mg/day or 70 mg/week Maximum: 70 mg/week	100–1,000
Neridronate (third generation)	Intravenous (in 200–250 mL saline in 3 hours)	1–2 mg/kg/day every 3–4 months Maximum: 100 mg/dose	100
Zoledronate (third generation)	Intravenous (in 50 mL saline in 30–45 minutes)	0.025–0.5 mg/kg every 6–12 months Maximum: 4 mg/dose	>10,000

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[38,41]. Compared to pamidronate, ZA treatment has a beneficial effect as it is generally infused over a shorter duration (30 minutes) with a longer interval (6–12 months) [42]. During bisphosphonate therapy, regular clinical monitoring using DXA and risk factor assessments should be conducted to determine whether to cease, reduce, or continue the same dose of bisphosphonate treatment [39].

Intravenous bisphosphonates may trigger acute phase reactions within 24–48 hours following the initial administration. These reactions can include symptoms such as fever, nausea, and malaise, which are typically self-limiting or can be managed with antipyretics. Iritis, characterized by red or painful eyes, is a rare side effect, particularly in patients with preexisting rheumatological conditions. Oral bisphosphonates, on the other hand, may cause esophagitis, dysphagia, and retrosternal pain. Transient hypocalcemia is a side effect common to both forms of bisphosphonates, necessitating the intake of calcium and vitamin D both before and after infusion. Bisphosphonates are retained in the bone, and as such, patients on long-term bisphosphonate therapy should be monitored due to an increased risk of atypical proximal fractures and jaw osteonecrosis. The use of bisphosphonates is contraindicated in children and adolescents with renal impairment, as the kidneys are responsible for the excretion of these drugs.

Denosumab received approval for the treatment of postmenopausal osteoporosis in 2010. Since then, it has emerged as a promising new therapy for skeletal diseases in pediatrics, although it has not yet received approval for pediatric use [43,44]. RANKL, expressed by osteoblasts, interacts with RANK on the surface of osteoclasts, thereby promoting osteoclast activity. Soluble OPG, also produced by osteoblasts, inhibits the interaction between RANKL and RANK. Denosumab, a monoclonal antibody, inhibits the binding between RANKL and its receptor RANK, effectively mimicking the effects of OPG [45]. To date, denosumab has been administered to a limited number of patients with various diseases such as OI, juvenile Paget disease, fibrous dysplasia, central giant-cell granuloma, metastatic giant cell tumor, and aneurysmal bone cyst in children. However, limited data are available regarding the dosage, duration, and response to denosumab therapy in children and adolescents. Furthermore, its efficacy and safety for pediatric use still need to be thoroughly investigated.

Conclusion

Personalized therapy, guided by a comprehensive risk factor assessment, is necessary for treating osteoporosis in children and adolescents. It is crucial to identify those at risk of osteoporotic fractures for early intervention. Conservative management can enhance BMD in this population, given the potential for spontaneous recovery of bone health. However, it is also essential to initiate an optimal pharmacological approach to prevent significant morbidity, such as irreversible bone deformity. Unkown etiology and mechanism of bone fragility need to be clarified. Additional research is needed to determine the efficacy, safety, dosage, and treatment duration of medical interventions, including new drugs.

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Conflict of Interest
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Case Report

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An Esophageal Leiomyoma with Cystic Degeneration Mimicking a Malignant Neoplasm

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Key Words
Endoscopic ultrasound; Esophagus; Leiomyoma; Mesenchymal tumors

Esophageal subepithelial tumors (SETs) are commonly encountered during screening endoscopy, and leiomyomas are the most common SET of the esophagus. Almost all patients with esophageal leiomyomas are asymptomatic; however, some present with dysphagia, depending on the size of the tumor and the extent to which it encroaches on the lumen. The typical endosonographic features of esophageal leiomyomas include well-demarcated, homogeneously hypoechoic lesions with echogenicity similar to that of the surrounding proper muscle layer, but without cystic changes. Histopathologically, esophageal leiomyomas do not undergo cystic or myxoid degeneration. This report presents a case involving a 65-year-old man with a symptomatic esophageal SET and endosonographic features indicative of malignant neoplasms, who was diagnosed with esophageal leiomyoma with cystic and myxoid degeneration following surgical resection.

Introduction

Esophageal subepithelial tumors (SETs) are commonly encountered during screening endoscopy, with an incidence of 0.4% (246/65,233), based on a recent Korean multicenter study [1]. Almost all esophageal SETs are asymptomatic and clinically insignificant, and leiomyomas are the most common. However, malignant SETs, such as gastrointestinal stromal tumors (GISTs) and SET-like carcinomas, can also occur in the esophagus. Endoscopic ultrasonography (EUS) is the most useful diagnostic modality for evaluating SETs of the gastrointestinal tract. The typical EUS features of leiomyomas include well-demarcated, homogeneously hypoechoic lesions with echogenicity similar to that of the surrounding proper muscle layer [2–4]. Calcifications are relatively common in leiomyomas (6.5%–18%); however, cystic changes are rarely observable [5,6]. In contrast, GISTs exhibit typical features on EUS, such as heterogeneously hypoechoic lesions with a marginal halo and hyperechoic spots, and slightly increased echogenicity compared to the surrounding proper muscle layer [5]. Furthermore, irregular margins and cystic changes have been suggested to be predictive factors of malignant potential [7]. Herein, we report a case of symptomatic esophageal leiomyoma with cystic changes on EUS that was managed successfully using thoracoscopic resection.

Case

A 65-year-old man presented with an esophageal SET that was incidentally detected during esophagogastroduodenoscopy. The patient had a 1-year history of chest discomfort and dyspepsia, and a 5-year history of diabetes. On endoscopy, the tumor was observed in the lower esophagus and no erosion or ulceration was noted on its surface (Fig. 1A). The tumor was hard and immovable when pressed with biopsy forceps. On EUS, the tumor measured 3.0 cm and had a heterogeneously hypoechoic appearance in the proper muscle layer (Fig. 1B). A cystic change, measuring 1.5 cm, was also noted on the inner side of the tumor (Fig. 1C). These EUS features are suggestive of malignant neoplasms such as GISTs. Physical examination revealed no abnormalities. Laboratory investigations revealed the following: white blood cell count, 5,470 cells/μL; hemoglobin, 15.0 g/dL; platelet count, 193,000 cells/μL; prothrombin time, 10.9 s (international normalized ratio 0.98); aspartate aminotransferase, 32 IU/L; alanine aminotransferase, 45 IU/L; total bilirubin, 0.62 mg/dL; total protein, 7.9 g/dL; albumin, 4.6 g/dL; blood urea nitrogen, 14.3 mg/dL; and creatinine, 0.9 mg/dL. Electrocardiography results were normal. Contrast-enhanced chest CT revealed asymmetric wall thickening with heterogeneous enhancement and a non-enhanced area in the lower esophagus, suggestive of malignant lesions (Fig. 2). Because the patient experienced symptoms, including chest discomfort, and EUS and CT findings were highly suspicious for malignant neoplasms, thoracoscopic resection was performed. Macroscopic examination revealed a well-defined, solid white ovoid mass with cystic changes, measuring 3.2 cm×2.2 cm, in the muscularis propria of the esophagus. Histopathological examination of the specimen revealed intersecting bundles or fascicles of bland spindle cells with eosinophilic cytoplasm (Fig. 3A). Cystic and myxoid degeneration was observed; however, significant cytological atypia, increased mitotic activity, and tumor necrosis were not detected (Fig. 3B, C). Immunohistochemical examination revealed that the tumor cells were positive for smooth muscle actin (Fig. 3D) and desmin, negative for c-kit, CD34, and S-100, and had a low Ki-67 proliferation index (<1%). Accordingly, the tumor was diagnosed as leiomyoma with cystic and myxoid degeneration. The patient's symptoms, including chest discomfort, subsided completely, and no recurrence was observed at the 24-month follow-up.

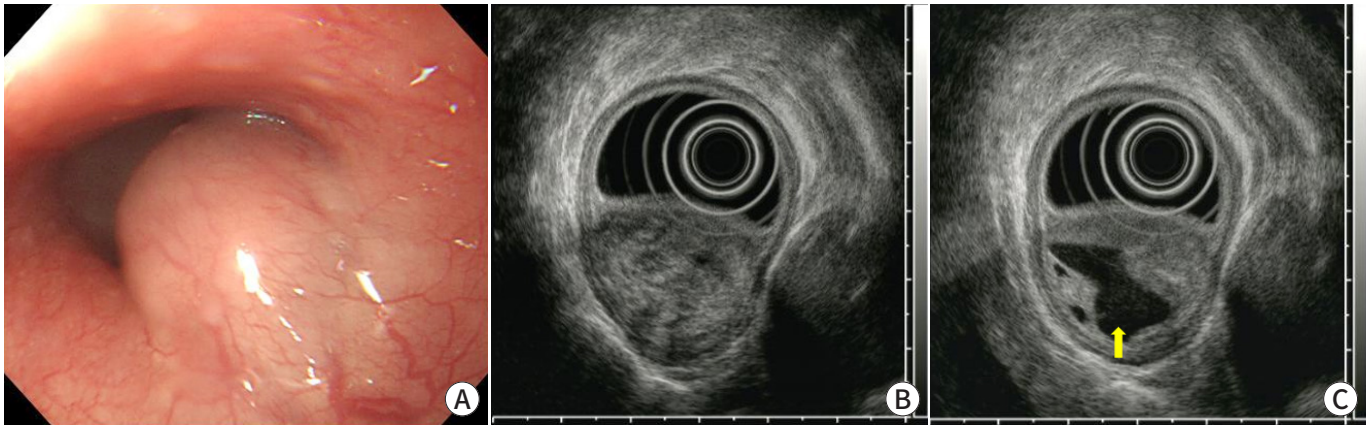

Fig. 1. Endoscopic and endosonographic findings. (A) A subepithelial tumor, measuring 3 cm, without surface erosion or ulceration is evident in the lower esophagus. (B, C) Endoscopic ultrasonography reveals a heterogeneously hypoechoic lesion with cystic changes (arrow) in the proper muscle layer.

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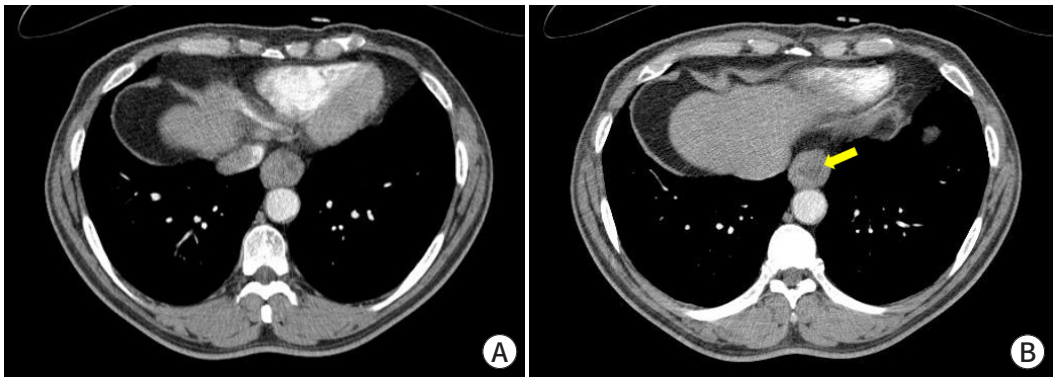

Fig. 2. Contrast-enhanced chest CT. (A, B) Asymmetric wall thickening with heterogeneous enhancement and a non-enhanced area (arrow) is evident in the lower esophagus.

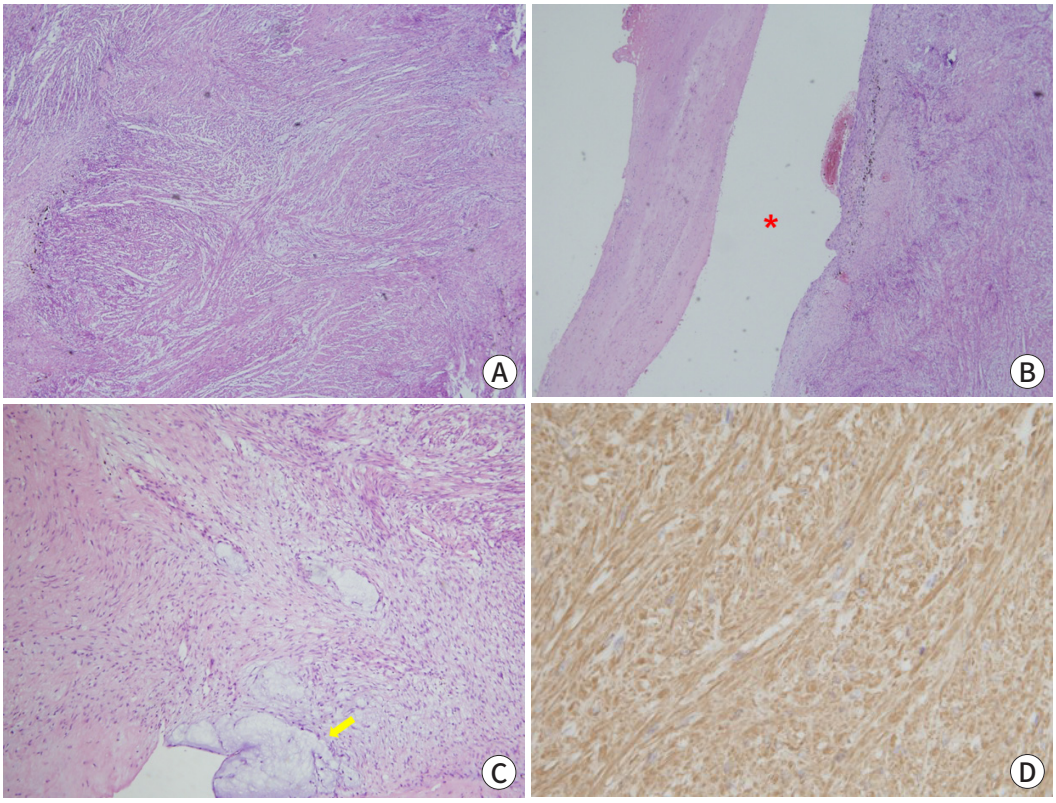

Fig. 3. Histopathological findings. (A) Intersecting bundles or fascicles of bland spindle cells with eosinophilic cytoplasm are observed (hematoxylin and eosin stain, ×40). (B, C) Cystic (asterisk) and myxoid degeneration (arrow) is evident; however, significant cytological atypia, increased mitotic activity, and tumor necrosis are not detected (hematoxylin and eosin stain, ×40 and ×100, respectively). (D) Tumor cells are positive for smooth muscle actin stain (×400).

Discussion

Esophageal leiomyomas are the most common benign SETs in the esophagus [8]. Unlike GISTs, esophageal leiomyomas do not undergo cystic or myxoid degeneration and are very rarely ulcerated [9]. Almost all patients with esophageal leiomyomas are asymptomatic, but some present with dysphagia, depending on the size of the tumor. In this case, the tumor was

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not ulcerated, but did exhibit cystic degeneration. This was believed to be the cause of the patient's symptoms (chest discomfort), which subsided after thoracoscopic resection.

Virtually all esophageal leiomyomas are well-demarcated, homogeneously hypoechoic lesions in the muscularis mucosa or proper muscle layer on EUS, and cystic changes are rarely observed [2,5]. However, in the present case, the esophageal leiomyoma appeared as a well-demarcated but heterogeneously hypoechoic lesion in the proper muscle layer. In addition, the echogenicity of the tumor was greater than that of the surrounding proper muscle layer, and extensive cystic changes were observed. These EUS features are usually highly suggestive of malignant stromal tumors such as GISTs. Chest CT also suggested a malignant rather than a benign lesion. However, EUS and CT cannot perfectly differentiate between benign and malignant SETs. Therefore, EUS-guided fine-needle biopsy has recently emerged as a commonly used diagnostic modality, with an acceptable yield (87.9%) [6,10,11]. In the present case, because the SET was symptomatic and the EUS and CT features were highly suggestive of malignancy, the tumor was surgically resected without histopathological confirmation via EUS-guided fine-needle biopsy.

Histopathologically, both leiomyomas and GISTs are mainly composed of spindle cells and display smooth muscle or nerve sheath differentiation; as such, immunohistochemical analysis is necessary for an accurate diagnosis. Leiomyomas are defined as desmin-positive and c-kit-negative tumors, whereas GISTs are defined as c-kit-positive [12]. The patient described in the present case was ultimately diagnosed with leiomyoma based on immunohistochemical staining.

Because esophageal leiomyomas are benign, resection is not required in most cases. However, when patients experience symptoms, such as dysphagia, the tumor size increases on follow-up examinations or, if the patient strongly desires to undergo tumor resection, resection is needed. In the past, surgical resection, such as thoracoscopic resection, was the primary treatment modality for esophageal leiomyomas located in the muscularis propria. However, endoscopic resection techniques, such as endoscopic submucosal dissection, endoscopic submucosal excavation, and submucosal tunneling endoscopic resection, have recently been introduced and have yielded high complete resection rates [13]. However, when a malignant SET is highly suspected, as in the present case, surgical resection is necessary to achieve satisfactory oncological outcomes.

Esophageal leiomyomas are often encountered as benign lesions during endoscopy. However, these tumors are sometimes symptomatic and do not exhibit the typical EUS and CT features of leiomyomas. In this situation, surgical resection is required to alleviate symptoms and rule out the possibility of malignancy.

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This case was previously published in Korean J Helicobacter Up Gastrointest Res 2021;21:152-155 in Korean. However, this case report includes different endoscopic, radiologic, and histopathologic images and is written in English to present different aspects. It is submitted with the approval of the editor of the Korean J Helicobacter Up Gastrointest Res.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Ethics Approval and Consent to Participate

Not applicable.

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Case Report

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A 12-Week Rehabilitation Protocol for the Management of Chronic Extensor Hallucis Longus Rupture Repaired with an Autograft of the Semitendinosus Tendon

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Key Words
Extensor hallucis longus tendon; Rupture; Hamstring tendons; Rehabilitation

Traumatic rupture of the extensor hallucis longus (EHL) is an uncommon finding in an outpatient setting. Surgical repair is typically necessary, particularly in chronic conditions that have persisted for six weeks or more. While several studies have reported EHL repair using autograft tendons, rehabilitation regimes vary, and standardized protocols have not yet been established. This case report presents with an inability to extend her left great toe. She underwent tendon reconstruction with an autograft semitendinosus tendon. At an 8-week follow-up, the patient reported greatly improved outcomes on the American Orthopaedic Foot and Ankle Society, Foot and Ankle Ability Measure, Foot and Ankle Disability Index questionnaire. Full recovery was achieved 12 weeks after surgery. The use of autograft semitendinosus tendon repair for chronic EHL tendon rupture, in conjunction with rehabilitation program, can be expected to yield favorable results.

Introduction

The rupture of the extensor hallucis longus (EHL) tendon is a rare occurrence, typically resulting from direct open trauma to the dorsum of the foot or ankle [1]. However, certain risk factors such as diabetes, rheumatoid arthritis, local steroid injections, and iatrogenic accidents during ankle arthroscopy may contribute to this type of injury [1,2]. The classic triad of clinical manifestations for this condition includes a hallux flexion deformity, an inability to actively extend the hallux interphalangeal joint, and normal passive mobility. We report a case of delayed presentation of chronic EHL tendon rupture that necessitated a reconstructive procedure using a semitendinosus autograft. One of the advantages of using the semitendinosus tendon as a graft is its easy accessibility and its strong resemblance to the EHL tendon [3,4].

Case

1. Preoperative evaluation

A 29-year-old woman was hospitalized after she sustained an injury from a falling kitchen knife, which punctured her left hallux metatarsophalangeal (MTP) joint. Initially, she was seen in the emergency department where she was diagnosed with an open laceration. The wound was primarily sutured at this time. During her recovery, she found herself unable to extend her left great toe while walking. As a result, she visited the surgery outpatient clinic and was subsequently referred to an orthopedic doctor due to a suspected tendon injury. This diagnosis was later confirmed through a clinical examination conducted by the orthopedic doctor.

The physical examination revealed that the patient had difficulty walking barefoot due to an issue with her left leg. Her left big toe displayed a plantar flexion deformity, and she was unable to actively dorsiflex her first interphalangeal joint (Fig. 1). However, passive dorsiflexion was possible with a full range of motion. The sensory function of the entire foot appeared to be normal. The MTP joint demonstrated a normal range of both active and passive motion. An ultrasound examination revealed a complete rupture of the EHL tendon, which had retracted approximately 6 cm from the tendon's edge (Fig. 2).

2. Surgical procedure

Surgery was performed with the patient in a supine position under regional anesthesia. A non-sterile thigh tourniquet was applied, set at 300 mmHg. An incision, measuring 8 cm, was made dorsally along the path of the EHL. This incision extended from the level of the MTP joint to the proximal EHL, with careful consideration to avoid the dorsocutaneous nerve. The proximal edge of the EHL tendon site was found to be adhered to the fat tissue. Dissection was carried out to liberate the proximal EHL from this adhesion. The gap between the proximal and distal stumps was measured to be 6 cm (Fig. 3).

A tendon stripper was used to harvest a 250-mm length of the semitendinosus tendon from the ipsilateral side. The harvested tendon was then sutured to the ends of the EHL tendon using the Pulvertaft and Kessler technique (Fig. 4A, B). After suturing, the tendon was carefully tensioned to ensure adequate extension of the great toe (Fig. 4C). The vitality and function of the EHL were assessed using a nerve stimulation machine set at 2.0 μV, which confirmed positive movement and functionality of the EHL tendon (Fig. 4D).

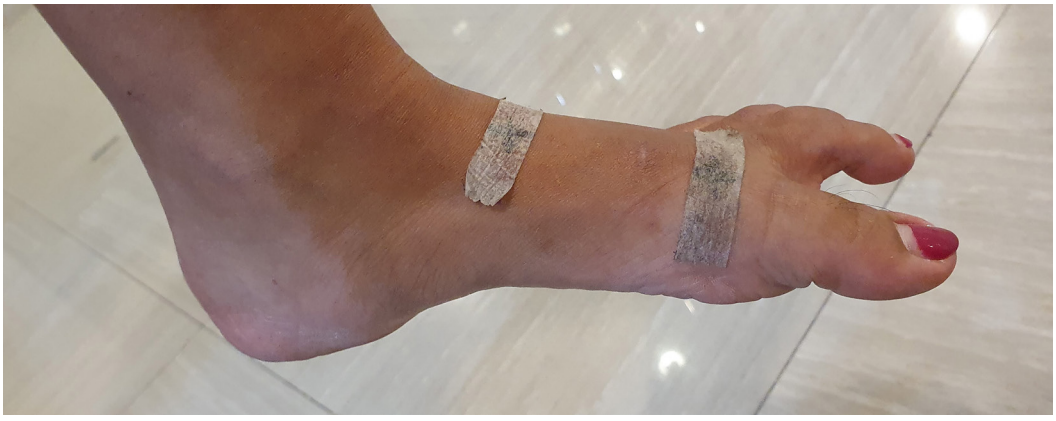

Fig. 1. Clinical presentation of the patient's left foot reveals hallux flexion deformity.

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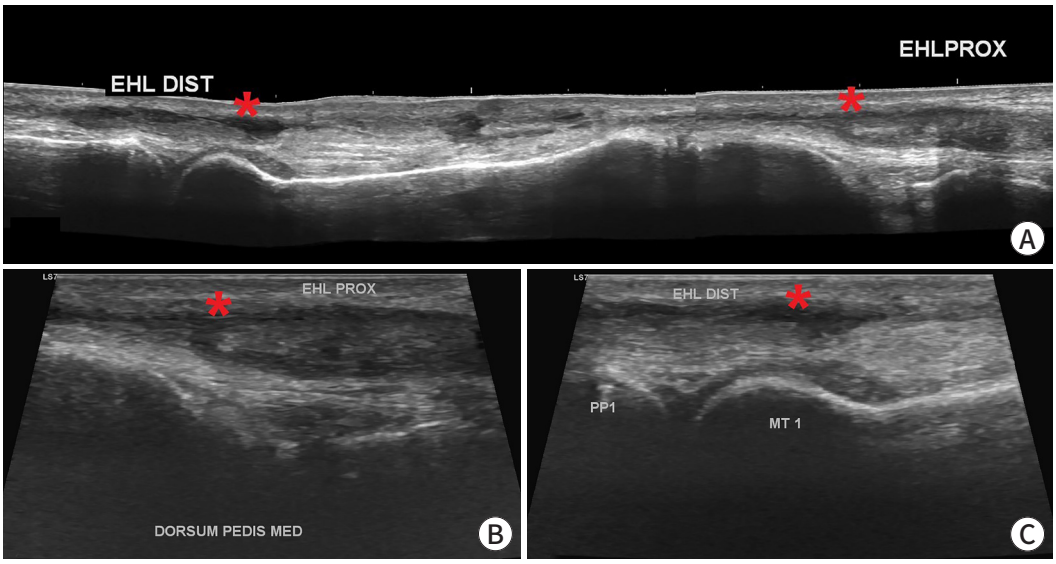

Fig. 2. Preoperative ultrasonography was performed to evaluate the integrity of the extensor hallucis longus (EHL). (A) Longitudinal ultrasound imaging of the dorsal aspect of the left ankle showed complete rupture of the EHL tendon with a gap between the stumps (asterisk). (B) The proximal stump (asterisk) of the torn EHL tendon was at the medial cuneiform level. (C) The distal stump (asterisk) of the torn EHL tendon was isolated at the metatarsal level. EHL DIST, distal EHL; EHL PROX, proximal EHL; DORSUM PEDIS MED, dorsum pedis medial; PP1, proximal phalanx 1; MT1, metatarsal 1.

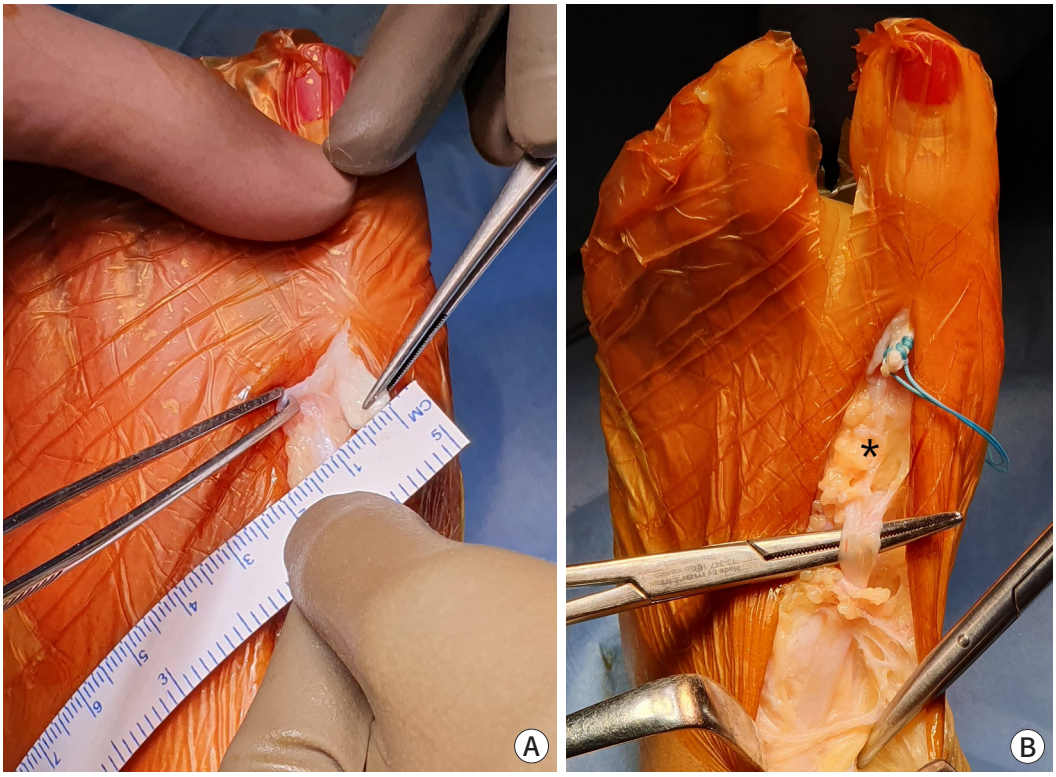

Fig. 3. Intraoperative findings. (A) Intraoperative view shows that the distal extensor hallucis longus (EHL) tendon width was 5 mm. (B) The gap between the proximal and distal EHL tendon stump was 6 cm; it is noteworthy that the proximal stump adhered to the fat tissue (asterisk).

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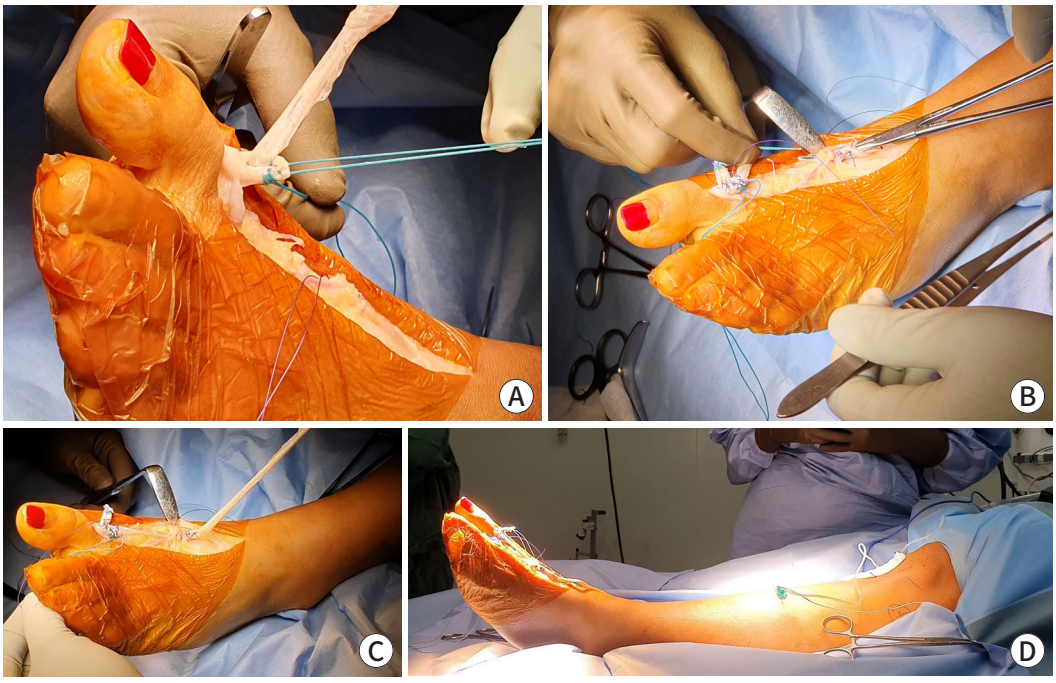

Fig. 4. Intraoperative findings. (A, B) The semitendinosus tendon graft was sutured to the proximal and distal extensor hallucis longus (EHL) stumps using the Pulvertaft and Kessler technique. (C) The sutured tendon was pulled to assess tendon tension and extension of the big toe. (D) EHL vitality and function were tested using a nerve stimulation machine and showed extension of the great toe.

3. Postoperative care

One week after surgery, the patient visited the surgical outpatient clinic for a wound assessment. Upon physical examination, her left great toe demonstrated ongoing weakness in active extension, prompting a recommendation for electrical muscle stimulation. The short leg splint was kept in place for six weeks post-surgery, after which it was substituted with a boot walker for an additional six weeks. By the second week after surgery, her left great toe showed slight improvement, with an extension of approximately 10°. The patient was then guided in passive dorsiflexion of the big toe. Four weeks post-surgery, there was a noticeable improvement in the left great toe, although some weakness remained. Active exercises for the great toe were introduced six weeks post-surgery, and the patient was given the go-ahead to participate in cycling. Additionally, transcutaneous electrical nerve stimulation was added to the program to address superficial nerve irritation on the dorsolateral aspect of the foot.

At an 8-week follow-up (Fig. 5), scores on the American Orthopaedic Foot and Ankle Society (AOFAS) hallux MTP scale ranged from 59 to 85. The Foot and Ankle Ability Measure activities of daily living subscale score varied between 43% and 85%, while the sport subscale score ranged from 25% to 79%. The Foot and Ankle Disability Index activities subscale score fluctuated between 56% and 86%, with the sport subscale score ranging from 31% to 81%. By the 10-week follow-up, improvements in pain and power were observed, and the patient was prepared to intermittently remove the boot walker. By the 12-week follow-up, the patient was given permission to completely discontinue the use of the boot walker. She exhibited near-normal active extension of the great toe without any pain. Further details of the postoperative rehabilitation protocol can be found in Table 1.

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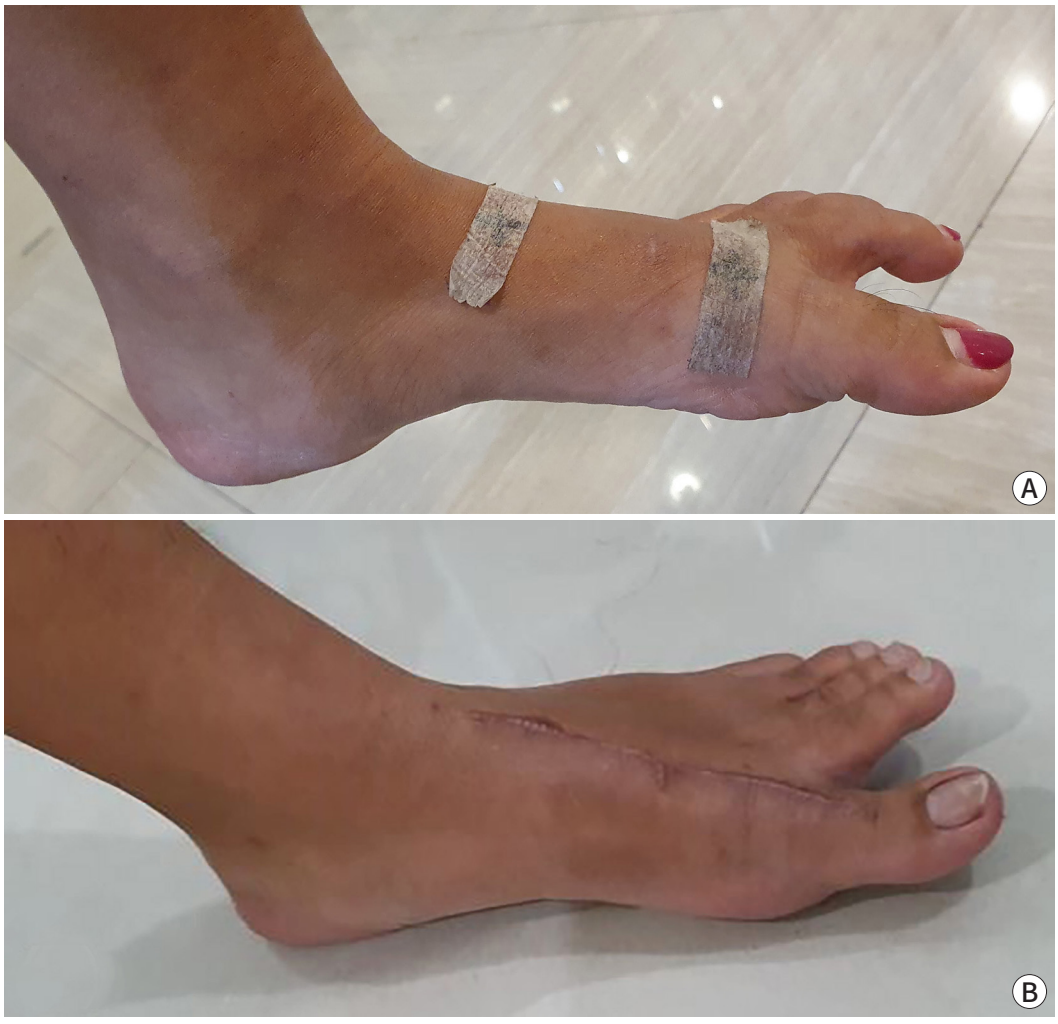

Fig. 5. An 8-week postoperative follow-up. (A) The left hallux position before surgery. (B) The hallux extension strength was nearly normal.

Discussion

A cohort study revealed an estimated 2% incidence of EHL rupture in the general population [5]. In this presented case, the injury was consistent with a zone 3 injury based on the Al-Qattan study (Table 2) [6]. Various methods exist for treating EHL ruptures, including primary suturing or reconstruction surgery with a tendon graft if primary suturing is not feasible [3]. Chronic EHL tendon ruptures (≥6 weeks) are commonly treated with reconstructive surgery involving a tendon graft or tendon transfer, as primary suturing can be challenging due to high tension, contracture, or degeneration of the ruptured tendon [7]. The etiology of EHL rupture is often associated with trauma, such as sharp objects falling onto the dorsum of the foot (e.g., a piece of glass, knife, mirror, or metal object) [1].

Commonly, autologous tendon grafts such as the semitendinosus, gracilis, plantaris, peroneus tertius, extensor digitorum longus, and extensor digitorum brevis are considered potential options for EHL repair [3,7]. The extensor digitorum longus and extensor digitorum brevis are typically used for shorter grafts, while the plantaris and peroneus tertius grafts are favored

Table 1. The 12-week rehabilitation protocol following extensor hallucis longus tendon reconstruction

Week	Program	Hallux range of motion (ROM) / Weight bearing (WB)
1	Wound healing and electrical muscle stimulation (EMS)	No ROM and no WB; a posterior splint was worn
2	Wound healing and EMS	No ROM and no WB; a posterior splint was worn
3–4	Passive at-home stretching of the hallux: 3 times daily, 10 minutes, with EMS.	No active ROM and partial WB; a posterior splint was worn
5–6	Passive at-home stretching of the hallux with increased power: 3 times daily, 10 minutes, with EMS.	No active ROM and partial WB; a posterior splint was worn
6	Active stretching of the hallux: 3 times daily, 10 minutes, with EMS. Static cycling: 3 times weekly, 15 minutes.	Start active ROM, remove the posterior splint, and start full WB on the boot walker everyday
8	Static cycling: 3 times weekly, 30 minutes. Gait cycle and toe crunch exercises were performed to improve stiffness and walking.	More active ROM, full WB on the boot walker for outdoor activity
10	Static cycling: 3 times weekly, 30 minutes. Gait cycle and toe crunch exercises were performed to improve stiffness and walking. Lower extremities strengthening routine.	Allow more active ROM, full WB on the boot walker at work
12	Static cycling: 4 times weekly, 30 minutes. Gait cycle and toe crunch exercises were performed to improve stiffness and walking. Lower extremities strengthening routine.	Remove boot walker and start full WB with comfortable shoes

Table 2. Anatomical zones of extensor hallucis longus (EHL) tendon laceration

Zone	Anatomical description
1	At EHL insertion on the distal phalanx
2	Between zones 1 and 3
3	Over metatarsophalangeal joint
4	At dorsal of foot between zones 3 and 5
5	Under the extensor retinaculum
6	Proximal to the extensor retinaculum

Data from Al-Qattan [6].

for longer grafts due to their sufficient length. However, these tend to have smaller diameters compared to the EHL tendon. The semitendinosus tendon, in contrast, offers both adequate length and a diameter similar to the EHL tendon, making it relatively easy to harvest. Moreover, it has shown superior regenerative results compared to the other options [3].

There is scarce information in the literature regarding the outcome of EHL reconstruction. Tuncer et al. reported a case study involving iatrogenic synovectomy of the EHL during ankle arthroscopy using radiofrequency thermal ablation. The study demonstrated that chronic EHL tendon rupture treated with autograft semitendinosus resulted in a positive outcome 12 weeks after tendon reconstruction, with the patient remaining symptom-free for a year [8]. Park et al. documented the case of a 15-year-old boy with chronic EHL rupture following a taekwondo match, who underwent tendon reconstruction with autograft semitendinosus. The study concluded that the semitendinosus tendon could serve as a potential graft material when primary suturing is challenging to perform [3]. Lohrer and Nauck reported various surgical

techniques for EHL tendon rupture involving tendon reconstruction or primary repair, aiming to minimize the need for skin incisions in sensitive areas. An autograft of the semitendinosus tendon appeared to yield better outcomes than a gracilis tendon autograft, tenodesis to a nearby tendon, or primary repair [9].

Bronner et al. published a report about mobilization protocols for EHL laceration rehabilitation. Regrettably, the report did not provide specific guidelines concerning the timing, duration, frequency, and intensity of hallux mobilization therapy. The general consensus for EHL rehabilitation recommends a three-week period of immobilization, followed by passive mobilization and resistance training for active mobilization [10]. Delaying active mobilization until 5 or 6 weeks postoperative or until the patient feels comfortable during passive mobilization is recommended as a way to reduce the risk of re-rupture [11]. The prolonged use of braces is also recommended to decrease the risk of re-rupture. The braces used for immobilization in cases of EHL rupture are those that limit ankle motion while keeping the foot in a natural or dorsiflexed position, thereby reducing the risk of excessive tension, strain, and friction on the tendon [12].

In instances where primary suturing is challenging due to a neglected case of EHL tendon rupture, the use of an autograft of the semitendinosus tendon has demonstrated favorable results. We selected the semitendinosus tendon for grafting because of its resemblance to the EHL tendon and its superior regenerative capabilities. A 12-week postoperative rehabilitation program is crucial to aid the healing process and guarantee satisfactory tendon mobility. This timeframe was considered adequate for patient recovery before discharge from our clinic.

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No potential conflict of interest relevant to this article was reported.

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Images and Solution

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Fibromuscular Dysplasia Involving the Iliac Artery and Mimicking Atresia of the Left Iliac Artery

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A 44-year-old woman was referred to the cardiology department due to experiencing heaviness in both legs during exertion and decreased ankle-brachial indexes of 0.83 and 0.78, respectively. She had a mild case of aplastic anemia. Lower extremity computed tomographic angiography (CTA) revealed a total occlusion of the left iliac artery from the bifurcation of the abdominal aorta, which was reconstructed at the level of the common femoral artery (Fig. 1A, red arrow). Atherosclerotic plaque was clearly visible at the abdominal aorta (Fig. 1B, C). However, the occluded iliac artery showed thread-like hypoplasia without any definitive atherosclerotic occlusion (Fig. 1D, red arrow).

Initially, we suspected congenital atresia of the iliac artery due to the patient's hypoplastic

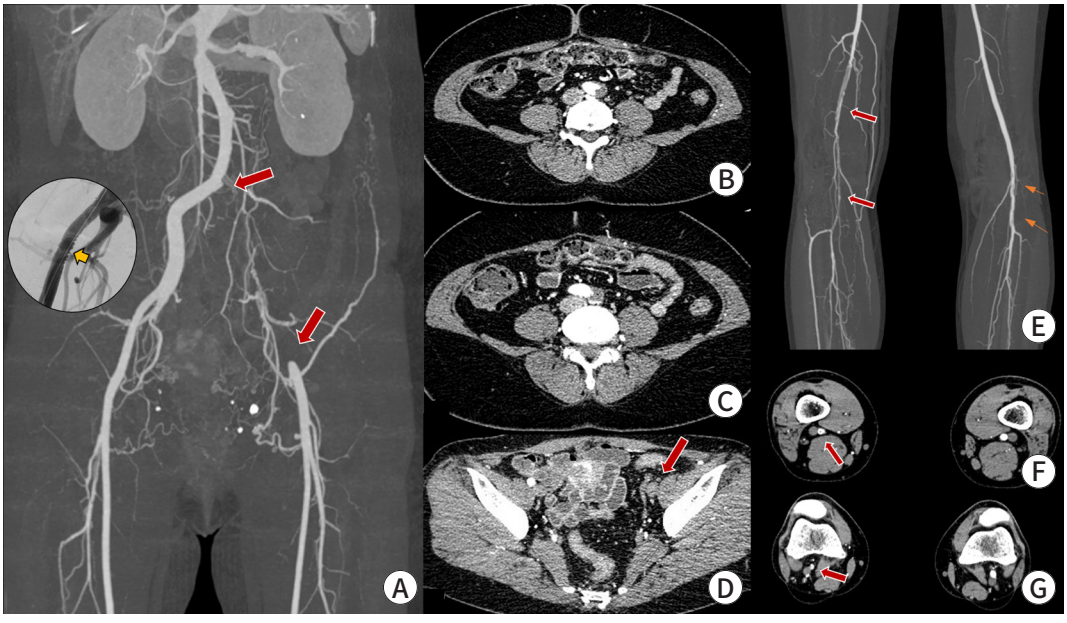

Fig. 1. CT angiography findings of the lower extremities. (A) The left iliac artery is completely occluded from the aortic bifurcation (circle; "string of beads" appearance of the right external iliac artery from invasive angiography). (B) Atherosclerotic plaques are present in the abdominal aorta and (C) at the bifurcation site. (D) A thread-like hypoplastic left iliac artery is visible. (E–G) Multiple layers of thread-like stenosis (red arrows) and a beaded appearance of the left popliteal artery are evident on CT angiography (orange arrows).

iliac artery, despite this being a rare condition. However, the renal arteries shown on CTA (Fig. 1A) suggested the possibility of fibromuscular dysplasia (FMD). We performed angiography on the candidate vessels. Both renal arteries displayed the typical "string of beads" appearance associated with FMD (Fig. 2A). The findings from intravascular ultrasonography were also consistent with FMD (Fig. 2B, C). Both carotid arteries were relatively normal in shape, but had tortuous courses. In contrast to CTA, the right external iliac artery exhibited a "string of beads" appearance on angiography (Fig. 1A, circle). Additionally, the right popliteal artery showed multiple layers of tread-like stenosis, and the left popliteal artery displayed a beaded appearance on CTA (Fig. 1E–G, red arrows).

FMD is a non-inflammatory and non-atherosclerotic arterial disease of unknown etiology.

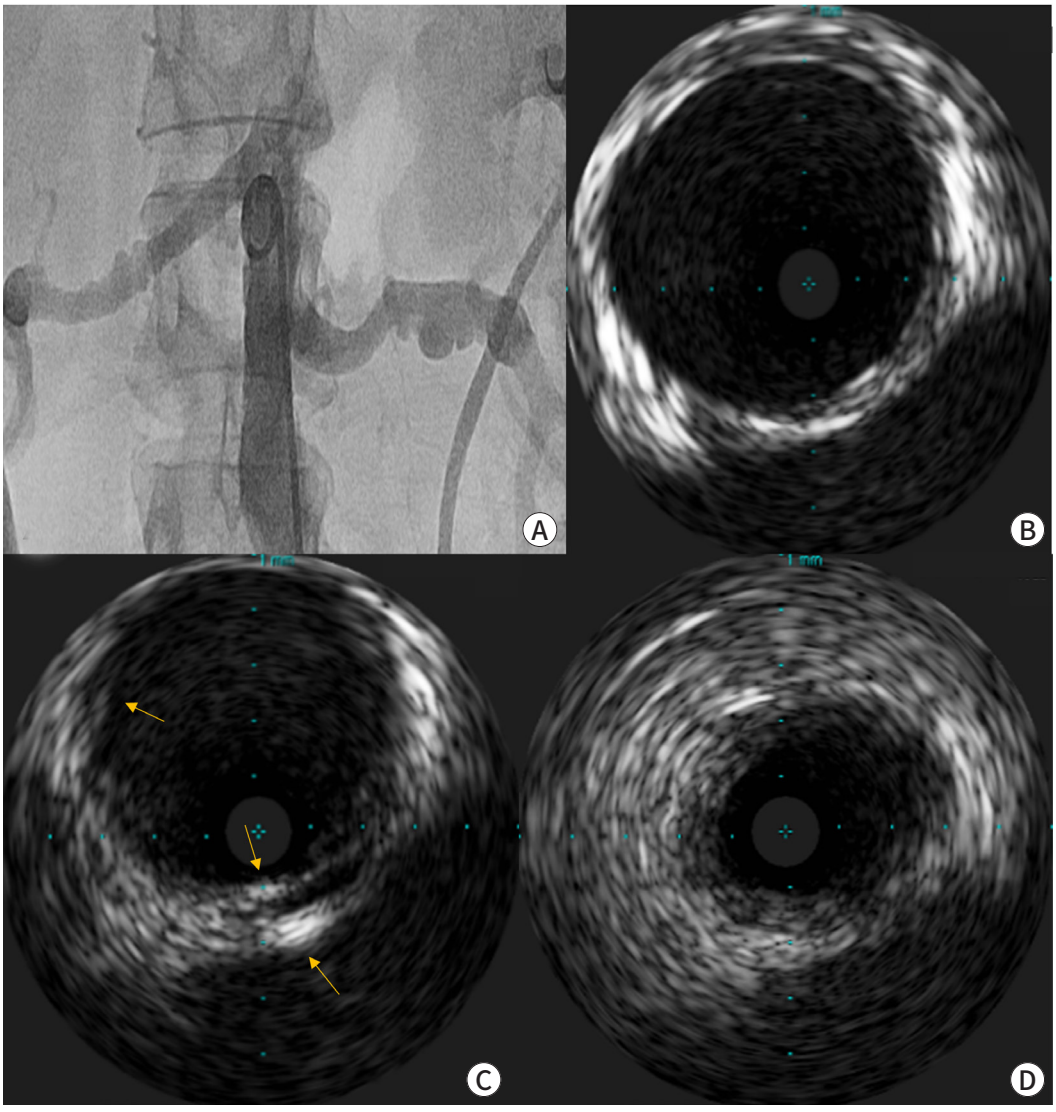

Fig. 2. Invasive images of the renal arteries. (A) Angiography reveals the typical "string of beads" appearance in both renal arteries. Intravascular ultrasonography indicates varied disease progression. (B) The vessel layers are relatively preserved. (C) There is an intimal fibromuscular ridge and increased medial echogenicity, as indicated by the arrows. (D) Circumferential hyperplasia of the intimal or medial layers is noted, accompanied by denudation of the vessel layers.

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Historically, FMD was categorized based on the arterial layers affected. However, obtaining pathological specimens is now a rare occurrence. Today, FMD is typically diagnosed through imaging studies, and an angiographic classification is commonly employed [1].

This patient exhibited tubular and multifocal stenosis, which is characteristic of FMD, and primarily showed lower extremity involvement. This article underscores the importance of considering FMD in middle-aged women presenting with peripheral artery obstructive disease but lacking traditional risk factors. It also highlights the utility of various imaging modalities in such cases.

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