ORIGINAL ARTICLE

Can the Neutrophil-Lymphocyte Ratio be Used as a Biomarker in Patients with Primary or Recurrent Pterygium?

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ABSTRACT

Purpose: The purpose of this study was to evaluate the inflammatory state in patients with primary or recurrent pterygium by utilizing the neutrophils-lymphocytes ratio (NLR).

Materials and Methods: We reviewed the medical records of the patients diagnosed with primary or recurrent pterygium retrospectively. The control group comprised of randomly selected patients who underwent strabismus or blepharoplasty surgery. Complete blood count values were obtained from routine preoperative laboratory examinations in the study and control groups. The NLR was calculated by dividing the neutrophils count by the lymphocytes count.

Results: The study enrolled 374 patients, including 178 patients with primary pterygium, 178 patients as controls, and 18 patients with recurrent pterygium. The average NLR was markedly higher in the recurrent pterygium group compared to the other groups (p=0.016). The primary pterygium and control groups were similar with respect to the mean NLR (p= 1.000). The area under the receiver operating characteristic (AUROC) curve value of the NLR, which distinguished patients with recurrent pterygium from those with primary pterygium, was found to be 0.699. The best cutoff value was 1.92, with a sensitivity of 77.8% and a specificity of 60.1%.

Conclusion: Patients with recurrent pterygium showed a higher NLR compared to those in the other groups. The NLR is not a reliable biomarker of primary pterygium. However, the NLR can be used as a reliable, simple, and inexpensive biomarker of recurrent pterygium.

Keywords: Inflammation, neutrophils-lymphocytes ratio, primary pterygium, pterygium, recurrent.

INTRODUCTION

Pterygium, a common ocular surface disorder which, is characterized by proliferation of altered limbal stem cells with inflammation and neovascularization of extracellular matrix (ECM).[1]Exposure to chronic UV light and oxidative stress play an important role in the pathogenesis of pterygium by disrupting limbal stem cell's function.[2-4] It was shown that pterygium cells expressed elevated levels of numerous inflammatory cytokines (IL-1, IL-6, IL-8), growth factors (FGF, TGF-β, VEGF) and MMPs (MMP-1, MMP-2 MMP-3, MMP-9) and these mediators contributed to the inflammation, fibrogenesis, vascularization and invasion of pterygium.[5] Additional hereditary, immunological and environmental factors (wind, dust or trauma) could also get involved in the development of pterygium.[5]

Different surgical techniques with various success rates were defined in the treatment of pterygium. Surgical techniques in pterygium are bare sclera technique, intraoperative MMC (Mitomycin C) application, conjunctival autograft technique and amniotic membrane grafting technique.[6-11]One of the most common complication of pterygium surgery is recurrence. Although predicting factors of recurrence were not fully understood, they probably depended on inflammation and other factors (genetics, surgical factors, young age, current active growth, and ocular motility restriction).[12,13]

Generally, inflammatory response associated with an increase in neutrophils to lymphocyte ratio.Therefore, several studies have showed that the increased neutrophils-lymphocytes ratio (NLR) could be used as a rapid and

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low-priced marker of systemic inflammation.[14] Previous studies have presented an association between NLR and some ophthalmological diseases such as age-related macular degeneration, idiopathic epiretinal membrane, keratoconus, dry eye, primary open angle glaucoma.[15-20]

In the current study, we aim to evaluate the influence of systemic inflamatuary process on primary and recurrent pterygium by utilising NLR.

MATERIALS AND METODS

A retrospective, clinical study was designed to evaluate NLR in patients with primary and recurrent pterygium. The local ethics committee approved this study which conformed to the Helsinki Declaration principles.

Patient Selection

Medical records of patients who underwent pterygium surgery at the Istanbul Education and Research Hospital between January 2015 and March 2020 were retrospectively analyzed. The control included consecutively selected patients who underwent strabismus or blepharoplasty surgery between January 2015 and January 2020.

Patients with diabetes mellitus, cardiovascular diseases, arterial hypertension, malignancies, hematological or autoimmune disorders, and chronic inflammatory disorders were excluded from the study. Patients having a history of ocular surgery other than the pterygium were also excluded.

Measurement Methods

Routine preoperative laboratory examination in both study and control groups were used to obtain complete blood count values. Neutrophil and leukocyte counts were measured using an automatic blood counter (Sysmex-XN 9000 Hematology Analyzer, Kobe, Japan). We calculated NLR by dividing the neutrophil count by the lymphocyte count.

Statistical Analyses

Statistical Package for the Social Sciences (SPSS) version 22.0 software program was used for statistical analysis. Descriptive statistics are presented as minimum, maximum and mean ± standard deviation.The kolmogorov-smirnov test was used to normal distribution compatibility of parameters. The parameters did not match to the normal distribution. Therefore, non-parametric tests were used for statistical analysis. The kruskal-wallis test was used for comparison of pterygium group, control group and recurrent pterygium group in terms of NLR and age. The chi-square test was used to compare gender. We performed receiver operating characteristic (ROC) analysis with Youden's index to evaluate the predictive performance of NLR. Given a 95% confidence interval, p-values lower than 0.05 indicated a statistically significant difference.

RESULTS

The present study enrolled 374 eyes of 374 patients, which consist of 178 eyes with primary pterygium, 178 eyes control group, and 18 eyes with recurrent pterygium. Demographic characteristics were similar in different groups, as presented in Table 1.

The neutrophil and lymphocyte count and NLR are shown in Table 2.The mean NLR was 1.87, 1.91 and 2.30 respectively primary pterygium group, control group and recurrent pterygium group. There was a statistically significant difference between the three groups (p = 0,016). Detailed statistical analysis between groups is shown in Table 3.

The ROC analyses were shown in Figure 1. According to the ROC curve, the AUROC value of the NLR to distinguish patients with primer pterygium group and control group was found to be 0.486, as shown in Figure 1A. The best cutoff value was 1.74, with a sensitivity of 45.5% and specificity of 45.5%. Furthermore, the AUROC value of the NLR to distinguish patients with primer pterygium group and recurrent pterygium group was found to be 0.699, as shown in Figure 1B. The best cutoff value was 1.92, with a sensitivity of 77.8% and specificity of 60.1%.

DISCUSSION

High neutrophil and low lymphocyte counts are biomarkers of systemic inflammation.[21]Also NLR is a simple, cheap,

Table 1: *Demographic Characteristics.*

Parameters	Primer pterygium group	Control group	Recurrent pterygium group	p
Patients/eye	178/178	178/178	18/18	
Female/male	93/85	95/83	11/7	0.389*
Age	55.1 ± 12.7	56.4 ± 14.1	58.1 ± 12.3	0.082**

*Chi-square test, **Kruskal-Wallis test

Table 2. *Neutrophil and lymphocyte count and NLR in different groups.*

Parameters	Primer pterygium group n:178	Control group n:178	Recurrent pterygium group n:18
Neutrophil 10^9/L Mean ± SD (Min-Max)	4.29 ±1.33 (1.84-10.59)	4.12 ±1.31 (1.46-7.84)	4.57±1.55 (2.95-7.72)
Lymphocyte 10^9/L Mean ± SD (Min-Max)	2.41 ±0.68 (0.86-5.30)	2.32±0.68 (0.89-4.90)	1.99 ±0.45 (1.52-2.93)
NLR Mean ± SD (Min-Max)	1.87±0.65 (0.50-4.45)	1.91± 0.79 (0.52-5.09)	2.30±0.68 (1.92-4.04)

NLR: Neutrophil-lymphocyte ratio, **SD**: Standard deviation, Min: Minimum value, Max: Maximum value, n: number of eyes

Table 3: *Statistical analysis between groups.*

Groups	p
Primary pterygium group - Control group - recurrent pterygium group	0.016
Primary pterygium group - Control group	1.000
Primary pterygium group - recurrent pterygium group	0.022
Control group - recurrent pterygium group	0.012

p = Kruskal-Wallis test
There was a statistically significant difference between the three groups (p = 0.016).
There was no statistically significant difference between the primary pterygium group and the control group (p = 1.000).
There was a statistically significant difference between the primary pterygium group and the recurrent pterygium group (p = 0.022).
There was a statistically significant difference between the control group and the recurrent pterygium group (p = 0.012).

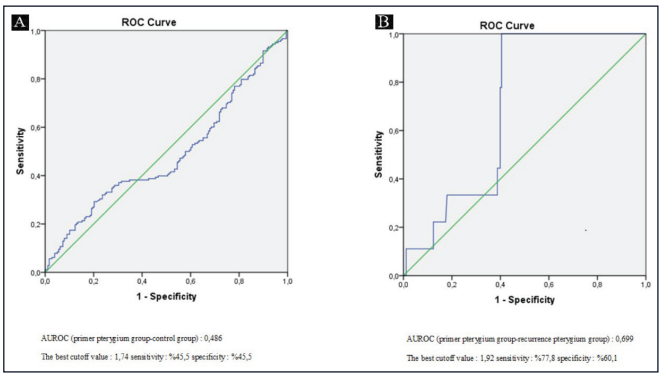

Figure 1: **A)** *AUROC value of the NLR to distinguish patients with the primer pterygium group and the control group,* **B)** *AUROC value of the NLR to distinguish patients with the primer pterygium group and the recurrent pterygium group.*

and reliable biomarkers of inflammation. NLR found to be high in some inflammatory conditions and is used as a biomarker such as cardiovascular, inflammatory, endocrinological diseases and malignancies.[21-26]Also NLR was found high in the patients with age-related macular degeneration, idiopathic epiretinal membrane, keratoconus, dry eye, primary open angle glaucoma. Therefore it supports that NLR can be used as a biomarker in the local inflammatory ophthalmological diseases. [15-20]

There are 2 studies in the literature evaluating the NLR in patients with pterygium.

In one of these two studies, NLR was higher in patients with pterygium than control group.[27]

In the other study, NLR was found similar to the control group in pterygium patients.[28]In these two studies, patients with recurrent pterygium were excluded from the study.

In the present study, no statistically significant difference was found between the pterygium group and the control group (p = 1,000). NLR value for distinguishing the patients with primer pterygium group from the control group was 0.486 with a cutoff value of 1,74 (sensitivity=45.5%, specifi city=45.5%). Therefore, NLR cannot distinguish the inflamatuar process reliably in primary pterygium and control group. On the other hand, NLR was significantly higher in the recurrent pterygium group than in the other two groups (p = 0,016). NLR value for distinguishing the patients with recurrent pterygium group from the primer pterygium group was 0.699 with a cutoff value of 1.92 (sensitivity=77.8%, specificity= 60.1%).

Pterygium is a local inflammatory and degenerative disease rather than systemic disease.Therefore, we think that there is no difference between the pterygium group and the control group in terms of NLR. However, immonuhistochemical studies has been reported that Cyclooxygenase-2 enzyme was observed to be higher in the recurrent pterygium group than primary pterygium group.[29]Cyclooxygenase-2 enzyme is known to play an important role in inflammation.[30,31] Therefore, we think that the NLR is higher in the recurrent pterygium group than the other 2 groups.

The present study show that NLR is not reliable biomarker in primary pterygium. On the other hand, high NLR in the

recurrent pterygium group suggests that NLR can be used as a simple and inexpensive biomarker.

CONCLUSION

We think that NLR is not reliable biomarker in primary pterygium. But NLR can be used as a reliable, simple and inexpensive biomarker in recurrent pterygium.That difference arise from that recurrent pterygium has higher inflamation than primary pterygium.

REFERENCES

1. Chui J, Di Girolamo N, Wakefield D, et al. The pathogenesis of pterygium: Current concepts and their therapeutic implications. Ocul Surf 2008 6: 24-43.
2. Bradley JC, Yang W, Bradley RH, et al. The science of pterygia. Br J Ophthalmol 2010; 94:815.
3. Taylor HR, West SK, Rosenthal FS, et al. Corneal changes associated with chronic UV irrradiation. Arch Ophthalmol. 1989;107:1481-4.
4. Tsai YY, Cheng YW, Lee H, et al. Oxidative DNA damage in pterygium. Mol Vis. 2005 11:71-5.
5. Wei-Ping Zhou, Yuan-Fang Zhu, Bei Zhang, et al. The Role of Ultraviolet Radiation in the Pathogenesis of Pterygia (Review) Mol Med Rep. 2016;14:3-15.
6. Essex RW, Snibson GR, Daniell M, et al Amniotic membrane grafting in the surgical management of primary pterygium. *Clin Exp Ophthalmol* 2004; 32:501-4.
7. Young AL. The use of conjunctival rotational autograft in the management of Pterygium. *Asia Pac J Ophthalmol (Phila)* 2013; 2:209-10.
8. Young AL, Ho M, Jhanji V, Cheng LL. Ten-year results of a randomized controlled trial comparing 0.02% mitomycin C and limbal conjunctival autograft in pterygium surgery. *Ophthalmology* 2013; 120:2390-5.
9. Young AL, Cao D, Chu WK, et al. The evolving story of pterygium. *Cornea* 2018; 37: (suppl 1): S55-S57.
10. Kaufman SC, Jacobs DS, Lee WB, et al. Options and adjuvants in surgery for pterygium: a report by the American Academy of Ophthalmology. *Ophthalmology* 2013; 120:201-8.
11. Aydemir O, Çatak O, Primer Pterjiyum Cerrahisinde Çıplak Sklera ve Konjonktival Otogreftleme Yönteminin Karşılaştırılması Fırat Tıp Dergisi 2011; 16: 129-31
12. Hovanesian JA, Starr CE, Vroman DT, The ASCRS Cornea Clinical Committee Surgical techniques and adjuvants for the management of primary and recurrent pterygia. J Cataract Refract Surg. 2017;43:405-19.
13. Kim KW, Kim JC. Current approaches and future directions in the management of pterygium. Int J Ophthalmol. 2018;11:709-11.
14. Zahorec R Ratio of neutrophil to lymphocyte counts—rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy 2001;102:5-14.
15. Ilhan N, Daglioglu MC, Ilhan O, et al. Assessment of neutrophil/lymphocyte ratio in patients with age-related macular degeneration. Ocul Immunol Inflamm. 2015;23:287-90.
16. Karaca EE, Özmen MC, Ekici F, et al. Neutrophil-to-lymphocyte ratio may predict progression in patients with keratoconus. Cornea. 2014;33:1168-73.
17. Elbey B, Yazgan UC, Yildirim A, et al. Mean platelet volume and neutrophil to lymphocyte ratio in patients with vernal keratoconjunctivitis. J Clin Exp Invest.s 2015;6:40-4.
18. Sekeryapan B, Uzun F, Buyuktarakci S, et al. Neutrophil-to lymphocyte ratio increases in patients with dry eye. Cornea. 2016;35:983-6.
19. Ozgonul C, Sertoglu E, Mumcuoglu T, et al. Neutrophil-to-lymphocyte ratio and platele-to-lymphocyte ratio as novel biomarkers of primary open-angle glaucoma. J Glaucoma. 2016;25:e815-e20.
20. Dikkaya F, Karaman Erdur S, Ozsutcu M, et al. The significance of neutrophil-to-lymphocyte ratio in idiopathic epiretinal membrane.Int Ophthalmol. 2018;38:1393-1397.
21. Papa A, Emdin M, Passino C, et al. Predictive value of elevated neutrophil-lymphocyte ratio on cardiac mortality in patients with stable coronary artery disease. Clin Chim Acta. 2008;395:27-31.
22. Buyukkaya E, Karakas MF, Karakas E, et al. Correlation of neutrophil to lymphocyte ratio with the presence and severity of metabolic syndrome. Clin Appl Thromb Hemost. 2014;20:159-63.
23. Azab B, Daoud J, Naeem FB, et al. Neutrophil-tolymphocyte ratio as a predictor of worsening renal function in diabetic patients (3-year follow-up study). Ren Fail. 2012;34:571-6.
24. Seretis C, Gourgiotis S, Gemenetzis G, et al. The significance of neutrophil/lymphocyte ratio as a possible marker of underlying papillary microcarcinomas in thyroidal goiters: a pilot study. Am J Surg. 2013;205:691-6.
25. Torun S, Tunc BD, Suvak B, et al. Assessment of neutrophil-lymphocyte ratio in ulcerative colitis: a promising marker in predicting disease severity. Clin Res Hepatol Gastroenterol. 2012;36:491-7.
26. Suppiah A, Malde D, Arab T, et al. The prognostic value of the neutrophil-lymphocyte ratio (NLR) in acute pancreatitis: identification of an optimal NLR. J Gastrointest Surg. 2013;17:675-81.
27. Gokmen O, Gokmen A, Evaluation of Neutrophil-Lymphocyte Ratios, Mean Platelet Volumes, and Platelet-Lymphocyte Ratios in Pterygium Beyoglu Eye J 2019; 4: 163-7.
28. Atılgan CU, Kösekahya P, Tekin K, et al. The Evaluation of Neutrophil-to-Lymphocyte Ratio as a Novel Marker in Patients with Pterygium Turkiye Klinikleri J Ophthalmol. 2020;29:52-6.
29. Baser G, Sivrikoz, ON, Karahan E, et al. The Influence of Chemokine CXCR4 and Cyclooxygenase-2 in the Recurrence of Pterygium Ocul Immunol Inflamm 2017;25:328-32.
30. Ricciotti E, FitzGerald, G.A. Prostaglandins and Inflammation Arterioscler Thromb Vasc Biol. 2011; 31: 986-1000.
31. Dubois RN, Abramson SB, Crofford L, et al. Cyclooxygenase in biology and disease. FASEB J. 1998;12:1063-73.