Original Article

Predicting postoperative pain with neutrophil/ lymphocyte ratio after arthroscopic rotator cuff repair

Kerim Öner [a], Ahmet Emin Okutan [b, *], Muhammet Salih Ayas [c], Ahmet Emre Paksoy [a], Ferdi Polat [d]

[a] Yozgat Bozok University, School of Medicine, Orthopaedics and Traumatology Dept., Yozgat, Turkey
[b] Karadeniz Technical University, School of Medicine, Orthopaedics and Traumatology Dept., Trabzon, Turkey
[c] Erzurum Regional Training and Research Hospital, Orthopaedics and Traumatology Dept., Erzurum, Turkey
[d] Sorgun State Hospital, Dept. of Anesthesiology, Yozgat, Turkey

ARTICLE INFO

ABSTRACT

Background: Postoperative pain is well known and usually disturbing complication of arthroscopic shoulder surgery. Inflammation plays an important role in the development and progression of postoperative pain. The aim of this study was to evaluate the predictability of postoperative pain through the correlation of neutrophil/lymphocyte ratio (NLR) with inflammation. In addition, the correlation of parameters such as operative time, tear size, age and gender with postoperative pain was evaluated.
Methods: Sixty three patients, who underwent arthroscopic rotator cuff repair, were evaluated in this single-center-based retrospective study. The American Society of Anaesthesiologists I and II risk groups were determined as the inclusion criteria. NLR was calculated using preoperative one day hemogram values in all patients. The amounts of analgesic use and Numerical Rating Scale (NRS) scores at the 12th, 24th and 48th hours and on the 3rd and 7th days were recorded. Multivariate linear regression analysis was used to correlate postoperative NRS scores with multiple independent factors, including preoperative NLR, sex, age, tear size, repair type, operative time, block time, postoperative analgesic intake and length of hospital stay.
Results: Sixty three patients with a mean age of 59.4 years (range, 40—72 years) were evaluated. The mean tear size was 2.8 cm (range, 1—5 cm), the mean operative time was 84.1 min (range, 35—135 min), the mean duration of block was 7.6 hours (range, 4—12 hours) and the mean length of hospital stay was 1.7 days (range, 1—3 days). There was no significant correlation between age, sex, tear size, repair type, operative time and postoperative NRS ($p > 0.2$). The preoperative NLR was found to be a strong predictor of postoperative NRS ($p < 0.001$, rho $= 0.864$). There was a correlation between the NLR and mean analgesic intake ($p = 0.03$). The duration of block was decreased in patients with a NLR above 2, while it was prolonged in patients with a NLR below 2 ($p = 0.04$, rho $= -0.725$).
Conclusion: The preoperative NLR was found to be a strongest factor predicting high acute pain levels after arthroscopic rotator cuff surgery. Likewise, NLR was also predictive of postoperative block time and analgesic consumption.
© 2020 Asia Pacific Knee, Arthroscopy and Sports Medicine Society. Published by Elsevier (Singapore) Pte Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

With the advancement of arthroscopic techniques and advanced implant options, arthroscopic diagnosis and treatment of shoulder pathologies have moved ahead of open surgery as the primary treatment method. Arthroscopic technique allows to intervene in more space with a minimally invasive approach, especially in glenohumeral pathologies, and complications such as infection and bleeding are minimised. However, postoperative pain still remains as a problem. A similar analgesic requirement arises with open surgery within the first 24—48 h after shoulder arthroscopy, and one third of patients describe severe pain despite multimodal

* Corresponding author. Karadeniz Technical University, School of Medicine, Orthopedics and Traumatology Dept., 61080, Trabzon, Turkey.
E-mail address: ahmeteokutan@yahoo.com (A.E. Okutan).

analgesia.[7] Postoperative pain is a consequence of the inflammatory response to surgical trauma. Local inflammatory mediators triggered by incision, dissection, etc. cause an increase in the nociceptor sensitivity and hyperalgesia, resulting in postoperative pain perception.[10]

Neutrophil/lymphocyte ratio (NLR) has been used as a marker for monitoring of diagnosis and treatment in a wide spectrum from systemic diseases such as hypertension, diabetes to inflammatory diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis, coronary heart disease, pancreatic, gastric, colorectal cancers, and a significant literature has been created.[8,12—15,17,19] For example, NLR reflect inflammatory response and disease activity in SLE patients. Increased NLR was observed in systemic lupus erythematosus patients and NLR level of 2.065 was determined as predictive cut-off value of SLE.[16] The aim of this study, similarly in previous studies, was to evaluate the predictability of postoperative pain through the correlation of NLR with inflammation. In addition, the correlation of parameters such as operative time, tear size, age and gender with postoperative pain was evaluated.

Patients and method

Eighty-six patients, who underwent arthroscopic rotator cuff repair and subacromial decompression by a single surgeon in our clinic between 2016 and 2018, were retrospectively analyzed. The study has been approved by an ethics committee (Ref no: 2016-KAEK-189_2019.01.09_11).

The American Society of Anaesthesiologists (ASA) I and II risk groups were determined as the inclusion criteria. Patients with massive and retracted cuff tears and moderate-to-severe acromioclavicular and glenohumereal joint degeneration were excluded, and 63 patients were included in the study. NLR was calculated using preoperative one day hemogram values, and the size of tear was determined by MRI images. Tears were classified as small (0—1 cm), medium (1—3 cm), large (3—5 cm) and massive (>5 cm) according to their sizes. All patients underwent single shot interscalene brachial plexus block and all patients were prepared in the beach chair position; following diagnostic arthroscopy,

subacromial bursectomy was performed. Transosseous-equivalent double-row or single-row repair was performed depending on the configuration of tear and tissue quality. Again, depending on the size of tear, 2 or 5 metallic anchors were used. Coracoacromial ligament release and anterior acromioplasty were performed on all patients. Postoperative immobilization of the shoulder was performed with the velpeau bandage. The duration of block and the onset times of pain were recorded. Depending on the pain level of the patients, opioid (tramadol hydrochloride 50 mg, every 6 h) or NSAID (dexketoprophen trometamol 50 mg, every 8 h, as needed) group of analgesics were administered intravenously until discharge. The amounts of analgesic use and Numerical Rating Scale (NRS) scores at the 12th, 24th and 48th hours and on the 3rd and 7th days were recorded. Multivariate linear regression analysis was used to correlate postoperative NRS scores with multiple independent factors, including preoperative NLR, sex, age, tear size, repair type, operative time, block time, postoperative analgesic intake and length of hospital stay.

Statistical analysis

The statistical analysis was performed using Statistical Package for Social Sciences (SPSS) Version 22.0 (SPSS, Chicago, IL) statistical analysis software. Normal distribution was defined by the Shapiro-Wilk test. The preoperative and postoperative comparisons were performed using the Student t-test as quantitative data. Patient factors were included in a multivariate regression analysis to determine the significant independent predictors of postoperative NRS score on days 1 and 7. The MannWhitney U test and Kruskal-Wallis test were used to compare the outcomes of subgroups.

Results

The study included 63 (35 females, 28 males) out of 86 patients meeting the criteria and undergone arthroscopic rotator cuff repair. The mean age of the patients was 59.4 years (range, 40—72 years). The mean tear size was 2.8 cm (range, 1—5 cm), the mean operative time was 84.1 min (range, 35—135 min), the mean duration of block

Table 1
Comparative postoperative NRS data by patient factors.

Parameters	No. of Patients (%)	Postoperative Day 1 NRS			Postoperative Day 7 NRS		
		Mean	SD	p	Mean	SD	p
Preoperative NLR							
≥2	30 (47,6%)	6,3	1,7	<0,001	3,1	0,9	<0,001
<2	33 (52,4%)	3,4	0,8		1,8	0,4	
Sex							
Female	35 (55,6%)	5,1	2,1	0,373	2,5	1,1	0,201
Male	28 (44,4%)	4,5	1,5		2,2	0,7	
Age							
≥60 yr	34 (54%)	4,5	1,7	0,393	2,2	0,8	0,213
<60 yr	29 (46%)	5,1	2,1		2,5	0,9	
Tear Size							
Small	6 (9,5%)	4,2	1,8	0,419	2,3	1,2	0,377
Medium	23 (36,5%)	5,1	2,2		2,4	1,1	
Large	28 (44,4%)	4,7	1,6		2,4	0,8	
Massive	6 (9,5%)	4,1	1,9		2,1	1,1	
Repair Type							
Single Row	31 (49,2%)	4,9	2,1	0,709	2,4	1,1	0,655
Double Row	32 (50,8%)	4,7	1,6		2,3	0,8	
Operative Time							
≥80 min	36 (57,1%)	4,5	1,7	0,277	2,2	0,8	0,357
<80 min	27 (42,9%)	5,1	2,1		2,5	0,9	
Block time							
<6 h	28 (44,4%)	6,6	1,5	0,02	3,3	0,8	0,03
≥6 h	35 (55,6%)	3,1	1,1		2,1	0,7	

NRS: Numerical Rating Scale; NLR: Neutrophil Leymphocyte Ratio; SD: Standart Deviation; p: Mann-Whitney U Test.
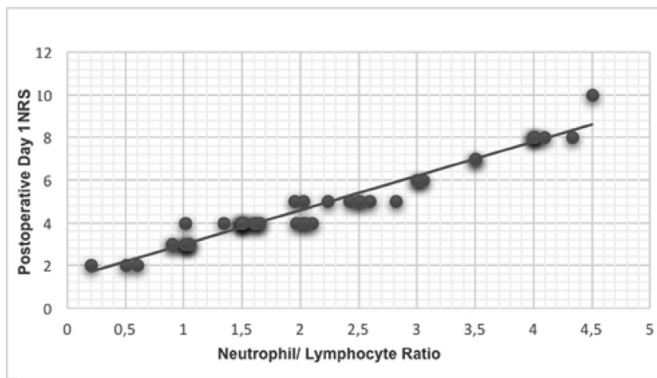
Fig. 1. A scatter dot chart shows the correlation between the NLR and the post-operative day 1 NRS scores (p < 0,001, rho = 0,864).

**Table 2**
NLR subgroups and daily mean analgesic intake and length of hospital stay.

NLR	Mean Opioid Intake (gr/day)	Mean NSAID Intake (gr/day)	Length of Hospital Stay (day)
<2	124,4 ± 12,6	95,6 ± 8,6	1,12 ± 0,3
≥2	184,5 ± 14,8	136,8 ± 13,5	1,95 ± 0,4
p	0,03	0,04	0,173

NLR: Neutrophil Leymphocyte Ratio; p: Kruskal-Wallis test.
Note: Table shows the correlation between the NLR and mean analgesic intake. There was no significant correlation between the NLR and length of hospital stay.
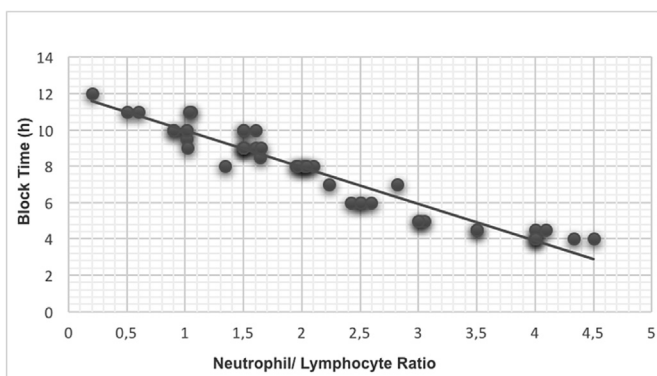
Fig. 2. A scatter dot chart shows the correlation between the NLR and the post-operative block time (p = 0,04, rho = −0,725).

was 7.6 h (range, 4–12 h) and the mean length of hospital stay was 1.7 days (range, 1–3 days). The mean preoperative NLR was 2.1 (range, 0.2–4.5). The mean postoperative NRS scores were determined to be 5.7 (range, 3–10) at the 12th hour, 4.8 (range, 3–10) at the 24th hour, 4.5 (range, 2–8) at the 48th hour and 2.4 (range, 1–5) on 7th day. The mean NRS scores of 33 patients with a NLR below 2 was 3.4 (range, 2–7) on the postoperative 1st day, 1.8 (range, 1–3) on the postoperative 7th day. The mean NRS scores of 30 patients with a NLR above 2 was 6.3 (range, 4–10) on the postoperative 1st day and 3 (range, 2–5) on the postoperative 7th day.

As can be seen from the parameters summarized in Table 1, there was no significant correlation between age, sex, tear size, repair type, operative time and postoperative NRS (p > 0.2). The preoperative NLR was found to be a strong predictor of postoperative NRS (p < 0.001, rho = 0.864) (Fig. 1). A detailed analgesic consumption and length of hospital stay is shown in Table 2. There was a correlation between the NLR and mean analgesic intake (p = 0,03 and 0,04). There was no significant correlation between

the NLR and length of hospital stay (p = 0,173). Likewise, there was a significant correlation between block duration and postoperative NRS; decreased NRS scores were found in those with a prolonged block duration, while increased NRS scores were observed in those with a short block duration (p = 0.02). The duration of block was decreased in patients with a NLR above 2, while it was prolonged in patients with a NLR below 2 (p = 0.04, rho = −0,725) (Fig. 2).

Discussion

In this study, the significance of preoperative NLR values in predicting postoperative pain after arthroscopic rotator cuff repair was determined, and its correlation was demonstrated. It was found that the patients with a NLR of 2 and above had high NRS scores and short block duration.

NLR is a marker of subclinical inflammation, and has been used in combination with other inflammatory markers to determine inflammation. The predictive role of NLR, as an inflammation marker, in several diseases such as coronary artery disease, colorectal cancers and other inflammatory diseases suggests that NLR can be a useful predictive indicator for postoperative pain resulted from inflammatory pathways secondary to surgical trauma and/or surgery-related direct nerve trauma.[18]

NLR, which is used as a predictor in the monitoring of numerous different diseases, has no definite cut-off value determined in the literature. There are studies taking the ratios such as 2, 3, 4 as a cut-off ratio.[2,9,16] With reference to two studies associated with postoperative pain, we also determined the cutoff value as 2 in this study.

Turgut et al.[18] retrospectively evaluated preoperative NLR and postoperative pain predictability in their study conducted on 140 patients who underwent orthognatic surgery. They divided the patients into two groups as those with a NLR of 2 and above and those with a NLR below 2, and found that the analgesic requirement of the group with a NLR of 2 and above was significantly high, and they interpreted this as the correlation of high NLR with increased postoperative pain.

Daoudia et al.[5] evaluated preoperative pain-related attitudes and postoperative analgesic requirement in their study on 60 patients who underwent laparoscopic cholecystectomy. They determined the individual attitudes against preoperative painful stimulation using "situational pain scale" and determined the emotional state using "hospital anxiety and depression scale". They recorded the total amount of analgesic requested for pain in the postoperative first 48 h as "unitary dosage". They demonstrated that the postoperative analgesic requirement of those with high situational pain scale scores was high, and that these were patients with a low NLR and poor emotional state. In conclusion, they stated that there was a correlation between postoperative unitary dosage and preoperative situational pain scale, and that hospital anxiety and depression scale representing the emotional state and NLR representing the inflammatory status were correlated with postoperative pain.

The effects of anesthesia types and some preoparative and operative parameters on postoperative pain in shoulder arthroscopy were investigated. For example, in one study, it was suggested that continuous-infusion device was effective in postoperative pain control,[1] whereas in another study, it was reported that interscalene block provided more relief in the early postoperative period compared to infusion pumps.[3] On the other hand, in the study by Kim et al.[11] evaluating 12-month follow-up scores of Visual Analogue Scale (VAS) of 84 patients who underwent rotator cuff repair, it was found that high VAS score and high-onset pain were correlated with high pain pattern. In the study by Dunn et al.[6] conducted on 394 patients with rotator cuff tear that they treated with physical therapy, it was indicated that pain levels were not

correlated with tear size, and that high pain levels were rather correlated with comorbidity, lower education levels and race.

The most important conclusion that can be drawn from many studies evaluating various parameters is the fact that pain is a subjective concept. The most obvious study revealing this was conducted by Cuff et al.[4] They evaluated the correlation of some preoperative and operative parameters with postoperative pain in 181 patients who underwent arthroscopic rotator cuff repair. They indicated that factors, such as preoperative narcotic use, smoking and young age of patients, were correlated with high pain scores in the first postoperative week. Interestingly, patients with a high preoperative subjective pain tolerance showed high pain scores in the postoperative period, and this correlation was determined to be strongly positive. In other words, patients who stated that they had a high pain threshold revealed high pain scores in the postoperative period. This is undoubtedly related to the subjectivity of the pain concept. As stated by the authors, patients may not have a high pain threshold as they really claimed, or those who thought they had a high pain threshold may have declared higher NRS values since they were exposed to more pain than they predicted postoperatively.

According to the conclusion we obtained from this study, it is possible to predict postoperative pain level with an objective parameter. Likewise, postoperative block time and requirement for analgesic consumption can be predicted preoperatively. Thus, unnecessary or excessive analgesic use can be prevented, early rehabilitation can be provided, patient satisfaction can be increased, the length of hospital stay can be shortened.

Limitations

The lack of different anesthesia modalities to be compared, the small number of patients are the main limitations of this study. On the other hand, the fact that NLR is changed in the presence of comorbidity or by many conditions defined and is very open to be affected, is an important limitation in terms of its widespread use, and requires a comprehensive study.

Conclusion

The preoperative NLR was found to be a strongest factor predicting high acute pain levels after arthroscopic rotator cuff surgery. Likewise, NLR was also predictive of postoperative block time and analgesic consumption.

Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.asmart.2020.03.001.

References

1. Barber FA, Herbert MA. The effectiveness of an anesthetic continuous-infusion device on postoperative pain control. *Arthroscopy*. 2002;18(1):76–81.
2. Bugada D, Lavand'homme P, Ambrosoli AL, et al. Effect of preoperative inflammatory status and comorbidities on pain resolution and persistent postsurgical pain after inguinal hernia repair. *Mediat Inflamm*. 2016;2016:5830347. https://doi.org/10.1155/2016/5830347.
3. Ciccone 2nd WJ, Busey TD, Weinstein DM, Walden DL, Elias JJ. Assessment of pain relief provided by interscalene regional block and infusion pump after arthroscopic shoulder surgery. *Arthroscopy*. 2008;24(1):14–19. https://doi.org/10.1016/j.arthro.2007.07.021.
4. Cuff DJ, O'Brien KC, Pupello DR, Santoni BG. Evaluation of factors affecting acute postoperative pain levels after arthroscopic rotator cuff repair. *Arthroscopy*. 2016;32(7):1231–1236. https://doi.org/10.1016/j.arthro.2015.12.021.
5. Daoudia M, Decruynaere C, Le Polain de Waroux B, Thonnard JL, Plaghki L, Forget P. Biological inflammatory markers mediate the effect of preoperative pain-related behaviours on postoperative analgesics requirements. *BMC Anesthesiol*. 2015;15:183. https://doi.org/10.1186/s12871-015-0167-9.
6. Dunn WR, Kuhn JE, Sanders R, et al. Symptoms of pain do not correlate with rotator cuff tear severity: a cross-sectional study of 393 patients with a symptomatic atraumatic full-thickness rotator cuff tear. *J Bone Jt Surg Am*. 2014;96(10):793–800. https://doi.org/10.2106/JBJS.L.01304.
7. Fredrickson MJ, Krishnan S, Chen CY. Postoperative analgesia for shoulder surgery: a critical appraisal and review of current techniques. *Anaesthesia*. 2010;65(6):608–624. https://doi.org/10.1111/j.1365-2044.2009.06231.x.
8. Han F, Liu Y, Cheng S, et al. Diagnosis and survival values of neutrophil-lymphocyte ratio (NLR) and red blood cell distribution width (RDW) in esophageal cancer. *Clin Chim Acta*. 2019;488:150–158. https://doi.org/10.1016/j.cca.2018.10.042.
9. Hong J, Mao Y, Chen X, et al. Elevated preoperative neutrophil-to-lymphocyte ratio predicts poor disease-free survival in Chinese women with breast cancer. *Tumour Biol*. 2016;37(3):4135–4142. https://doi.org/10.1007/s13277-015-4233-1.
10. Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia I: physiological pathways and pharmacological modalities. *Can J Anaesth*. 2001;48(10):1000–1010. https://doi.org/10.1007/BF03016591.
11. Kim CW, Kim JH, Kim DG. The factors affecting pain pattern after arthroscopic rotator cuff repair. *Clin Orthop Surg*. 2014;6(4):392–400. https://doi.org/10.4055/cios.2014.6.4.392.
12. Lou M, Luo P, Tang R, et al. Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients. *BMC Endocr Disord*. 2015;15:9. https://doi.org/10.1186/s12902-015-0002-9.
13. Mercan R, Bitik B, Tufan A, et al. The association between neutrophil/lymphocyte ratio and disease activity in rheumatoid arthritis and ankylosing spondylitis. *J Clin Lab Anal*. 2016;30(5):597–601. https://doi.org/10.1002/jcla.21908.
14. Ozturk C, Balta S, Balta I, Celik T. Neutrophil-lymphocyte ratio in behcet disease. *Angiology*. 2015;66(7):695. https://doi.org/10.1177/0003319715586290.
15. Paramanathan A, Saxena A, Morris DL. A systematic review and meta-analysis on the impact of pre-operative neutrophil lymphocyte ratio on long term outcomes after curative intent resection of solid tumours. *Surg Oncol*. 2014;23(1):31–39. https://doi.org/10.1016/j.suronc.2013.12.001.
16. Qin B, Ma N, Tang Q, et al. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. *Mod Rheumatol*. 2016;26(3):372–376. https://doi.org/10.3109/14397595.2015.1091136.
17. Templeton AJ, McNamara MG, Seruga B, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. *J Natl Cancer Inst*. 2014;106(6). https://doi.org/10.1093/jnci/dju124. dju124.
18. Turgut HC, Alkan M, Atac MS, et al. Neutrophil lymphocyte ratio predicts postoperative pain after orthognathic surgery. *Niger J Clin Pract*. 2017;20(10):1242–1245. https://doi.org/10.4103/1119-3077.181399.
19. Xiao WK, Chen D, Li SQ, Fu SJ, Peng BG, Liang LJ. Prognostic significance of neutrophil-lymphocyte ratio in hepatocellular carcinoma: a meta-analysis. *BMC Canc*. 2014;14:117. https://doi.org/10.1186/1471-2407-14-117.