Post-operative non-steroidal anti-inflammatory drugs do not affect clinical outcomes of rotator cuff repair

Joel Wei-An Lim*, Ming Han Liow, Andrew Hwee Chye Tan

Sports Service, Department of Orthopaedic Surgery, Singapore General Hospital, Outram Road, Singapore, 169865, Singapore

ARTICLE INFO

Keywords:

Rotator cuff repair
NSAIDs
Postoperative
Analgesia
Shoulder

ABSTRACT

Background: The administration of non-steroidal anti-inflammatory drugs (NSAIDs) to patients is thought to impair rotator cuff healing and clinical outcomes.

Methods: 36 patients who underwent rotator cuff repair were divided into 3 groups based on their post-operative analgesia regimes.

Results: At 4.4 years postoperative, there was significant improvement in SST and UCLA scores ($p < 0.001$). There were no significant differences in post-operative clinical outcome scores between the groups ($p > 0.05$). Administration of NSAIDs and duration of their use did not influence outcomes of rotator cuff repair ($p = 0.151$).

Conclusion: NSAIDs has no significant influence on clinical outcomes of rotator cuff repair.

1. Introduction

Rotator cuff disease is amongst the most common musculoskeletal conditions seen with its incidence expected to increase due to an aging population. Consequently, the rate of rotator cuff repairs performed is also expected to rise. Despite advances in surgical techniques and instrumentation in rotator cuff repairs, documented rotator cuff re-tear rates were observed in 25% of patients at a mean of 2 years after surgery (range 0.0%–94.4%).^{1–3} The reason behind rotator cuff repair failure is multifactorial and could be broadly divided into biological factors where there is a failure of healing despite strong fixation i.e. older age, fatty infiltration, nonsteroidal anti-inflammatory drugs (NSAIDs) use, and mechanical failures such as large tear size, traditional double-row fixation and inappropriate rehabilitation regimes.⁴

NSAIDs function by inhibiting cyclooxygenase and the subsequent synthesis of prostaglandins which effect the inflammatory cascade.⁵ NSAIDs are commonly prescribed after surgery for pain control, including post-rotator cuff repair. However, there are multiple animal studies that have shown their detrimental effect on bone-tendon healing with resultant early failure.^{6–9} Conversely, the pathogenesis of fatty infiltration is largely unknown and evidence has shown that it can even worsen after rotator cuff repair. Interestingly, inflammation and fibroproliferative processes have been implicated in the development of fatty infiltration, so inhibiting the inflammation pathway with NSAIDs might hypothetically reduce rotator cuff repair failure rates.^{10–12}

The aim of this study is to determine if the administration of post-

operative NSAIDs affects clinical outcomes after rotator cuff repair.

2. Materials and methods

Between 2004 and 2009, the senior author (AHCT) performed 'deltoid-on' rotator cuff repairs on 36 patients with symptomatic full-thickness supraspinatus tears. These 36 patients, comprising of 12 Males and 24 Females, aged from 42 to 71, were followed up for at least 2 years (ranging from 2 to 7 years post-operatively, with a mean duration 4.4years). Inclusion criteria for surgery were as follows: Patients with full-thickness supraspinatus tears, clinical weakness (graded by Medical Research Council (MRC) Scale) and experienced pain to the extent that it affected their activities of daily living. All patients had radiographic evidence of a full-thickness rotator cuff tear documented by either magnetic resonance imaging or ultrasound imaging of the shoulder. The Simple Shoulder Test (SST) scores and the UCLA shoulder scores were prospectively collected preoperatively and 2 years postoperatively.^{13,14}

The SST is a self-administered questionnaire to assess functional disability of the shoulder. It consists of 12 yes-no questions which relate to shoulder pain, range of motion and function, with a maximum score of 12 correlating with better shoulder comfort and function.¹⁵ SST was chosen as it has been used widely in numerous studies since its introduction in 1993. The SST is a self-evaluation of activities of daily living that is easy to administer in less than 3 min in a clinical setting. It has a high degree of reproducibility and is applicable to a wide range of

* Corresponding author.

E-mail addresses: joel.lim2@mohh.com.sg (J.W.-A. Lim), lincoln.liow.m.h@sgh.com.sg (M.H. Liow), andrew.tan.h.c@singhealth.com.sg (A.H.C. Tan).

<https://doi.org/10.1016/j.jor.2019.06.009>

Received 15 April 2019; Accepted 4 June 2019

Available online 05 June 2019

0972-978X/ © 2019 Professor P K Surendran Memorial Education Foundation. Published by Elsevier B.V. All rights reserved.

causes for shoulder dysfunction.¹⁵ Although it received criticism for being too simple, when compared to other shoulder outcome measures such as the Shoulder Pain and Disability Index (SPADI) and the American Shoulder and Elbow Surgeons form (ASES), the SST showed better convergent validity and correlation to patient satisfaction.^{16–18} Its validated simplicity, practicality and reproducibility makes it a popular and easily administered test.

The UCLA shoulder rating scale has been used in various studies for numerous shoulder conditions, including rotator cuff repairs. The UCLA score comprises of five components assessing pain, function, range of motion, strength and patient satisfaction. With a maximum score of 35, a score of 34–35 is considered excellent, 29–33 good, 21–28 fair and < 20 as poor function. As more than 50% of the scale is based on comfort (pain) and function, it can provide accurate data on patients who have undergone rotator cuff repair.^{15,19}

2.1. Surgical procedure

All 36 patients, who had isolated supraspinatus tears, underwent a deltoid raphe-splitting open rotator cuff repair. The surgical procedure began with a patient positioned supine with head raised at 30°. A 3-cm incision was made 1 cm distal to the anterolateral border of the acromion, parallel to the lateral border of the acromion. After dividing the subcutaneous fat layers, a split was made in the anterior deltoid raphe of the deltoid muscle near its origin at the acromion.²⁰ The bursa was subsequently resected and the rotator cuff tear was defined and debrided. The tendon was mobilized on both bursal and articular sides. The footprint on the greater tuberosity was prepared with 2 double-loaded bio-absorbable suture anchors inserted along the subchondral bone. The cuff repair was then done with the arm in neutral position without tension. The wound was subsequently closed in layers, including repair of the deltoid split.

Post-operatively, the shoulder was put in a universal arm sling. Post-operative analgesics, either NSAIDs (Etoricoxib, Naproxen, Mefenamic Acid or Celecoxib) or opiate derivatives (Tramadol), were prescribed for all patients. All patients were admitted on the day of surgery and discharged on the following day. On the day of discharge, patients were reviewed by the physiotherapist and started on passive range-of-motion exercises. For the first 6 weeks, patients underwent passive forward elevation of 140° and external rotation of 40° strictly. The subsequent 6 weeks involved active range-of-motion exercises. Patients were counseled to resume normal activities at 3 months. They were reviewed in the outpatient specialist clinic by the senior author at two weeks, six weeks, three, six, twelve and twenty-four months post-surgery.

None of our patients had any surgical or post-operative complications.

2.2. Statistical analysis

Assessment of differences in outcome scores between the groups was compared using one way analysis of variance with post hoc Bonferroni test. All continuous data are expressed in terms of mean and standard deviations from the mean. Statistical significance was defined as p value < 0.05. Statistical analysis was carried out with SPSS software, version 20 (SPSS Inc, Chicago, Illinois).

3. Results

There were 23 patients who received less than 2 weeks of NSAIDs, 6 patients who received more than 2 weeks of NSAIDs and 7 patients who were prescribed opioid derivatives post-surgery. Patient demographics were similar in all 3 groups (Table 1) and patients had similar pre-operative clinical parameters and scores (Table 2).

After a minimum of 2 years of follow-up, there was significant improvement in SST score, UCLA shoulder rating scale, abduction range of motion and abductor strength for all patients ($p < 0.05$). For patients

Table 1
Demographic data.

	< 2 weeks NSAIDs	> 2 weeks NSAIDs	Opioid derivatives	p-value
No. of Patients	23	6	7	
Age	56.2 ± 7.3	55.2 ± 7.0	58.7 ± 9.2	0.673
Gender (Male: Female)	8:15	3:3	1:6	0.384
Operated Side (Left: Right)	10:13	0:6	2:5	0.126

Table 2
Functional outcome scores.

	< 2 weeks NSAIDs	> 2 weeks NSAIDs	Opioid derivatives	p-value
Simple Shoulder Test				
Preoperative	1.0 ± 1.4	1.3 ± 1.8	0.6 ± 1.1	0.627
Postoperative	9.8 ± 2.6	10.3 ± 4.0	11 ± 1.0	0.572
Change	8.8 ± 2.6	9.0 ± 3.8	10.4 ± 1.5	0.366
UCLA Shoulder Rating Scale				
Preoperative	10.0 ± 3.7	11.1 ± 6.2	8.0 ± 3.9	0.385
Postoperative	29.4 ± 5.4	31.3 ± 8.5	30.7 ± 3.4	0.692
Change	19.4 ± 6.0	20.2 ± 10.6	22.7 ± 6.2	0.545
Abduction Strength (MRC Grade)				
Preoperative	2.6 ± 1.0	3.1 ± 1.7	2.3 ± 1.6	0.450
Postoperative	3.6 ± 1.6	3.8 ± 1.9	3.0 ± 2.1	0.660
Abduction Range of Motion (°)				
Preoperative	87.6 ± 33.4	98.0 ± 59.7	82.0 ± 13.0	0.774
Postoperative	148.6 ± 6.5	135.0 ± 30.0	145.0 ± 12.2	0.149

who received less than 2 weeks of NSAIDs, the SST score improved from 1.0 ± 1.4 pre-operatively to 9.8 ± 2.6 post-operatively, with the UCLA shoulder rating scale improving from 10.0 ± 3.7 to 29.4 ± 5.4. For patients who received more than 2 weeks of NSAIDs, the SST score improved from 1.3 ± 1.8 pre-operatively to 10.3 ± 4.0 post-operatively with the UCLA shoulder rating scale improving from 11.1 ± 6.2 to 31.3 ± 8.5. For patients who received opioid derivatives, the SST score improved from 0.6 ± 1.1 preoperatively to 11.0 ± 1.0 postoperative with the UCLA shoulder rating scale improving from 8.0 ± 3.9 to 30.7 ± 3.4 postoperative. There was no significant difference in the magnitude of improvement of clinical outcome scores between the 3 groups. (Table 2).

No significant difference was found between the post-operative abductor strength ($p = 0.660$) and post-operative abduction range of motion ($p = 0.149$). At a mean of 4.4 years post-surgery, 1 patient from the group that received more than 2 weeks of NSAIDs and 1 patient from the group that received opioid derivatives suffered rotator cuff tears which were diagnosed on magnetic resonance imaging.

100% of patients achieved the minimally clinical important difference (MCID) for SST and UCLA shoulder rating scale.

4. Discussion

Our study aims to investigate if the use of post-operative NSAIDs in rotator cuff repairs would affect clinical outcomes and we found that neither the use nor duration of use of NSAIDs affected outcomes.

Rotator cuff surgery is associated with significant post-operative pain that might necessitate prolonged opioid use. Opioid use is not without its adverse side effects, such as nausea, vomiting, pruritus, drowsiness and decreased gastrointestinal motility. Nonsteroidal anti-inflammatory drugs, both non-selective and selective, have analgesic and anti-inflammatory properties which are useful post-operatively to reduce inflammation, allowing patient to begin rehabilitation earlier.⁶ Usage of post-operative NSAIDs can reduce opioid requirements via a multimodal pain therapy. However, there are several well-published side effects such as renal impairment, gastrointestinal bleeding,

allergies and even acute myocardial infarction.^{21–23}

There are numerous animal studies in orthopaedic literature that have reported deleterious effects of NSAIDs on tendon-to-bone healing.^{6–9} Cohen et al. reported that rats which underwent tendon repairs and received Indomethacin or Celecoxib had significant reduction of loads to failure as well as a lack of collagen organization when examined under a microscope.⁶ Recent studies that have shown that muscle atrophy and fatty infiltration persist and even worsens after rotator cuff repair. These factors have been associated with failure of rotator cuff repairs and increased COX-2 expression has been implicated with the findings.⁴

Current clinical literature examining the use of NSAIDs and duration of their use on patients undergoing rotator cuff repair is sparse. Oh et al. found that patients who received celecoxib, ibuprofen or tramadol had similar clinical outcomes and function scores at 12-months post-surgery.²³ In our study, the use of post-operative NSAIDs did not result in poorer clinical outcomes and NSAIDs' use exceeding 2 weeks did not seem to have a detrimental effect on clinical outcomes either. A recent animal study on inhibition of COX-1, COX-2 and 5-LOX using Licoferone, a selective COX inhibitor, has shown increased strength and higher loads to failure after rotator cuff repairs.²⁴ The detrimental effects of NSAIDs on tendon healing is still controversial, as translating results from laboratory to clinical practice and from animals to humans is difficult due to the differences in physiology, varied study methodologies and end-points.²⁵

There are several limitations to our study. Firstly, this is a retrospective study and therefore the risk of selection bias is present. However, in this study, through the use of specific inclusion criteria, a standardized operative and rehabilitation protocol, we have attempted to mitigate the risk of bias. Secondly, general post-operative complications which may be attributed to use of NSAIDs was available from our orthopaedic diagnostic centre registry. However, this may not pick up the entire spectrum of potential systemic side-effects which would be important. Thirdly, routine MRI was not performed for patients after surgery to assess healing of the rotator cuff repair, and the actual rate of re-tears may be under-estimated. However, all patients underwent a comprehensive battery of clinical outcomes and quality-of-life assessment measures which allowed us to identify and manage patients with suspected re-tears.

5. Conclusion

The use of NSAIDs and duration of their use did not appear to affect the clinical outcomes after rotator cuff repairs in our study. We recommend that while surgeons must be cognizant of the potential side effects of NSAIDs, their use as a good modality of post-operative pain relief need not be precluded in patients after rotator cuff repair.

Conflicts of interest

The Authors declare that there is no conflict of interest.

References

- Galatz LM, Ball CM, Teefey SA, Middleton WD, Yamaguchi K. The outcome and repair integrity of completely arthroscopically repaired large and massive rotator cuff tears. *J Bone Joint Surg Am.* 2004;86(2):219–224.
- Boileau P, Brassart N, Watkinson DJ, Carles M, Hatzidakis AM, Krishnan SG. Arthroscopic repair of full-thickness tears of the supraspinatus: does the tendon really heal? *J Bone Joint Surg Am.* 2005;87(6):1229–1240.
- Gerber C, Fuchs B, Hodler J. The results of repair of massive tears of the rotator cuff. *J Bone Joint Surg Am.* 2000;82(4):505–515.
- McElvany MD, McGoldrick E, Gee AO, Neradilek MB, Matsen 3rd FA. Rotator cuff repair: published evidence on factors associated with repair integrity and clinical outcome. *Am J Sports Med.* 2015;43(2):491–500.
- Seibert K, Zhang Y, Leahy K. Pharmacological and biochemical demonstration of the role of cyclooxygenase 2 in inflammation and pain. *Proc Natl Acad Sci USA.* 1994;91(25):12013–12017.
- Cohen DB, Kawamura S, Ehteshami JR, Rodeo SA. Indomethacin and celecoxib impair rotator cuff tendon-to-bone healing. *Am J Sports Med.* 2006;34(3):362–369.
- Dolkart O, Liron T, Chechik O, et al. Statins enhance rotator cuff healing by stimulating the COX2/PGE2/EP4 pathway: an in vivo and in vitro study. *Am J Sports Med.* 2014;42(12):2869–2876.
- Lu Y, Li Y, Li FL, Li X, Zhuo HW, Jiang CY. Do different cyclooxygenase inhibitors impair rotator cuff healing in a rabbit model? *Chin Med J (Engl).* 2015;128(17):2354–2359.
- Chechik O, Dolkart O, Mozes G, Rak O, Alhajjara F, Maman E. Timing matters: NSAIDs interfere with the late proliferation stage of a repaired rotator cuff tendon healing in rats. *Arch Orthop Trauma Surg.* 2014;134(4):515–520.
- Gladstone JN, Bishop JY, Lo IK, Flatow EL. Fatty infiltration and atrophy of the rotator cuff do not improve after rotator cuff repair and correlate with poor functional outcome. *Am J Sports Med.* 2007;35(5):719–728.
- Goutallier D, Postel JM, Gleyze P, Leguilloux P, Van Driessche S. Influence of cuff muscle fatty degeneration on anatomic and functional outcomes after simple suture of full-thickness tears. *J Shoulder Elb Surg.* 2003;12(6):550–554.
- Kang JR, Gupta R. Mechanisms of fatty degeneration in massive rotator cuff tears. *J Shoulder Elb Surg.* 2012;21(2):175–180.
- Lippitt SB, Harryman II DT, Matsen III FA. A Practical Tool for Evaluating Function. *The Simple Shoulder Test.* AAOS; 1993:501–518.
- Amstutz HC, Sew Hoy AL, Clarke IC. UCLA anatomic total shoulder arthroplasty. *Clin Orthop Relat Res.* 1981;155:7–20.
- Matsen III FA, Ziegler DW, DeBartolo SE. Patient self-assessment of health status and function in glenohumeral degenerative joint disease. *J Shoulder Elb Surg.* 1995;4:345–351.
- Roach KE, Budiman-Mak E, Songsiridej N, Lertratanakul Y. Development of a shoulder pain and disability index. *Arthritis Care Res.* 1991;4(4):143–149.
- Richards RR, An KN, LU Bigliani, et al. A standardized method for the assessment of shoulder function. *J Shoulder Elb Surg.* 1994;3(6):347–352.
- Romeo AA, Mazzocca A, Hang DW, Shott S, Bach Jr BR. Shoulder scoring scales for evaluation of rotator cuff repair. *Clin Orthop Relat Res.* 2004;427:107–114.
- Budoff J, Nirschl RP, Guidi EJ. Current Concepts Review – debridement of partial thickness tears of the rotator cuff without acromioplasty. Long-term follow-up and review of literature. *J Bone Joint Surg Am.* 1998;80(5):733–748.
- Matsen III FA, Lippitt SB. *Procedure: Rotator Cuff Repair. Shoulder Surgery: Principles and Procedures.* Philadelphia: Saunders; 2004:347–377.
- Larkai EN, Smith JL, Lidsky MD, Graham DY. Gastrointestinal mucosa and dyspeptic symptoms in arthritic patients during chronic steroidal antiinflammatory drug use. *Am J Gastroenterol.* 1987;15:1153–1158.
- Huerta C, Castellsague J, Varas-Lorenzo C, García Rodríguez LA. Nonsteroidal anti-inflammatory drugs and risk of ARF in the general population. *Am J Kidney Dis.* 2005;45:531.
- Oh JH, Seo HJ, Lee YH, Choi HY, Kim SH. The effect of selective COX-2 inhibitor on pain control and rotator cuff healing following arthroscopic repair: prospective randomized comparative study. *J Shoulder Elb Surg.* 2015;24(4):e106.
- Bally M, Dendukuri N, Rich B, et al. Risk of acute myocardial infarction with NSAIDs in real world use: bayesian meta-analysis of individual patient data. *BMJ.* 2015;357:j1909.
- Chen MR, Dragoo JL. The effect of nonsteroidal anti-inflammatory drugs on tissue healing. *Knee Surg Sport Traumatol Arthrosc.* 2012;21(3):540–549.