Acta Medica Alanya

Research Article

Araştırma

Acta Medica Alanya 2023;7(3): 226-231
Doi: 10.30565/medalanya.1376796

Lymphocyte-to-Monocyte Ratio is a Good Marker of Adhesive Capsulitis in Rotator Cuff Tears

Lenfosit-Monosit Oranı Rotator Manşet Yırtıklarında Adeziv Kapsülitin İyi Bir Belirtecidir

İlhan Çelik[1], Hümeyra Çelik[2], Tacettin Ayanoğlu[3], Emre Arıkan[4], Seyit Ali Kayış[5]

[1] Alanya Education and Training Hospital, Department of Orthopaedics and Traumatology, Antalya, Türkiye
[2] Alanya Alaaddin Keykubat University Medical School, Department of Physiology, Alanya, Antalya, Türkiye
[3] Bolu Abant Izzet Baysal University Medical School, Department of Orthopaedics and Traumatology, Bolu, Türkiye
[4] Bursa Yuksek Ihtisas Training and Research Hospital, Department of Orthopaedics and Traumatology, Bursa, Türkiye
[5] Bolu Abant Izzet Baysal University Medical School, Department of Biostatistics and Medical Informatics, Bolu, Türkiye

ABSTRACT

Purpose: The aim of the study is to evaluate the prediction of adhesive capsulitis in the preoperative period of rotator cuff tear (RCT) by neutrophil-lymphocyte (NLR), platelet-lymphocyte (PLR), neutrophil-monocyte (NMR), lymphocyte-monocyte (LMR) ratios.

Methods: This study was designed as a retrospective case-control study. After ethical approval, preoperative hemogram and biochemistry data of 128 patients who were operated on for RCT were collected from the archive of hospitale. Among the patients who underwent arthroscopy due to RCT, those with signs of adhesive capsulitis in the intraoperative period were included in the RCT+Adhesive capsulitis group. Age, blood glucose, CRP, sedimentation, white blood cell, neutrophil, monocytes, lymphocytes, platelets, fasting blood glucose, hemoglobin and hematocrit values, and NLR, PLR, NMR, and LMR ratios were compared between healthy control and RCT+Adhesive capsulitis. Logistic regression analysis of the ratios was also performed.

Results: A total of 64 healthy RCT (group 1) and 64 patients with RCT+Adhesive capsulitis (group 2) were included in the study. Fasting blood glucose, lymphocyte, CRP values, and NMR and LMR were found to be higher in patients with adhesive capsulitis ($p<0.05$); and monocyte, NLR and PLR were found to be lower in group 2 compared to group 1 ($p<0.05$). According to ROC analysis, it was revealed that LMR was the best predictor of adhesive capsulitis in RCT.

Conclusion: It has been demonstrated that the inflammation rate LMR obtained from the hemogram, which is an easy, low-cost, and reproducible method, is a variable that predicts adhesive capsulitis in RCT.

Key Words: Adhesive capsulitis; rotator cuff tear; lymphocyte-monocyte rate

ÖZET

Amaç: Çalışmanın amacı, rotator manşet yırtığındaki (RMY) adeziv kapsüliti preoperatif olarak ölçülen nötrofil-lenfosit (NLO), trombosit-lenfosit (PLO), nötrofil-monosit (NMO), lenfosit-monosit (LMO) oranlarından öngörmektir.

Yöntem: Bu çalışma retrospektif vaka kontrol çalışması olarak tasarlandı. Etik onay alındıktan sonra, RMY amacıyla ameliyat edilen 128 hastanın ameliyat öncesi hemogram ve biyokimya verileri hastane arşivinden toplandı. RMY nedeniyle artroskopi yapılan hastalardan intraoperatif dönemde adeziv kapsülit bulguları olanlar RMY+Adeziv kapsülit grubuna dahil edildi. Sağlıklı kontrol ve RMY+Adeziv kapsülit grupları arasında yaş, kan şekeri, CRP, sedimantasyon, beyaz kan hücresi, nötrofil, monositler, lenfositler, trombositler, açlık kan şekeri, hemoglobin ve hematokrit değerleri ile NLO, PLO, NMO ve LMO oranları karşılaştırıldı. Oranların lojistik regresyon analizi yapıldı.

Bulgular: Çalışmaya toplam 64 sağlıklı RMY (grup 1) ve 64 RMY+Adeziv kapsülit hastası (grup 2) dahil edildi. Açlık kan şekeri, lenfosit, CRP değerleri, NMO ve LMO adeziv kapsülitli hastalarda yüksek bulundu ($p<0,05$); monosit, NLO ve PLO ise grup 2'de grup 1'e göre daha düşük bulundu ($p<0,05$). ROC analizine göre RMY'de adeziv kapsülitin en iyi belirleyicisinin LMO olduğu ortaya çıktı.

Sonuç: Kolay, düşük maliyetli ve tekrarlanabilir bir yöntem olan hemogramdan elde edilen LMO'nun inflamatuar bir oran olarak RMY'de adeziv kapsüliti öngören bir değişken olduğu gösterilmiştir.

Anahtar Kelimeler: Adeziv kapsülit; rotator manşet yırtığı; lenfosit-monosit oranı

Recieved Date: 16.10.2023 / **Accepted Date:** 09.12.2023 / **Published (Online) Date:** 31.12.2023

Corresponding author: Hümeyra Çelik, MD, Assisstant Professor, Alanya Alaaddin Keykubat University Medical School, Department of Physiology, Alanya, Antalya, Turkey
Phone: +905530522807 / **mail:** humeyra.colaker@gmail.com
ORCID: 0000-0002-3394-2438

To cited: Çelik İ, Çelik H, Ayanoğlu T, Arıkan E, Kayış SA. Lymphocyte-to-Monocyte Ratio is a Good Marker of Adhesive Capsulitis in Rotator Cuff Tears. Acta Med. Alanya 2023;7(3): 226-231 doi: 10.30565/medalanya.1376796

Acta Medica Alanya 2023;7(3): 226-231
Doi: 10.30565/medalanya.1376796

Introduction

Adhesive capsulitis, also known as 'frozen shoulder', is known as the presence of significant limitation and pain in active and passive shoulder range of motion due to inflammatory fibrotic contracture of the glenohumeral joint capsule.[1] Although it has an increasing incidence with age[2], it has been reported to be more common, especially in adults between the ages of 52 and 72[3], and to be associated with some diseases such as diabetes mellitus, hypo-hyperthyroidism, myocardial infarction.[4] Non-infectious and limited chronic low-grade inflammation and fibrosis formation without necrosis are suggested for the formation of adhesive capsulitis.[5] Inflammation-based histopathology of adhesive capsulitis has been supported by magnetic resonance imaging (MRI).[6]

For the diagnosis of adhesive capsulitis, when abduction-external rotation restriction is detected in the physical examination, it is supported by MRI, but the definitive diagnosis is made during the repair of RCT (rotator cuff tear) in arthroscopy.[7] To support the diagnosis, it is known that blood glucose and HbA1c elevation among laboratory findings[8] are associated with adhesive capsulitis, and C-reactive protein[9] shows high sensitivity in adhesive capsulitis, but there are no preoperative and specific laboratory findings for it. The formation of adhesive capsulitis based on inflammation is a guide for the investigation of inflammatory markers supporting the diagnosis.

It has been demonstrated that neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), neutrophil-monocyte ratio (NMR), and lymphocyte-monocyte ratios (LMR) reflect the level of systemic inflammation, and have recently been suggested as inflammatory markers.[10] These parameters, which can be easily calculated from blood samples collected under simple laboratory conditions, represent low-cost and reproducible tests, and are included in the hemogram for preoperative routine examination.[11, 12] These parameters can be associated with adhesive capsulitis, which has a hypothesis of inflammation in its etiopathogenesis. If the adhesive capsulitis accompanying rotator cuff tendinitis was diagnosed during the preoperative preparation, additional measures such as frozen shoulder manipulation could be added before arthroscopy, and the preoperative preparation process could be strengthened.

In light of this information, we aim to contribute to the diagnostic approach of adhesive capsulitis by evaluating NLR, PLR, NMR, and LMR in preoperative hemograms of patients with RCT.

Material-Method

Ethical approval of the study was obtained from Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (decision number: 78/2021). This study was designed as a retrospective case-control study. Demographic and clinical data of the patients were obtained from Bolu Abant İzzet Baysal University Medical Faculty Hospital Orthopaedics-Traumatology Department in the hospital database. Patients who have undergone surgery and fracture, have rheumatic disease, septic arthritis and diagnosed with degenerative arthritis excluded the study. Two groups were formed in the study as RCT (Group 1) and RCT+Adhesive capsulitis (Group 2). Those included in the RCT+adhesive capsulitis group applied to Bolu Abant İzzet Baysal University Training and Research Hospital Polyclinics between 2021-2022 and were randomly selected from the patient population who diagnosed with adhesive capsulitis according to physical examination, MRI, and arthroscopic findings. RCT patients were randomly selected from those who did not show signs of intraoperative adhesive capsulitis. Preoperative hemograms taken routinely from the patients were used in the study. The age, gender, blood glucose value, CRP, sedimentation, white blood cell, neutrophil, monocytes, lymphocyte, platelet values and neutrophil-to-lymphocyte, platelet-to-lymphocyte, lymphocyte-to-monocyte and neutrophil-to-monocyte ratios were evaluated in the study. Physical examination findings suggestive of adhesive capsulitis: Impaired range of motion with forward flexion, abduction, and external and internal rotation the MRI findings of the RCT+adhesive capsulitis group may include : thickening of the coracohumeral ligament, inflammation and edema, accumulation of fibrous tissue, thickening of the joint capsule, narrowing of the joint space, increased synovial fluid, involvement of the rotator cuff capsule. All patients were operated on in the lateral decubitus position with traction. A diagnosis of RCT was made by standard glenohumeral examination. The diagnosis of adhesive capsulitis was made arthroscopically with intraoperative visualization: synovial inflammation concentrated in the rotator interval and hypertrophy, reactive capsular fibrosis, increased capsule and coracohumeral ligament thickness.[13] Rotator interval excision was additionally applied based on RCT.

Statistical Analysis

As descriptive statistics, numbers and percentages were used for categorical data, and mean±standard deviation or median (min.-max.) was used for continuous data. The

distributional properties of the continuous data were evaluated using the Shapiro-Wilk Test. Control and adhesive capsulitis groups were compared t-test for normally distributed variables and via Mann Whitney U test for non-normally distributed variables. Bivariate comparisons of categorical data were conducted using Chi-square tests. Initially, a single explanatory variable logistic regression analysis model was fit for all variables. Than multiple explanatory variable logistic regression analysis model, was fitted by including all significant independent variables. A backward-elimination approach in the multiple explanatory variable logistic regression model was conducted to evaluate the model for potential confounding effects. In this model, the factors/covariates were removed one at a time, starting with the factor/covariate that had the largest P value, until all remaining factors had a two-sided P value <0.05. The goodness of fit was tested using the Hosmer–Lemeshow Test.

Results

CRP:C-reactive protein, WBC:White blood cell, HMG: Hemoglobin, HCT: Hematocrit, Group 1: RCT, Group 2: RCT+Adhesive capsulitis

Descriptive statistics of Groups 1 and 2 are given in Table 1. No statistically significant difference were found between groups 1 and 2 for hemoglobin (p=0.100) and hematocrit (p=0.080), but for fasting blood glucose was found higher statistically in Group 2 (p=0.009). There was no difference between the white blood cell (p=0.520), neutrophil (p=0.860) and platelet (p=0.334) values of the groups evaluated in the hemogram. In Group 2, lymphocytes (p=0.033) were found higher statistically and monocytes (p=0.000) were found lower statistically. The sedimentation used to assess systemic inflammation was similar between groups (p=0.090) and CRP (p=0.040) was found higher in Group 2 (Figure 1).

NLR (p=0.024), NMR (p=0.000), LMR (p=0.000) and PLR (p=0.011), which are thought to be helpful in diagnosis, were statistically different between groups 1 and 2. While LMR and NMR were higher in group 2, NLR and PLR were higher in group 1 (Figure 1).

In the logistic regression analysis, the cut-off value for LMR was determined as 3.02, this value was found to be 0.83 sensitive and 0.61 specific (Tables 2 and 3, Figure 2).

Discussion

To summarize the findings of the study, preoperative blood glucose, CRP, lymphocyte, NMR and LMR were found to be significantly higher in the preoperative RCT+Adhesive capsulitis group; monocytes, NLR, and PLR values were found to be high in the RCT group. In addition, LMR was found to have the highest sensitivity and specificity among the NMR, LMR, NLR and PLR to predict adhesive capsulitis in the preoperative period in RCT patients.

Diabetes mellitus is known as a condition predisposing to the formation of adhesive capsulitis[14], and chronic low-grade inflammation caused by diabetes is estimated to constitute the pathophysiology of adhesive capsulitis.[15] For this purpose, adhesive capsulitis has been included among the skeletal system complications caused by diabetes[16], HbA1c has been shown to be correlated with the increasing incidence of diabetes mellitus[8], and it has been reported that there is a relationship between adhesive capsulitis and the hyperglycemia component of the metabolic syndrome.[4] In our study, consistent with the literature, plasma glucose levels were found to be high in

Table 1. The descriptive statistics of Group 1 (RCT) and Group 2 (RCT+Adhesive capsulitis)

Variable	Group 1(n=63)	Group 2 (n=63)	*P* value
Age, year[b]	57 (50-65)	59 (44-67)	0.742
Plasma glucose, gr/dL[b]	115 (96-153)	102 (93-117)	0.009
CRP, mg/dL[b]	3.2 (0.5-6.6)	1.4 (0.2-3.5)	0.040
Sedimentation, mm/h[b]	14 (10-20)	18 (12-26)	0.090
Neutrophil, K/µL[b]	4.20 (3.6-4.8)	3.9 (3.3-5.1)	0.860
Lymphocyte, K/µL[b]	2.3 (1.8-3.0)	2.0 (1.6-2.6)	0.033
Monocyte, K/µL[b]	0.5 (0.4-0.6)	0.6 (0.5-0.9)	0.000
Platelet, K/µL[b]	255 (214-303)	264 (229-306)	0.334
WBC, K/µL[b]	7.3 (6.0-8.7)	7.0 (5.9-8.4)	0.520
HGB, g/dL[a]	14.3±1.73	13.8±1.46	0.100
HCT, %[a]	43.5±4.67	42.2±4.19	0.080

[a] Means SD; P values were determined via t-test.

[b] Values are median (Q1-Q3); P values were determined via Mann Whitney U test.

Acta Medica Alanya 2023;7(3): 226-231
Doi: 10.30565/medalanya.1376796

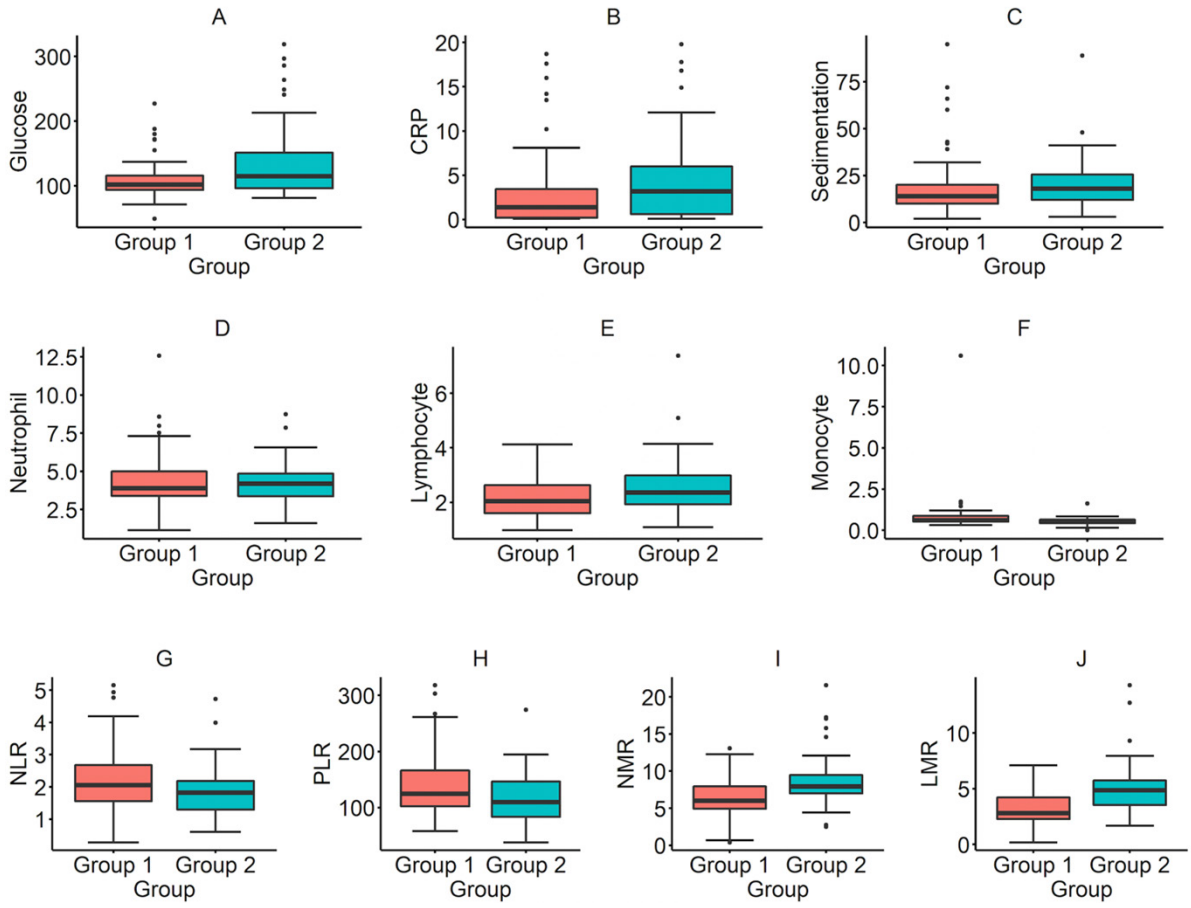

Figure 1. Comparison of glucose (A), CRP (B), sedimentation (C), neutrophil (D), lymphocyte (E), monocytes (F), NLR (G), PLR (H), NMR (I) and LMR (J) between groups. (Group 1:RCP; Group 2:RCP+Adhesive capsulitis; CRP: C-reactive protein; NLR:Neutrophil-Lymphocyte Ratio; PLR:Platelet-Lymphocyte Ratio; NMR: Neutrophil-Monocyte Ratio; LMR: Lymphocyte-Monocyte Ratio.)

Table 2. Results of the single explanatory variable logistic regression analysis for inflammation rates
[a] Values are median (Q1-Q3).

Variable	Group 1 (n=63)	Group 2 (n=63)	Odds ratio	(95 % CI)	P value
NLR[a]	2.05 (1.5-2.7)	1.82 (1.2-2.2)	1.64	1.09-2.57	*0.02*
NMR[a]	6.0 (4.9-7.9)	7.95 (6.9-9.5)	0.76	0.64-0.88	*0.00*
PLR[a]	124.8 (101.7-169.0)	109.9 (82.9-146.3)	1.01	1.00-1.02	*0.00*
LMR	2.0 (2.2-4.2)	4.8 (3.4-5.7)	0.49	0.36-0.65	*0.00*

Table 3. Results of the multiple explanatory variable analysis for inflammation rates

Variable	Odds ratio (95 % CI)	P value
NLR	1.25 (0.34-5.42)	0.745
NMR	0.87 (0.72-1.04)	0.14
PLR	1.00 (0.99-1.01)	0.31
LMR	0.68 (0.31-1.42)	*0.00*

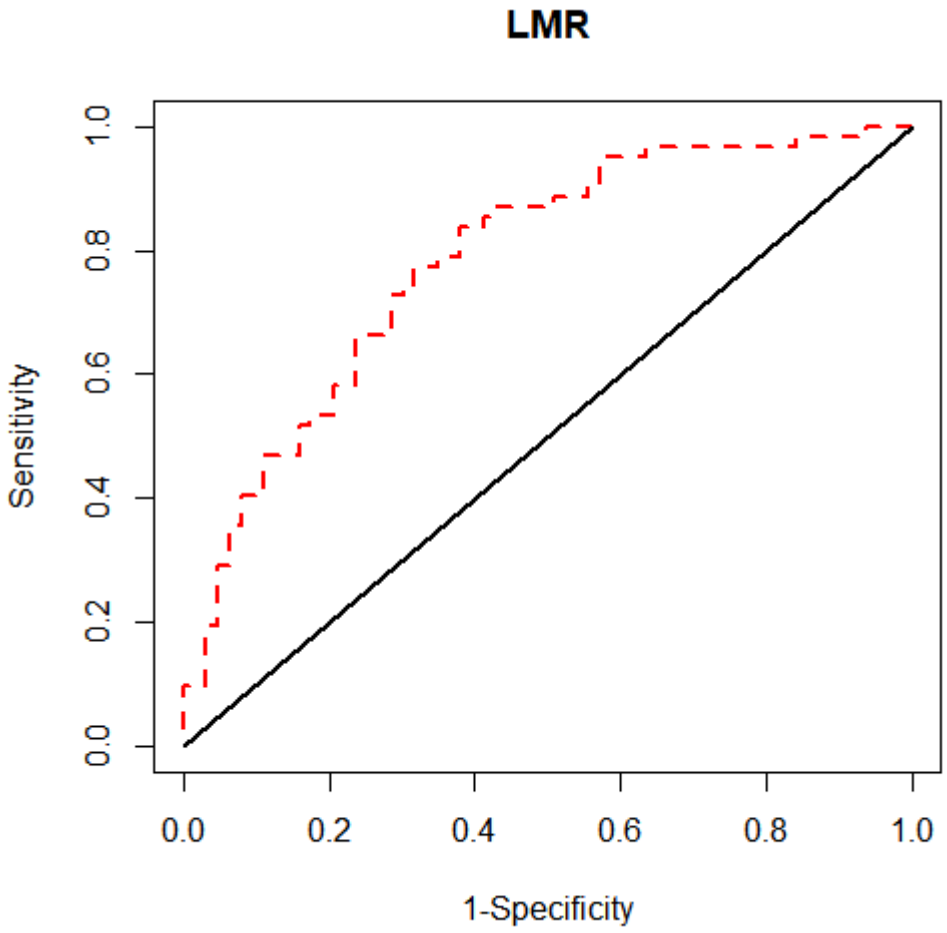

Figure 2. ROC curve for separating RCT and RCT+Adhesive capsulitis for LMR (Area Under the Curve 0.783, p value 0.00).

patients with adhesive capsulitis, and the formation of adhesive capsulitis based on hyperglycemia was confirmed.

Capsular fibrosis of adhesive capsulitis develops against the background of chronic low-grade inflammation.[17] C-reactive protein and erythrocyte sedimentation rate are frequently used as markers of systemic inflammation in clinical practice. Although there are studies showing that C-reactive protein is normal[18] and high[19] in adhesive capsulitis, a more sensitive form of CRP, called high sensitivity-CRP, shows high sensitivity.[9] There are studies reporting that ESR is normal[18] and high[19] in adhesive capsulitis. In our study, CRP was high and ESR was normal in the RCT+Adhesive capsulitis group. Here, sedimentation normality associated with CRP elevation may be used in differential diagnosis to predict preoperative adhesive capsulitis in patients with RCT.

Lymphocytes provide cell-mediated immunity as part of adaptive immunity and play a role in chronic inflammation.[20] Neutrophils[21] and monocytes[22] represent acute inflammation as part of innate immunity. Inflammatory rates, which are easily and inexpensively obtained under basic laboratory conditions by routine hemogram evaluation from automated systems such as NLR, PLR, NMR and LMR, are studied for biomarker purposes in diseases whose symptoms are not within sharp limits and many methods are used for diagnosis.[23] These markers have been studied in many diseases such as inflammatory bowel diseases, malignancies, cardiovascular diseases, and acute pancreatitis, and significant results have been obtained in this regard.[24] In relation to the pathophysiology of chronic low-grade inflammation of adhesive capsulitis, our results showed high lymphocyte value and low monocyte value. In connection with these values, LMR and NMR were high, and NLR and PLR were low in patients with RCT+Adhesive capsulitis. When we measured which rate could better predict adhesive capsulitis in the preoperative period in patients with RCT with the highest sensitivity and specificity, we revealed that LMR may be the best biomarker candidate. The definitive diagnosis of adhesive capsulitis is made by arthroscopic intervention, but our study revealed that the correct interpretation of inflammatory rates in the hemogram, as well as physical examination during the preoperative planning period, will contribute to supporting the diagnosis.

Acta Medica Alanya 2023;7(3): 226-231
Doi: 10.30565/medalanya.1376796

Limitations: The lack of clinical data in cases of adhesive capsulitis in our study constituted the limitation; of the study. The advantage of the present study was that inflammatory rates in adhesive capsulitis were studied for the first time with sensitivity and specificity values.

Conclusion: Easy and inexpensive diagnostic approaches to predict whether adhesive capsulitis accompanies a rotator cuff tear in the preoperative period can strengthen the perioperative strategy and contribute to the surgical organization. We believe that future multicenter studies with more patients and groups will contribute to the early diagnosis and treatment of adhesive capsulitis with RCT.

Conflict of Interest: No conflict of interest was declared by the authors.

Funding sources: The authors declared that this study has received no financial support.

Ethics Committee Approval: In this study, national and international ethical rules are observed.

Ethic Board: Bolu Abant İzzet Baysal University Clinical Research Ethics Committee 2021/78

ORCID and Author contribution: H. Ç. (0000-0002-3394-2438), İ. Ç. (0000-0003-3709-2511),T. A. (0000-0002-3089-9913),E. A. (0000-0001-5033-893X),S.A.K. (0000-0003-4791-8946). All the authors had contribution to all stages of the article, read the final version, and approved it.

Peer-review: Externally peer reviewed.

References

1. Neviaser AS, Neviaser RJ. Adhesive capsulitis of the shoulder. J Am Acad Orthop Surg. 2011;19:536-42. doi: 10.5435/00124635-201109000-00004.
2. Balci N, Balci MK, Tüzüner S. Shoulder adhesive capsulitis and shoulder range of motion in type II diabetes mellitus: association with diabetic complications. J Diabetes Complications. 1999;13:135-40. doi: 10.1016/s1056-8727(99)00037-9.
3. Bridgman JF. Periarthritis of the shoulder and diabetes mellitus. Ann Rheum Dis. 1972;31:69-71. doi: 10.1136/ard.31.1.69.
4. Austin DC, Gans I, Park MJ, Carey JL, Kelly JD 4th. The association of metabolic syndrome markers with adhesive capsulitis. J Shoulder Elbow Surg. 2014;23:1043-51. doi: 10.1016/j.jse.2013.11.004
5. Nathan C, Ding A. Nonresolving inflammation. Cell. 2010;140:871-82. doi: 10.1016/j.cell.2010.02.029.
6. Sofka CM, Ciavarra GA, Hannafin JA, Cordasco FA, Potter HG. Magnetic resonance imaging of adhesive capsulitis: correlation with clinical staging. HSS J. 2008;4:164-9. doi: 10.1007/s11420-008-9088-1.
7. Ramirez J. Adhesive Capsulitis: Diagnosis and Management. Am Fam Physician. 2019;99:297-300. PMID: 30811157
8. Chan JH, Ho BS, Alvi HM, Saltzman MD, Marra G. The relationship between the incidence of adhesive capsulitis and hemoglobin A_{1c}. J Shoulder Elbow Surg. 2017;26:1834-7. doi: 10.1016/j.jse.2017.03.015
9. Park HB, Gwark JY, Jung J, Jeong ST. Association Between High-Sensitivity C-Reactive Protein and Idiopathic Adhesive Capsulitis. J Bone Joint Surg Am. 2020;102:761-8. doi: 10.2106/JBJS.19.00759.
10. Fusar-Poli L, Natale A, Amerio A, et al. Neutrophil-to-Lymphocyte, Platelet-to-Lymphocyte and Monocyte-to-Lymphocyte Ratio in Bipolar Disorder. Brain Sci. 2021;11:58. doi: 10.3390/brainsci11010058.
11. Sun Y, Lin J, Luo Z, Chen J. Preoperative Lymphocyte to Monocyte Ratio Can Be a Prognostic Factor in Arthroscopic Repair of Small to Large Rotator Cuff Tears. Am J Sports Med. 2020;48:3042-50. doi: 10.1177/0363546520953427.
12. Sarıçam G. Neutrophil/Lymphocyte, Platelet/Lymphocyte and Neutrophil/Monocyte Rates in Carpal Tunnel Syndrome. Turkiye Klinikleri J Cardiovasc Sci. 2018;30:107-12. doi: 10.5336/cardiosci.2018-62886
13. Le HV, Lee SJ, Nazarian A, Rodriguez EK. Adhesive capsulitis of the shoulder: review of pathophysiology and current clinical treatments. Shoulder Elbow. 2017;9:75-84. doi: 10.1177/1758573216676786.
14. Dias R, Cutts S, Massoud S. Frozen shoulder. BMJ. 2005;331:1453-6. doi: 10.1136/bmj.331.7530.1453.
15. Milgrom C, Novack V, Weil Y, Jaber S, Radeva-Petrova DR, Finestone A. Risk factors for idiopathic frozen shoulder. Isr Med Assoc J. 2008;10:361-4. PMID: 18605360
16. Gordon JA, Farooqi AS, Rabut E, et al. Evaluating whole-genome expression differences in idiopathic and diabetic adhesive capsulitis. J Shoulder Elbow Surg. 2022;31:e1-13. doi: 10.1016/j.jse.2021.06.016.
17. Pietrzak M. Adhesive capsulitis: An age related symptom of metabolic syndrome and chronic low-grade inflammation? Med Hypotheses. 2016;88:12-7. doi: 10.1016/j.mehy.2016.01.002.
18. Hamdan TA, Al-Essa KA. Manipulation under anaesthesia for the treatment of frozen shoulder. Int Orthop. 2003;27:107-9. doi: 10.1007/s00264-002-0397-6.
19. Bulgen DY, Binder A, Hazleman BL, Park JR. Immunological studies in frozen shoulder. J Rheumatol. 1982;9:893-8. PMID: 7161781
20. Miller BJ, Gassama B, Sebastian D, Buckley P, Mellor A. Meta-analysis of lymphocytes in schizophrenia: clinical status and antipsychotic effects. Biol Psychiatry. 2013;73:993-9. doi: 10.1016/j.biopsych.2012.09.007.
21. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. Innate Immunity.Available from: https://www.ncbi.nlm.nih.gov/books/NBK26846/
22. Fogg DK, Sibon C, Miled C, et al. A clonogenic bone marrow progenitor specific for macrophages and dendritic cells. Science. 2006;311:83-7. doi: 10.1126/science.1117729.
23. Balta S, Demirkol S, Unlu M, Arslan Z, Celik T. Neutrophil to lymphocyte ratio may be predict of mortality in all conditions. Br J Cancer. 2013;109:3125-6. doi: 10.1038/bjc.2013.598.
24. Posul E, Yilmaz B, Aktas G, Kurt M. Does neutrophil-to-lymphocyte ratio predict active ulcerative colitis? Wien Klin Wochenschr. 2015;127:262-5. doi: 10.1007/s00508-014-0683-5.