Original Article

Long-Term Preoperative Nonsteroidal Anti-inflammatory Drug Use Does Not Impact Revision Rate After Repair of Rotator Cuff, Achilles, Distal Biceps, or Quadriceps Tendon

Romir Parmar, B.S., Sailesh V. Tummala, M.D., Alejandro Holle, B.S., Jose Iturregui, M.D., Alexander J. Hoffer, M.D., and John M. Tokish, M.D.

Purpose: To determine whether long-term preoperative nonsteroidal anti-inflammatory drug (NSAID) use affected the revision rates after primary tendon repair for the following common sports medicine surgical procedures: rotator cuff repair (RCR), Achilles tendon repair (ATR), distal biceps repair (DBR), or quadriceps tendon repair (QTR). **Methods:** A retrospective comparative study using a national insurance database was performed. Patients who underwent major tendon repair, including RCR, ATR, DBR, or QTR, with at least 2-year follow-up were identified. Those who had a diagnosis of long-term NSAID use prior to the index operation were identified and matched 1:4 to controls without NSAID use based on age, sex, specific tendon repaired, and Elixhauser Comorbidity Index. The revision repair rates of the 2 groups were compared. **Results:** A total of 36,068 patients underwent major tendon repair. Of these, 7,246 (20%) met the long-term NSAID use criteria prior to tendon repair (NSAID users). After RCR, 3.2% of NSAID users (n = 190) and 2.6% of controls (n = 617) underwent revision surgery within 2 years (odds ratio [OR], 1.15; 95% confidence interval [CI], 0.97-1.36; $P = .10$). After ATR, NSAID users had a revision rate of 3.9% (n = 24) versus 2.5% (n = 62) in the control cohort (OR, 1.47; 95% CI, 0.89-2.38; $P = .12$). After DBR, both NSAID users and controls had fewer than 11 revision cases (OR, 1.54; 95% CI, 0.49-4.16; $P = .42$). After QTR, the revision rate was 5.9% (n = 30) for NSAID users compared with 4.8% (n = 95) for the control group (OR, 1.22; 95% CI, 0.77-1.86; $P = .38$). None of the observed differences in revision rates between NSAID users and controls were significant. **Conclusions:** Patients with a diagnosis of and coding for long-term preoperative NSAID use do not have greater revision rates within 2 years of primary tendon repair than patients without this diagnosis. **Level of Evidence:** Level III, retrospective case-control study.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used in the management of inflammation and associated pain.[1,2] Musculoskeletal system–related conditions affect a large proportion of the United States population, and approximately 95% of patients with chronic musculoskeletal pain have been prescribed NSAIDs at least once.[3-5] Disorders associated with long-term pain can have major negative impacts on an individual's physical, social, and psychological health, as well as his or her overall quality of life.[6] Many patients with chronic pain due to inflammatory and degenerative conditions use NSAIDs regularly to assist in daily pain management.[7]

The primary mechanism of action of NSAIDs occurs through blocking cyclooxygenase (COX), which is an important enzyme in the production of prostaglandins, inflammatory mediators from arachidonic acid.[8] Although NSAIDs are beneficial in reducing pain to allow movement and function,[9] they may have a negative impact on soft-tissue integrity.[10] When a soft-tissue injury occurs, the natural response of the human body is to upregulate the inflammatory pathways, which play an important role in tissue healing.[11,12] However, NSAIDs reduce the production of inflammatory mediators such as prostaglandins and are thought to interfere with these physiological soft-tissue healing processes.[13]

From The University of Arizona College of Medicine–Phoenix, Phoenix, Arizona, U.S.A. (R.P.); and Department of Orthopaedic Surgery, Mayo Clinic, Phoenix, Arizona, U.S.A. (S.V.T., A.H., J.I., A.J.H., J.M.T.).

Received August 1, 2024; accepted October 14, 2024.

Address correspondence to Sailesh V. Tummala, M.D., Department of Orthopaedic Surgery, Mayo Clinic, 5777 E Mayo Blvd, Phoenix, AZ 85054, U.S.A. E-mail: tummala.sailesh@mayo.edu

2666-061X/241217

https://doi.org/10.1016/j.asmr.2024.101034

A number of animal studies investigated the effect of NSAIDs on tendon and ligament healing, but the results were conflicting.[1,14-24] There remains a paucity of literature on the effect of long-term NSAID use on soft-tissue healing in humans. One recent randomized controlled trial by Tangtiphaiboontana et al.[25] showed that patients who were prescribed postoperative ibuprofen for 2 weeks after rotator cuff surgery did not have an increased risk of tendon retear compared with the control group. Prostaglandins play a role in bone healing given that they are produced by osteoblasts after COX-2 upregulation.[26]

Similar to tendon and ligament healing, there is conflicting evidence surrounding NSAID use and bone healing.[27] A recent meta-analysis by Al Farii et al.[28] suggested that NSAID use may be associated with fracture nonunion and the dose duration may have an inverse relation with the risk of nonunion. However, a study by Kim et al.[29] showed that NSAIDs have no short-term impact (<3 weeks) on bone healing. Bone healing is also of interest in tendon repair surgical procedures because they rely on healing of the bone-tendon interface through onlay or inlay fixation methods such as suture anchors, bone tunnels, or interference screws.[30,31]

Although the effect of postoperative NSAID use on soft-tissue healing after orthopaedic sports medicine procedures has been assessed,[22] there is limited evidence on the effect of preoperative long-term NSAID use. The purpose of this study was to determine whether long-term preoperative NSAID use affected the revision rates after primary tendon repair for the following common sports medicine surgical procedures: rotator cuff repair (RCR), Achilles tendon repair (ATR), distal biceps repair (DBR), or quadriceps tendon repair (QTR). We hypothesized that there would be no difference in the revision rates after tendon repair in long-term NSAID users compared with individuals who did not regularly use NSAIDs on a long-term basis preoperatively.

Methods

Data Source

This study used patient data from the PearlDiver Mariner Database (PearlDiver, Colorado Springs, CO), a commercially available administrative claims database that contains deidentified data from 2010 to 2022. The M165 data set within the PearlDiver system contains data on approximately 165 million patients. This data set allows users to follow certain procedures, diagnoses, and complications longitudinally using *International Classification of Diseases, Ninth Revision* (ICD-9), *International Classification of Diseases, Tenth Revision* (ICD-10), and Current Procedural Terminology (CPT) codes. All data within the database are tracked using these *International Classification of Diseases* (ICD) and CPT codes, without any patient-identifying information included. Thus, all data from this data set are Health Insurance Portability and Accountability Act compliant and were deemed exempt from institutional review board approval. Studies using this database have been published in the orthopaedic literature.[32,33]

Study Design and Cohort Formation

Using CPT codes, we identified all patients who underwent RCR, ATR, DBR, or QTR (Appendix Table 1). Patients were excluded if they were younger than 18 years. Additionally, only patients with at least 2-year follow-up within the database were included.

Long-term NSAID users were identified by ICD code ICD-9-V5864 or ICD-10-D-Z791 for "Long-term (current) use of non-steroidal anti-inflammatories." According to ICD-10 coding guidelines, this code is used for patients who received NSAIDs for an extended period as a prophylactic measure or for treatment of a chronic condition requiring a lengthy course of NSAIDs. This code is not used for medications being administered over a brief period or for the treatment of an acute illness or injury. Although this code does not specify the exact NSAID used, aspirin is not included under this code.[34] To maximize the probability that patients were actively taking NSAIDs before the index procedure, only patients with a diagnosis of chronic NSAID use prior to the index procedure (NSAID users) were included in this group. Patients in whom long-term NSAID use was diagnosed after the procedure were excluded. Controls were identified as any patients who met the inclusion criteria and did not have a diagnosis code for long-term current use of NSAIDs. In 4 separate matching processes, 1 for each procedure included, NSAID users were exactly matched to controls in a 1:4 ratio based on age, sex, and Elixhauser Comorbidity Index.

Outcome Measures

The rate of ipsilateral revision retear surgery within 2 years of the index procedure was obtained for each of the included tendon repairs. The reoperation procedures only included those that addressed the tendon retear itself, excluding any other common revision procedures for infection, joint replacement, and so on. Laterality was ensured by only including patients who had ICD-10 codes for a tendon tear that specified laterality on the same day of the index procedure and revision procedure. Thus, patients whose laterality could not be determined or those who underwent bilateral procedures on the same day were excluded.

Statistical Analysis

Demographic variables and comorbidities were compared between cohorts for each procedure separately using independent *t* tests for continuous variables

and χ^2 tests for categorical variables. Multivariable logistic regression analyses were used to determine the effect of long-term NSAID use on the rate of revision surgery, accounting for demographic variables or comorbidities that were significantly different between groups. The level of significance was set at $P < .05$, and all data were presented as mean and standard deviation. All analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria) provided within the PearlDiver database.

Results

Study Cohort

A total of 36,068 patients were included in the analysis. Of those included, 7,246 (20%) had a diagnosis claim for long-term current NSAID use prior to tendon repair. When evaluated by procedure, 5,940 RCR patients, 620 ATR patients, 175 DBR patients, and 511 QTR patients took long-term NSAIDs prior to the index procedure. After matching, there were no significant differences between NSAID users and the control group for age, sex, or Elixhauser Comorbidity Index for any procedure (Table 1). Patients in the RCR NSAID subgroup were aged 61.0 ± 9.4 years, with 56.4% of the patients being women. Patients in the ATR NSAID subgroup were aged 55.1 ± 11.3 years, with 35.2% of patients being women. Patients in the DBR NSAID subgroup were aged 55.0 ± 9.9 years, with 1.7% of patients being women. Patients in the QTR NSAID subgroup were aged 63.2 ± 10.9 years, with 33.9% of patients being women. Across all procedures, NSAID users were significantly more likely to use tobacco compared with controls (RCR, $P < .001$; ATR, $P = .003$; DBR, $P = .006$; and QTR, $P < .001$).

Rates of Revision Surgery

After RCR, 3.2% of NSAID users (n = 190) and 2.6% of controls (n = 617) underwent revision surgery within 2 years, with an adjusted odds ratio (OR) of 1.15 (95% confidence interval [CI], 0.97-1.36; $P = .10$) (Table 2). After ATR, the NSAID users had a revision rate of 3.9% (n = 24) versus 2.5% (n = 62) in the control cohort, with an OR of 1.47 (95% CI, 0.89-2.38; $P = .12$). Patients who underwent DBR experienced fewer than 11 revision cases in both the chronic NSAID cohort and the control cohort. On multivariable regression, the OR was 1.54 (95% CI, 0.49-4.16; $P = .42$). After QTR, the revision rate was 5.9% (n = 30) for NSAID users compared with 4.8% (n = 95) for the control group. On multivariable regression, the OR was 1.22 (95% CI, 0.77-1.86; $P = .38$).

Discussion

The main finding of this study was that patients with a diagnosis of long-term NSAID use did not have

Table 1. Demographic Variables and Comorbidities Compared Between NSAID Users and Controls Separated by Procedure

	Rotator Cuff Repair			Achilles Tendon Repair			Distal Biceps Repair			Quadriceps Tendon Repair		
	NSAID Users (n = 5,940)	Controls (n = 23,695)	*P* Value	NSAID Users (n = 620)	Controls (n = 2,446)	*P* Value	NSAID Users (n = 175)	Controls (n = 684)	*P* Value	NSAID Users (n = 511)	Controls (n = 1,997)	*P* Value
Mean age (SD), yr	61.0 (9.4)	61.0 (9.4)	.91	55.1 (11.3)	55.1 (11.2)	.94	55.0 (9.9)	54.9 (9.9)	.90	63.2 (10.9)	63.3 (10.8)	.88
Sex												
Male	2,587 (43.6)	10,326 (43.6)	.98	218 (35.2)	859 (35.1)	.99	172 (98.3)	676 (98.8)	.85	338 (66.1)	1,330 (66.6)	.89
Female	3,353 (56.4)	13,369 (56.4)		402 (64.8)	1,587 (64.9)		3 (1.7)	8 (1.2)		173 (33.9)	667 (33.4)	
Mean ECI (SD)	5.7 (3.4)	5.7 (3.5)	.68	5.0 (3.0)	4.9 (2.9)	0.62	3.8 (2.4)	3.8 (2.2)	.66	5.4 (3.1)	5.3 (3.0)	.42
Alcohol abuse	588 (9.9)	2,223 (9.4)	.23	43 (6.9)	180 (7.5)	0.78	26 (14.9)	66 (9.6)	.060	58 (11.4)	168 (8.4)	.047*
CKD	1,038 (17.5)	4,457 (18.8)	.019*	85 (13.7)	457 (18.7)	.005*	28 (16.0)	81 (11.8)	.18	113 (22.1)	573 (28.7)	.003*
COPD	2,680 (45.1)	10,446 (44.1)	.16	268 (43.2)	1,097 (44.8)	.50	54 (30.9)	214 (31.3)	.99	207 (40.5)	817 (40.9)	.91
CHF	342 (5.8)	1,741 (7.3)	<.001*	32 (5.2)	205 (8.4)	.009*	<11	26 (3.8)	.71	40 (7.8)	253 (12.7)	.003*
CAD	1,860 (31.3)	8,058 (34.0)	<.001*	141 (22.7)	746 (30.5)	<.001*	43 (24.6)	208 (30.4)	.16	174 (34.1)	857 (42.9)	<.001*
Obesity	3,581 (60.3)	13,568 (57.3)	<.001*	455 (73.4)	1,651 (67.5)	.006*	101 (57.7)	371 (54.2)	.46	318 (62.2)	1,147 (57.4)	.056
Depression	3,350 (56.4)	11,998 (50.6)	<.001*	338 (54.5)	1,228 (50.2)	.061	67 (38.3)	234 (34.2)	.36	242 (47.4)	888 (44.5)	.26
Diabetes	2,708 (45.6)	12,466 (52.6)	<.001*	272 (43.9)	1,360 (55.6)	<.001*	60 (34.3)	268 (39.2)	.27	237 (46.4)	1,094 (54.8)	<.001*
Hypertension	4,846 (81.6)	19,916 (84.1)	<.001*	496 (80.0)	2,065 (84.4)	.010*	136 (77.7)	550 (80.4)	.49	427 (83.6)	1,765 (88.3)	.004*
Tobacco use	3,313 (55.8)	10,910 (46.0)	<.001*	288 (46.5)	975 (39.9)	.003*	97 (55.4)	298 (43.6)	.006*	283 (55.4)	858 (43.0)	<.001*

NOTE. Data are reported as number (percentage) unless otherwise indicated.

CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ECI, Elixhauser Comorbidity Index; NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation.

*Statistically significant.

Table 2. Rates of Revision Surgery Compared Between Long-Term NSAID Users and Controls Separated by Procedure

	NSAID Users	Controls	OR	95% CI	*P* Value
Rotator cuff repair	190 (3.2)	617 (2.6)	1.15	0.97-1.36	.10
Achilles tendon repair	24 (3.9)	62 (2.5)	1.47	0.89-2.38	.12
Distal biceps repair	<11	<11	1.54	0.49-4.16	.42
Quadriceps tendon repair	30 (5.9)	95 (4.8)	1.22	0.77-1.86	.38

NOTE. Data are reported as number (percentage) unless otherwise indicated.
CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio.

greater revision rates after major tendon repair compared with matched controls without this diagnosis. A subgroup analysis of RCR, ATR, DBR, and QTR revealed no difference in revision surgery rates in any subgroup between the NSAID users and the controls. These findings suggest that long-term NSAID use may not adversely affect tendon healing after primary repair.

NSAIDs are commonly used for pain control in orthopaedic sports medicine.[35,36] Although they are effective at reducing pain from acute injuries, they may delay or decrease tendon healing owing to the involvement of the inflammatory pathway.[37] Additional research has shown a potential negative impact of NSAIDs on bone healing after fracture or surgery, although these effects may be dose and duration dependent.[38-40] Recently, given the harmful adverse effects and concerns with opioid addiction, the use of NSAIDs has increased postoperatively.[41-43] Given the potential negative effects on tendon healing and common postoperative use, recent research has investigated the relation between revision rates and postoperative NSAID use after tendon repairs. Most studies have shown no differences in retear or complication rates with a short course of postoperative NSAIDs.[25,44,45]

However, there is still a paucity of literature exploring the effect of long-term preoperative NSAID use on tendon repair outcomes. Chronic pain is a common and difficult problem to manage, with some reports suggesting that up to 20.5% of adults in America experience daily, chronic pain.[46,47] NSAIDs, often chosen as a first-line treatment for chronic pain, are very effective at helping in managing symptoms.[9] However, the use of these medications has known adverse effects such as damage to the gastric lining,[48] renal system,[49] and cardiovascular system.[50] NSAID adverse effects on the musculoskeletal system must not be overlooked either.

Physiological tendon healing occurs in 3 phases, including an inflammatory phase, which removes necrotic tissue; a proliferative phase; and a remodeling phase.[51] During the inflammatory phase, mediators such as prostaglandins are produced to provide a vasodilatory effect and allow the migration of other important proinflammatory molecules to the injured site.[52] Because the main mechanism of action of NSAIDs is to reduce the number of prostaglandins, the inflammatory phase of tendon healing may be the most impacted. However, tendon healing is an extensive, multifactorial process with numerous key pathways and molecules. During the proliferative phase, tendon cells synthesize new collagen type III molecules, which are then replaced by more durable collagen type I fibers during the final remodeling phase.[53] Prior in vivo research has shown that although NSAID administration does inhibit tenocyte proliferation, it does not inhibit collagen synthesis.[54] Additionally, growth factors such as transforming growth factor β are heavily involved through all phases of tendon healing.[55] One study showed that ibuprofen treatment in tendinopathic human tendon did not lead to any changes in transforming growth factor β or collagen expression.[56] Thus, the negative effects of NSAIDs on the prostaglandin pathway may not be detrimental enough to clinically impact tendon healing given that other essential processes in tendon healing are not affected. Our study findings strengthen this hypothesis because long-term NSAID use did not significantly affect the revision rates of major tendon repair compared with controls.

It is important to note that the effects of NSAIDs depend on duration, dose, and type of medication. For instance, a randomized controlled trial by Oh et al. found high rotator cuff retear rates in patients who were taking postoperative celecoxib but not in patients who were taking ibuprofen.[57] Although both medications are considered NSAIDs, they have different selectivity for the COX enzyme, leading to different downstream effects. A scoping review of both clinical and animal studies by Ghosh et al. found that selective COX-2 inhibitors, such as celecoxib, were associated with negative effects on soft-tissue healing after surgery compared with nonselective COX inhibitors, such as ibuprofen, which had no negative effects on soft-tissue healing.[58] Whereas most of the research on NSAID use and tendon healing is focused on the effects of acute NSAID use on tendon healing, this study explored long-term preoperative NSAID use. Our study findings suggest that preoperative long-term NSAID use is safe and will not result in an increased risk of tendon rerupture after surgical repair.

The largest subgroup in this study comprised patients who underwent RCR, with 5,940 patients in the NSAID

group and 23,695 patients in the control group. Shoulder pain is one of the most common musculoskeletal pain syndromes, and use of NSAIDs as a first-line modality is common owing to pain control efficacy and quality-of-life improvement.[59-61] Thus, even after a long trial of NSAIDs to manage symptoms, many of these patients ultimately undergo RCR.[62] In the current literature, revision rates for rotator cuff surgery range from 3.8% to 21%, and depend on various aspects including age, tear size, and muscle quality.[63,64] Our study found revision rates of 3.2% for the NSAID group and 2.6% for the control group, which is consistent with previous literature. These findings are reassuring, showing that the use of NSAIDs prior to rotator cuff surgery may not increase the risk of needing a revision procedure.

The other subgroups in this study were DBR, QTR, and ATR. The revision rate for each of these repairs was below 6%, which is similar to the previous rates reported in the literature.[65-67] Although patients undergoing these surgical procedures made up a lower percentage of the study population (17.8% total), the outcomes of these procedures are still important to discuss to assess for any differences in the effects of NSAIDs based on tendon location and/or function. Moreover, the sparse amount of clinical research that discusses NSAID use effects on these specific tendons makes it an interesting area of future research.

Limitations

This study is not without limitations. The use of a large retrospective database has associated limitations. Because the PearlDiver database is dependent on administrative data, such as ICD and CPT codes, any coding errors made by providers will result in inaccuracies that cannot be addressed. Furthermore, this database does not typically include patient-reported outcome measures, which are important to discuss when assessing a patient's perspective on his or her health and surgical outcomes. Because the diagnosis code used in this study was for "Long-term (current) use of non-steroidal anti-inflammatories," it included all types of NSAIDs, and it was not possible to evaluate what kinds of NSAIDs were used with more granularity. NSAIDs can be subcategorized based on their specificity for the COX isozyme, which can result in different biochemical effects. Addressing the different types of NSAIDs and their effects on revision rates is an important topic for future research. Despite the ICD code stating "long-term," it was not possible to determine the exact amount of time during which the patient cohort was taking NSAIDs or the amount of NSAIDs taken. Furthermore, it is important to mention that although patients with a diagnosis of long-term NSAID use after the initial procedure were excluded, this does not completely omit all patients who may have taken NSAIDs postoperatively for pain control or other reasons. This also does not account for patients who may have taken NSAIDs without consulting a physician or reporting this to another health care provider because they are over-the-counter medications. Moreover, demographic analysis of the study cohorts showed that patients in the NSAID group were more likely to be tobacco users, which could be a confounding variable. Particularly in terms of the RCR group, there may have been patients who underwent reverse total shoulder arthroplasty instead of revision RCR, given the age group in this study. Thus, the omission of patients who underwent reverse total shoulder arthroplasty may have resulted in an underrepresentation of the number of RCRs that failed. Additionally, the data were not able to be disaggregated by sex and/or gender owing to the nature of data query.

Conclusions

Patients with a diagnosis of and coding for long-term preoperative NSAID use do not have greater revision rates within 2 years of primary tendon repair than patients without this diagnosis.

Disclosures

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: S.V.T. receives support for education from ImpactOrtho and receives hospitality payments from Stryker. J.M.T. receives intellectual property royalties from Arthrex; is a paid consultant for Arthrex; is a paid presenter or speaker for Arthrex; is a board or committee member of Arthroscopy Association of North America: is on the editorial or governing board of *Journal of Shoulder and Elbow Surgery* and *Orthopedics Today*; and receives publishing royalties and financial or material support from *Journal of Shoulder and Elbow Surgery*. All other authors (R.P., A.H., J.I., A.J.H.) declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Dahners LE, Mullis BH. Effects of nonsteroidal anti-inflammatory drugs on bone formation and soft-tissue healing. *J Am Acad Orthop Surg* 2004;12:139-143.
2. Abdul-Hadi O, Parvizi J, Austin MS, Viscusi E, Einhorn T. Nonsteroidal anti-inflammatory drugs in orthopaedics. *J Bone Joint Surg Am* 2009;91:2020-2027.
3. Horton R. GBD 2010: Understanding disease, injury, and risk. *Lancet* 2012;380:2053-2054.
4. Andersson G. *United States Bone and Joint Initiative: The burden of musculoskeletal diseases in the United States (BMUS)*. Ed 4. *Rosemont, IL: United States Bone and Joint Initiative, 2020. http://www.boneandjointburden.org. Accessed October 13, 2024.*

5. Rasu RS, Sohraby R, Cunningham L, Knell ME. Assessing chronic pain treatment practices and evaluating adherence to chronic pain clinical guidelines in outpatient practices in the United States. *J Pain* 2013;14:568-578.
6. Tüzün EH. Quality of life in chronic musculoskeletal pain. *Best Pract Res Clin Rheumatol* 2007;21:567-579.
7. Machado GC, Abdel-Shaheed C, Underwood M, Day RO. Non-steroidal anti-inflammatory drugs (NSAIDs) for musculoskeletal pain. *BMJ* 2021;372:n104.
8. Vane JR, Botting RM. Anti-inflammatory drugs and their mechanism of action. *Inflamm Res* 1998;47:78-87.
9. Ong CKS, Lirk P, Tan CH, Seymour RA. An evidence-based update on nonsteroidal anti-inflammatory drugs. *Clin Med Res* 2007;5:19-34.
10. Solaiman RH, Dirnberger J, Kennedy NI, et al. The effect of nonsteroidal anti-inflammatory drug use on soft tissue and bone healing in the knee: A systematic review. *Ann Joint* 2024;9:3.
11. Kurmis AP, Kurmis TP, O'Brien JX, Dalén T. The effect of nonsteroidal anti-inflammatory drug administration on acute phase fracture-healing: A review. *J Bone Joint Surg Am* 2012;94:815-823.
12. Cheng H, Huang H, Guo Z, Chang Y, Li Z. Role of prostaglandin E2 in tissue repair and regeneration. *Theranostics* 2021;11:8836-8854.
13. Hertel J. The role of nonsteroidal anti-inflammatory drugs in the treatment of acute soft tissue injuries. *J Athl Train* 1997;32:350-358.
14. Dahners LE, Gilbert JA, Lester GE, Taft TN, Payne LZ. The effect of a nonsteroidal antiinflammatory drug on the healing of ligaments. *Am J Sports Med* 1988;16:641-646.
15. Elder CL, Dahners LE, Weinhold PS. A cyclooxygenase-2 inhibitor impairs ligament healing in the rat. *Am J Sports Med* 2001;29:801-805.
16. Ferry ST, Dahners LE, Afshari HM, Weinhold PS. The effects of common anti-inflammatory drugs on the healing rat patellar tendon. *Am J Sports Med* 2007;35:1326-1333.
17. Forslund C, Bylander B, Aspenberg P. Indomethacin and celecoxib improve tendon healing in rats. *Acta Orthop Scand* 2003;74:465-469.
18. Cohen DB, Kawamura S, Ehteshami JR, Rodeo SA. Indomethacin and celecoxib impair rotator cuff tendon-to-bone healing. *Am J Sports Med* 2006;34:362-369.
19. Hanson CA, Weinhold PS, Afshari HM, Dahners LE. The effect of analgesic agents on the healing rat medial collateral ligament. *Am J Sports Med* 2005;33:674-679.
20. Dimmen S. Effects of COX inhibitors on bone and tendon healing: Experimental studies of fracture healing, tendon healing and tendon-to-bone healing in the rat. *Acta Orthop* 2011;82:1-22 (suppl 342).
21. Dimmen S, Engebretsen L, Nordsletten L, Madsen JE. Negative effects of parecoxib and indomethacin on tendon healing: An experimental study in rats. *Knee Surg Sports Traumatol Arthrosc* 2009;17:835-839.
22. Dimmen S, Nordsletten L, Engebretsen L, Steen H, Madsen JE. The effect of parecoxib and indometacin on tendon-to-bone healing in a bone tunnel: An experimental study in rats. *J Bone Joint Surg Br* 2009;91-B:259-263.
23. Randelli P, Randelli F, Cabitza P, Vaienti L. The effects of COX-2 anti-inflammatory drugs on soft tissue healing: A review of the literature. *J Biol Regul Homeost Agents* 2010;24:107-114.
24. Thomas J, Taylor D, Crowell R, Assor D. The effect of indomethacin on Achilles tendon healing in rabbits. *Clin Orthop Relat Res* 1991;272:308-311.
25. Tangtiphaiboontana J, Figoni AM, Luke A, Zhang AL, Feeley BT, Ma CB. The effects of nonsteroidal anti-inflammatory medications after rotator cuff surgery: A randomized, double-blind, placebo-controlled trial. *J Shoulder Elbow Surg* 2021;30:1990-1997.
26. Chen MR, Dragoo JL. The effect of nonsteroidal anti-inflammatory drugs on tissue healing. *Knee Surg Sports Traumatol Arthrosc* 2013;21:540-549.
27. Pountos I, Georgouli T, Calori GM, Giannoudis PV. Do nonsteroidal anti-inflammatory drugs affect bone healing? A critical analysis. *Sci World J* 2012;2012:1-14.
28. Al Farii H, Farahdel L, Frazer A, Salimi A, Bernstein M. The effect of NSAIDs on postfracture bone healing: A meta-analysis of randomized controlled trials. *OTA Int* 2021;4:e092.
29. Kim H, Kim DH, Kim DM, et al. Do nonsteroidal anti-inflammatory or COX-2 inhibitor drugs increase the nonunion or delayed union rates after fracture surgery?: A propensity-score-matched study. *J Bone Joint Surg Am* 2021;103:1402-1410.
30. Lui P, Zhang P, Chan K, Qin L. Biology and augmentation of tendon-bone insertion repair. *J Orthop Surg Res* 2010;5:59.
31. Li X, Xiao Y, Shu H, Sun X, Nie M. Risk factors and corresponding management for suture anchor pullout during arthroscopic rotator cuff repair. *J Clin Med* 2022;11:6870.
32. Becker A, van Tulder M, Öberg B, et al. Guidelines for the management of non-specific low back pain in primary care: An update of the 1999 guidelines. *Eur Spine J* 2009;18:193-200.
33. Miller LE, Cummings TM. Pain management in the elderly: The role of non-steroidal anti-inflammatory drugs. *Br J Pain* 2014;8:56-62.
34. Centers for Medicare & Medicaid Services (U.S.). *ICD-10-CM Official Guidelines for Coding and Reporting FY 2023 – UPDATED April 1, 2023 (October 1, 2022 - September 30, 2023)* 2023. https://stacks.cdc.gov/view/cdc/126426.
35. Paoloni JA, Milne C, Orchard J, Hamilton B. Non-steroidal anti-inflammatory drugs in sports medicine: guidelines for practical but sensible use: Table 1. *Br J Sports Med* 2009;43:863-865.
36. Ziltener JL, Leal S, Fournier PE. Non-steroidal anti-inflammatory drugs for athletes: An update. *Ann Phys Rehabil Med* 2010;53:278-288.
37. Chan KM, Fu SC. Anti-inflammatory management for tendon injuries - friends or foes? *BMC Sports Sci Med Rehabil* 2009;1:23.
38. Gerstenfeld LC, Thiede M, Seibert K, et al. Differential inhibition of fracture healing by non-selective and cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs. *J Orthop Res* 2003;21:670-675.
39. Li Q, Zhang Z, Cai Z. High-dose ketorolac affects adult spinal fusion: A meta-analysis of the effect of perioperative nonsteroidal anti-inflammatory drugs on spinal fusion. *Spine* 2011;36:E461-E468.

40. Simon AM, O'Connor JP. Dose and time-dependent effects of cyclooxygenase-2 inhibition on fracture-healing. *J Bone Joint Surg Am* 2007;89:500-511.
41. Ilyas AM, Sundaram P, Plusch K, Kasper A, Jones CM. Multimodal pain management after outpatient orthopedic hand surgery: A prospective randomized trial. *J Hand Surg Glob Online* 2024;6:16-20.
42. The NO PAin Investigators, Duong A, Ponniah AK, et al. Effect of a postoperative multimodal opioid-sparing protocol vs standard opioid prescribing on postoperative opioid consumption after knee or shoulder arthroscopy: A randomized clinical trial. *JAMA* 2022;328:1326.
43. Thompson KA, Klein D, Alaia MJ, Strauss EJ, Jazrawi LM, Campbell KA. Opioid use is reduced in patients treated with NSAIDs after arthroscopic bankart repair: A randomized controlled study. *Arthrosc Sports Med Rehabil* 2021;3:e15-e22.
44. Hadro A, Huyke-Hernandez FA, Kleinsmith RM, et al. Effect of post-operative NSAID use on rotator cuff repair outcomes. *J Orthop* 2024;56:119-122.
45. Constantinescu DS, Campbell MP, Moatshe G, Vap AR. Effects of perioperative nonsteroidal anti-inflammatory drug administration on soft tissue healing: A systematic review of clinical outcomes after sports medicine orthopaedic surgery procedures. *Orthop J Sports Med* 2019;7:232596711983887.
46. Yong RJ, Mullins PM, Bhattacharyya N. Prevalence of chronic pain among adults in the United States. *Pain* 2022;163:e328-e332.
47. Nahin RL, Feinberg T, Kapos FP, Terman GW. Estimated rates of incident and persistent chronic pain among US adults, 2019-2020. *JAMA Netw Open* 2023;6:e2313563.
48. Sostres C, Gargallo CJ, Arroyo MT, Lanas A. Adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs, aspirin and coxibs) on upper gastrointestinal tract. *Best Pract Res Clin Gastroenterol* 2010;24:121-132.
49. Whelton A. Nephrotoxicity of nonsteroidal anti-inflammatory drugs: physiologic foundations and clinical implications. *Am J Med* 1999;106:13S-24S.
50. Harirforoosh S, Asghar W, Jamali F. Adverse effects of nonsteroidal antiinflammatory drugs: An update of gastrointestinal, cardiovascular and renal complications. *J Pharm Pharm Sci* 2014;16:821.
51. Jiang L, Liu T, Lyu K, et al. Inflammation-related signaling pathways in tendinopathy. *Open Life Sci* 2023;18:20220729.
52. Marsolais D, Frenette J. Inflammation et réparation tendineuse. *Med Sci (Paris)* 2005;21:181-186.
53. Darrieutort-Laffite C, Blanchard F, Soslowsky LJ, Le Goff B. Biology and physiology of tendon healing. *Joint Bone Spine* 2024;91:105696.
54. Tsai WC, Hsu CC, Chou SW, Chung CY, Chen J, Pang JHS. Effects of celecoxib on migration, proliferation and collagen expression of tendon cells. *Connect Tissue Res* 2007;48:46-51.
55. Molloy T, Wang Y, Murrell GAC. The roles of growth factors in tendon and ligament healing. *Sports Med* 2003;33:381-394.
56. Heinemeier KM, Øhlenschlæger TF, Mikkelsen UR, et al. Effects of anti-inflammatory (NSAID) treatment on human tendinopathic tissue. *J Appl Physiol* 2017;123:1397-1405.
57. Oh JH, Seo HJ, Lee YH, Choi HY, Joung HY, Kim SH. Do selective COX-2 inhibitors affect pain control and healing after arthroscopic rotator cuff repair? A preliminary study. *Am J Sports Med* 2018;46:679-686.
58. Ghosh N, Kolade OO, Shontz E, et al. Nonsteroidal anti-inflammatory drugs (NSAIDs) and their effect on musculoskeletal soft-tissue healing: A scoping review. *JBJS Rev* 2019;7. e4-e4.
59. Adebajo AO, Nash P, Hazleman BL. A prospective double blind dummy placebo controlled study comparing triamcinolone hexacetonide injection with oral diclofenac 50 mg TDS in patients with rotator cuff tendinitis. *J Rheumatol* 1990;17:1207-1210.
60. AlRuthia Y, Alghadeer S, Balkhi B, et al. Efficacy of acetaminophen versus ibuprofen for the management of rotator cuff-related shoulder pain: Randomized open-label study. *Saudi Pharm J* 2019;27:882-888.
61. Sun Y, Chen J, Li H, Jiang J, Chen S. Steroid injection and nonsteroidal anti-inflammatory agents for shoulder pain: A PRISMA systematic review and meta-analysis of randomized controlled trials. *Medicine* 2015;94:e2216.
62. Keener JD, Patterson BM, Orvets N, Chamberlain AM. Degenerative rotator cuff tears: Refining surgical indications based on natural history data. *J Am Acad Orthop Surg* 2019;27:156-165.
63. Davey MS, Hurley ET, Carroll PJ, et al. Arthroscopic rotator cuff repair results in improved clinical outcomes and low revision rates at 10-year follow-up: A systematic review. *Arthroscopy* 2023;39:452-458.
64. Longo UG, Carnevale A, Piergentili I, et al. Retear rates after rotator cuff surgery: a systematic review and meta-analysis. *BMC Musculoskelet Disord* 2021;22:749.
65. Grewal G, Bernardoni ED, Cohen MS, et al. Clinical outcomes after revision distal biceps tendon surgery. *Orthop J Sports Med* 2021;9:232596712098175.
66. Trivedi NN, Varshneya K, Calcei JB, et al. Achilles tendon repairs: Identification of risk factors for and economic impact of complications and reoperation. *Sports Health* 2023;15:124-130.
67. Rao S, Johnson EE, D'Amore T, Szeto S, Otlans P, Cohen SB. Outcomes after Rerpair of quadriceps tendon rupture in patients aged 40 years and younger. *Orthop J Sports Med* 2022;10:232596712210971.