Original Article

Ibuprofen Use Did Not Affect Outcome Metrics After Arthroscopic Rotator Cuff Repair,

Nicholas R. Kraus, M.S., B.A., Kirsten D. Garvey, M.S., B.A., Laurence D. Higgins, M.D., M.B.A., and Elizabeth Matzkin, M.D.

Purpose: To determine whether patients who are prescribed ibuprofen after arthroscopic rotator cuff repair have significantly different patient-reported outcomes for pain, function, and overall health at baseline and 1 and 2 years after operation relative to patients only prescribed opioids. **Methods:** Patients who underwent a rotator cuff repair by a total of 3 surgeons and participated in the outcomes registry from 2012 to 2016 were screened for inclusion in this study. Inclusion criteria were primary arthroscopic rotator cuff repair, at least 2 years from the date of surgery and over the age of 18. Exclusion criteria were revision and open rotator cuff repair. All patients followed the standard postoperative rehabilitation protocol for rotator cuff repair. Patients were divided into 2 cohorts. Group I included patients who received ibuprofen/nonsteroidal anti-inflammatory agents (NSAID) after surgery (n = 281), and Group II consisted of patients who did not receive ibuprofen/NSAID after surgery (n = 182). Patient-reported outcome measures for Visual Analogue Scale, American Shoulder Elbow Surgeons score, Single Assessment Numeric Evaluation score, Simple Shoulder Test and The Veterans Rand 12-Item Health Survey were collected preoperatively and at 3 and 6 months, 1 year, and 2 years after surgery. Statistical analysis was performed to compare patient-reported outcome measures between Group I and II. **Results:** This study consisted of 463 patients who underwent arthroscopic rotator cuff repair, and patients were divided into 2 cohorts. There were 281 patients who did not receive ibuprofen/NSAID after operation in Group I and 182 patients who did receive ibuprofen in Group II. There were no statistically significant differences between the 2 groups in age at treatment, mean body mass index, gender, ethnicity, diabetes, and number of rotator cuff tendons involved; however, there was a statistically significant difference in receiving worker's compensation ($P = .005$), and this was subsequently adjusted for in our analysis. There were no significant differences in patient-reported outcomes for all metrics between the group prescribed ibuprofen and the group that was not prescribed ibuprofen at 1 and 2 years after surgery or in change from baseline. **Conclusion:** Patients receiving ibuprofen did as well as patients who did not receive ibuprofen after arthroscopic rotator cuff repair on patient-reported outcome measures assessing shoulder pain, function, and overall health. **Level of Evidence:** Level III, retrospective comparative study.

Rotator cuff injury is one of the most widespread musculoskeletal disorders, accounting for more than 4.5 million physician visits and 250,000 surgeries per year in the United States.[1-4] Injury to the rotator cuff often causes shoulder pain, loss of strength, complex sequelae, and partial or total inability to work, thus reducing a patient's quality of life.[5-8]

The treatment algorithm for rotator cuff tears is multifactorial.[9] The rotator cuff has a limited ability for intrinsic repair, in part due to poor vascularization of the tendon tissue.[2,10,11] Management depends on the presence and severity of impingement, extent of tendon tear, degree of retraction, and functional demands.[12] Nonoperative treatment can lead to tear progression, tendon retraction, and muscle degeneration.[11] Surgical rotator cuff repair has demonstrated satisfactory long-term clinical results,[13] with more than 90% good or excellent results at 10 years after surgery.[14]

The ideal rotator cuff repair restores kinematics, improves strength and function while decreasing pain.[15,16] Despite advances in both open and arthroscopic surgical

From Tufts University School of Medicine (N.R.K., K.D.G.) and Department of Orthopaedic Surgery, Brigham and Women's Hospital (N.R.K., K.D.G., L.D.H., E.M.), Boston, Massachusetts.

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Address correspondence to Elizabeth Matzkin, M.D., Harvard Medical School, 75 Francis St., Boston, MA 02115. E-mail: ematzkin@bwh.harvard.edu

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techniques, shoulder surgery is frequently associated with severe postoperative pain.[17,18] Traditional pain management for shoulder injuries has included local injection of analgesics, nerve blocks, intravenous patient-controlled analgesia, opioid drugs, and nonsteroidal anti-inflammatory agents (NSAIDs), with the latter two being the most frequently used.[19,20] Despite the widespread use of opioids and NSAIDs in the postoperative setting, both have risks, limitations, and side effects.

Opioids are associated with adverse effects including nausea and vomiting, pruritus, sleep disturbance, constipation, and dependency.[21] Conversely, NSAIDs function by inhibiting cyclooxygenase (COX) enzymes, reducing the synthesis of inflammatory prostaglandins[22] but diminishing platelet counts, leading to bleeding and gastric ulceration.[23] Although NSAIDs have been shown to minimize pain and decrease opioid requirements after surgery,[24] they have traditionally been avoided by orthopedic surgeons. This avoidance could be based on past studies that have shown that selective NSAIDs (COX-2 inhibitors) impede fracture and tendon healing.[25-28] Additionally, in vitro NSAID treatment has been shown to impede proliferation and migration of tendon cells that are necessary for tendon repair after injury.[29] Despite literature indicating NSAID use leads to adverse in vitro and clinical outcomes, other studies have shown neutral or positive effects of selective and nonselective NSAID use.[30-33]

Given the widespread use of NSAIDs for postoperative pain relief, it is important to identify what effects NSAID use has on patient-reported outcomes for pain, function, and overall health after arthroscopic rotator cuff repair. There is limited information regarding the direct effect of NSAIDs on clinical and patient-reported outcomes in rotator cuff repair.[34] The purpose of this study is to determine whether patients that are prescribed ibuprofen after arthroscopic rotator cuff repair have significantly different patient-reported outcomes for pain, function, and overall health at baseline and 1 and 2 years after surgery relative to patients only prescribed opioids. We hypothesized that patients who were prescribed ibuprofen after arthroscopic rotator cuff repair would not have significantly different patient-reported outcome measures as those that were instructed not to take ibuprofen after surgery.

Methods

Approval by the institutional review board was obtained before the initiation of the present study. Data were collected prospectively on consecutive surgeries performed by 3 surgeons at an academic medical center and retrospectively reviewed for the present study. All patients signed an informed consent. An electronic surgical outcomes registry was used for data collection. Patients who underwent a rotator cuff repair and participated in the outcomes registry from 2012 to 2016 were screened on the basis of inclusion and exclusion criteria reviewed. Inclusion criteria were primary arthroscopic rotator cuff repair during the study period, at least 2 years from the date of surgery, and age over 18 years. Exclusion criteria were revision rotator cuff repair and open rotator cuff repair. All patients followed the standard postoperative rehabilitation protocol for rotator cuff repair.

Patients included in the study were divided into two cohorts based on post-operative analgesic therapy: Group I (no ibuprofen/NSAID use) and Group II (ibuprofen use). Group I patients were instructed to avoid ibuprofen/NSAIDs after surgery for 12 weeks and were provided opioids for pain management. Group II patients were sent home with a prescription for 800 mg of Ibuprofen and instructed to take regularly and use opioid pain medication when needed. The groups were predetermined by surgeon preference; all patients undergoing surgery with a particular surgeon either were prescribed ibuprofen or were instructed to avoid ibuprofen/NSAIDs for 3 months after surgery.

All participants were administered a preoperative survey consisting of the following outcome-measuring tools: (i) Visual Analog Scale (VAS) used to measure overall pain level, (ii) the Veterans Rand 12-Item Health Survey (VR-12), a standard self-reported global health measure tool that is used to assess a patient's overall perspective of their health, (iii) the American Shoulder and Elbow Surgeons Shoulder Score (ASES) used to measure functional limitations and pain of the shoulder, (iv) standard preoperative form consisting of 4 questions regarding their expectations of recovery, (v) Single Assessment Numeric Evaluation (SANE) shoulder score used to determine a patient self-assessment of their shoulder function, and (vi) Simple Shoulder Test used to assess functional disability of the shoulder based on a 12-item score card. The same outcome measures were reassessed at 3 and 6 months and 1 and 2 years after surgery. At each data collection point, participants were e-mailed an electronic survey with one e-mail reminder and one phone call reminder by a research assistant if outcome measures were not completed in a timely manner. Paper-based questionnaires were not used in this study.

Statistical Analysis

The scores for all functional assessment metrics were tallied for each cohort at each of the time points of data collection pre- and post-operatively. Baseline differences in covariates were assessed using the *t*-test (continuous) and χ^2 test (categorical variables). A linear mixed effects model to compare outcomes between the groups at each timepoint accounted for all available data and did not require that subjects have complete data at all timepoints. Multivariable models adjusted for covariates that were imbalanced at baseline (worker's compensation status). Statistical analysis was performed to determine

Table 1. Patient Demographics

Demographic characteristics	No ibuprofen/NSAIDS Use (281 patients)	Ibuprofen use (182 patients)	*P* value
Age at treatment (mean ± SD)	57.01 ± 9.13	55.93 ± 9.72	.229
BMI, median (IQR)	28 (22.14-33.86)	27.90 (20.8-35.0)	.805
Gender			.157
Males (% of total)	162 (58%)	94 (51%)	
Females (% of total)	117 (42%)	89 (49%)	
Missing	2	0	
Ethnicity			.525
Hispanic (% of total)	7 (3%)	6 (3%)	
Non-Hispanic White (% of total)	221 (81%)	143 (79%)	
Non-Hispanic Black (% of total)	8 (3%)	2 (1%)	
Other (% of total)	38 (14%)	29 (16%)	
Missing	7	3	
Diabetic			.465
No (% of total)	269 (96%)	172 (95%)	
Yes (% of total)	10 (4%)	9 (5%)	
Missing	2	2	
Workers compensation			.005
No	263 (94%)	156 (87%)	
Yes	16 (6%)	24 (13%)	
Missing	2	3	
Number of tendons involved			.897
1	82 (42.3%)	81 (44.5%)	
2	77 (39.7%)	72 (39.6%)	
3	31 (16.0)	27 (14.8%)	
4	4 (2.1%)	2 (1.1%)	
Missing	89	6	

BMI, body mass index; IQR, interquartile range, NSAID, nonsteroidal anti-inflammatory agent; SD, standard deviation.

whether there was any correlation between ibuprofen use and functional outcome measures collected. Statistical significance was set at $P < .05$.

Results

Patient Characteristics

In total, 591 patients undergoing primary rotator cuff repair were initially identified. Of these patients, 471 were included (80%), and 120 did not have complete preoperative and 1- and 2-year postoperative PROMs data (20%) and were therefore excluded. For patients who underwent multiple surgeries, only the first surgery was included, leaving an analytic dataset of 463.

Differences in baseline characteristics between the included subjects are presented in Table 1. There were no statistically significant differences between the 2 groups in terms of age at treatment, mean body mass index, gender, ethnicity, and diabetes; however, there was a statistically significant difference between both groups with regard to worker's compensation status ($P = .005$).

There was a total of 281 patients in Group I (no NSAIDs use) and 182 patients in Group II (ibuprofen/NSAID use) who underwent rotator cuff repair during the data collection period. These patients were administered the preoperative and postoperative surveys at each of the study time points. Clinical characteristics of

Table 2. Improvement in VAS Pain Ratings Across All Groups After Rotator Cuff Repair (Adjusted for Worker's Compensation Status) and in ASES Pain Ratings Across All Groups After Rotator Cuff Repair (Adjusted for Worker's Compensation Status)

PRO	Time	No ibuprofen/NSAIDs use	Ibuprofen use	*P* value
VAS	Baseline	5.0 (4.6, 5.4)	5.4 (5.0, 5.8)	.112
VAS	Year 1	1.4 (1.1, 1.7)	1.6 (1.3, 1.9)	.279
VAS	Year 2	1.2 (0.9, 1.5)	1.3 (1.0, 1.6)	.629
VAS	Year 1 change from BL	−3.6 (−4.0, −3.2)	−3.8 (−4.2, −3.4)	.437
VAS	Year 2 change from BL	−3.8 (−4.2, −3.4)	−4.1 (−4.5, −3.7)	.274
ASESI	Baseline	47.1 (44.0, 50.2)	44.0 (41.0, 47.1)	.110
ASESI	Year 1	83.3 (80.6, 85.9)	82.4 (79.9, 84.9)	.559
ASESI	Year 2	85.6 (82.8, 88.4)	85.9 (82.9, 88.9)	.846
ASESI	Year 1 change from BL	36.2 (33.4, 39.1)	38.4 (35.4, 41.4)	.297
ASESI	Year 2 change from BL	38.5 (35.5, 41.5)	41.9 (38.5, 45.3)	.142

BL, baseline; ASES, American Shoulder and Elbow Surgeons Shoulder; NSAID, nonsteroidal anti-inflammatory agent; VAS, Visual Analog Scale.

Table 3. Improvement in SANE Ratings Across All Groups After Rotator Cuff Repair (Adjusted For Worker's Compensation Status) And In SST Ratings Across All Groups After Rotator Cuff Repair (Adjusted For Worker's Compensation Status)

PRO	Time	No ibuprofen/NSAIDs use	Ibuprofen use	*P* value
SANE	Baseline	35.1 (31.6, 38.5)	34.8 (31.4, 38.2)	.890
SANE	Year 1	77.6 (73.8, 81.4)	77.1 (73.4, 80.8)	.833
SANE	Year 2	79.6 (75.4, 83.8)	79.7 (74.8, 84.5)	.987
SANE	Year 1 change from BL	42.6 (38.3, 46.8)	42.4 (38.0, 46.7)	.947
SANE	Year 2 change from BL	44.6 (40.0, 49.1)	44.9 (39.6, 50.2)	.924
SST	Baseline	37.1 (32.5, 41.7)	31.7 (27.3, 36.2)	.053
SST	Year 1	77.4 (73.2, 81.5)	76.0 (72.1, 80.0)	.577
SST	Year 2	79.7 (75.2, 84.3)	78.2 (73.5, 83.0)	.588
SST	Year 1 change from BL	40.3 (36.0, 44.6)	44.3 (40.0, 48.6)	.198
SST	Year 2 change from BL	42.7 (38.0, 47.3)	46.5 (41.4, 51.5)	.275

BL, baseline; NSAID, nonsteroidal anti-inflammatory agent; SANE, Single Assessment Numeric Evaluation; SST, Simple Shoulder Test.

each group were assessed to evaluate major differences in rotator cuff tear size by comparing number of tendons torn. There were no statistical differences between the 2 NSAID use groups in terms of the number of tendons involved.

Postoperative Pain

Table 2 presents the VAS pain scores after adjusting for worker's compensation status. Patients experienced significant improvement in VAS pain scores at 1- and 2-years after rotator cuff repair in both Group I (no NSAID use) and Group II (ibuprofen/NSAID use). Patients in Group I had an average baseline VAS pain score of 5.0 (confidence interval [CI] 4.6-5.4), a 1-year pain score of 1.4 (CI 1.1-1.7), and a 2-year pain score of 1.2 (CI 0.9-1.5). Patients in Group II had an average baseline VAS pain score of 5.4 (CI 5.4-5.8), a 1-year pain score of 1.6 (CI 1.3-1.9) and a 2-year pain score of 1.3 (CI 1.0-1.6). Both Group I and Group II postoperative VAS pain scores meet the Minimal Clinically Important Differences measure. There is no significant difference in VAS pain score between patients in group I and group II at 1 year ($P = .279$) and 2 years after operation ($P = .629$). Patients across both groups demonstrated a similar magnitude of pain improvement at 1 and 2 years after rotator cuff repair.

Pain improvement was also measured with the ASES assessment tool. After adjusting for worker's compensation status, there were no statistically significant intergroup differences in pain improvement at baseline, 1-year, and 2-years following rotator cuff repair ($P = .110$, .559,.846, respectively). Patients in Group I improved their ASES shoulder function score by 38.5 points at 2 years after surgery and Group II improved by 41.9 points at the same time interval (Table 2).

Postoperative Function

All patients demonstrated improvement in shoulder function after rotator cuff repair as reported by the SANE and Simple Shoulder Test (SST) outcome measures before and after adjusting for worker's compensation status. SANE and SST outcome measures were used to assess functional disability experienced by patients because of rotator cuff tear. Both groups experienced a significant increase in SANE score: Group I improved by 44.6 points at 2 years after surgery, and Group II improved by 44.9 points at 2 years. There were no statistically significant intergroup differences in SANE score improvement over the course of the study. There were no significant intergroup differences in SST score improvement or at baseline and 1 and 2 years after operation (Table 3).

Table 4. Improvement in the VR-12M and VR-12P Ratings Across All Groups After Rotator Cuff Repair (Adjusted For Worker's Compensation Status)

PRO	Time	No ibuprofen/NSAIDs use	Ibuprofen use	*P* value
VR12M	Baseline	53.4 (51.6, 55.2)	52.8 (51.1, 54.5)	.541
VR12M	Year 1	54.9 (53.2, 56.5)	54.9 (53.4, 56.5)	.962
VR12M	Year 2	54.9 (53.2, 56.7)	54.3 (52.5, 56.2)	.569
VR12M	Year 1 change from BL	1.5 (0.0, 2.9)	2.1 (0.6, 3.6)	.531
VR12M	Year 2 change from BL	1.5 (0.0, 3.1)	1.6 (-0.2, 3.3)	.987
VR12P	Baseline	34.7 (33.2, 36.2)	34.1 (32.7, 35.6)	.501
VR12P	Year 1	46.3 (44.9, 47.8)	46.2 (44.8, 47.6)	.846
VR12P	Year 2	47.6 (46.0, 49.1)	47.0 (45.4, 48.6)	.550
VR12P	Year 1 change from BL	11.6 (10.4, 12.9)	12.0 (10.8, 13.3)	.654
VR12P	Year 2 change from BL	12.9 (11.5, 14.2)	12.9 (11.3, 14.4)	.998

BL, baseline; NSAID, nonsteroidal anti-inflammatory agent; VR-12M, Veterans Rand 12-Item Health Survey for Mental Health; VR-12P, Veterans Rand 12-Item Health Survey for Physical Health.

Overall Health Assessment

The VR-12 assessment tool was used to assess patient's overall health. The VR-12 form consisted of a series of questions about mental, emotional, and physical health, as well as social functioning. The VR-12 is separated into a physician component score and a mental component score. The higher the score, the better the patient's perception of their overall health. Patients in both groups demonstrated improvement in the VR-12 physician component score and mental component score after rotator cuff repair. There were no statistically significant intergroup differences at baseline and 1 and 2 years after surgery. Similarly, there were no statistically significant intergroup differences in improvement at 1 and 2 years after surgery (Table 4).

Discussion

In this study, we found no significant difference in patient-reported outcome measures between patients who were instructed to use ibuprofen after surgery and patients who were instructed not to use NSAIDs following surgery for rotator cuff repair. This supports the hypothesis that patients would have similar reported outcomes at 1- and 2-years following arthroscopic rotator cuff repair.

Postoperative pain control is a critical component of patient care and leads to faster rehabilitation and increased function after surgical repair. There is a broad range of analgesic therapies for pain control. The traditional management of postoperative pain after rotator cuff repair is with opioid drugs, and many consider it the gold standard for analgesia after orthopedic surgery.[17] Opioids also have a high potential for abuse, and thus there have been significant efforts to reduce the rate of opioids prescribed.[35]

Historically NSAID use has been avoided in rotator cuff repair surgery because of the potential to inhibit tendon healing.[36] NSAIDs have been shown to decrease opioid requirements after surgical procedures[24,37] but concern for lack of healing and inferior postoperative outcomes has prevented many surgeons from using them.

In a Level I RCT, Oh et al.[34] determined there were no significant differences in pain intensity or incidence of adverse effects at 2 weeks after rotator cuff repair in individuals randomized to a selective NSAID group (celecoxib), a nonselective NSAID group (ibuprofen), or an opioid group (tramadol). However, the study determined that the selective NSAID celecoxib was correlated with a significantly higher re-tear rate compared with those taking the nonselective NSAID ibuprofen or the opioid tramadol.[34]

Despite the efficacy of NSAIDs in postoperative pain control, these agents are not without risk. NSAIDs reduce pain and inflammation by inhibiting cyclooxygenase activity in the arachidonic pathway, decreasing the synthesis of proinflammatory prostaglandin molecules.

The effects of NSAIDs on bone, tendon, and muscle healing have been studied in animal models and to a lesser extent in human models. Conflicting evidence exists in support of and against the use of NSAIDs in bony and tendinous healing processes. A study by Carlstedt et al.[32] demonstrated the positive effect of NSAIDs on tendon healing. Carlstedt et al.[32] conducted an in vitro study that examined the effects of the nonspecific NSAID indomethacin on the biomechanical properties of plantaris longus tendon healing in rabbits. The study found that indomethacin therapy significantly increased tendon tensile strength.[32] Leadbetter[38] demonstrated the importance of cell proliferation, migration, and collagen synthesis for tendon repair. In animal models, Tsai et al.[39] showed that NSAIDs impeded the proliferation and migration of tendon cells, delaying the healing process. Almekinders et al.[30] investigated the in vitro effects of NSAIDs on human tendon fibroblasts and found that these drugs may inhibit the proliferative phase of tendon healing by impeding DNA synthesis. However, the study also found that NSAIDs stimulated protein synthesis in these same cells, demonstrating that NSAIDs may be beneficial in the remodeling phase of the healing process.[30] Ferry et al.[40] found that NSAIDs, with the exception of ibuprofen, had a detrimental effect on healing strength at the bone-tendon junction in animal models. A meta-analysis by Wheatley et al.[41] found that NSAID exposure delayed bone union in the adult population. These studies indicate that NSAID use plays a hindering role in tendinous and bony healing processes, but there are fewer studies that identify the direct impact of NSAID use on rotator cuff repair healing.

Despite the theoretical concerns on healing processes, there is not any strong evidence to avoid the use of NSAIDs after rotator cuff surgery. This article supports the use of ibuprofen after arthroscopic rotator cuff repair and demonstrates no difference in clinical outcomes 2 years after surgery. This should encourage surgeons to prescribe ibuprofen after surgery to potentially minimize the use of opioids.

Limitations

There are several limitations to this study. Although our patient response rate was sufficient at 80%, nonresponse bias is a limitation of any retrospective review of prospectively collected data. Surgical technique was not taken into consideration, but even with variability in technique, we demonstrate that outcomes are not affected with postoperative ibuprofen use. VAS scores were collected to assess pain, but number of opioids used with or without ibuprofen was not the aim of this study, rather only patient-reported outcome measures, so we are unable to comment on whether ibuprofen use decreased opioid use after surgery. We did not assess the total consumption of ibuprofen after operation, so we cannot comment on what the patients actually consumed

but only what was prescribed. This study looked at patient reported outcome measures only, and postoperative magnetic resonance imaging to assess healing was not performed. Also, the lack of a priori power analysis leaves the potential for a type II or beta error.

Conclusion

Patients receiving ibuprofen did as well as patients who did not receive ibuprofen after arthroscopic rotator cuff repair on patient-reported outcome measures assessing shoulder pain, function, and overall health.

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