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ARAŞTIRMA / RESEARCH

Neutrophil/lymphocyte ratio as a predictor of severe postoperative edema and ecchymosis in open rhinoplasty surgery

Açık rinoplasti cerrahisinde postoperatif şiddetli ödem ve ekimozun bir göstergesi olarak nötrofil/lenfosit oranı

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Abstract

Purpose: This study investigated the relationship between preoperative neutrophil-to-lymphocyte ratio (NLR) and severe postoperative edema and ecchymosis after open rhinoplasty.

Materials and Methods: The study was carried out retrospectively in 165 ASA I-II patients aged 18-45 years who underwent open rhinoplasty in the Department of Plastic and Reconstructive Surgery. The patients were grouped based on their scores on the edema and ecchymosis scales. The degree of edema and ecchymosis was considered "minimal" (Group M) in those scoring 0-2 points and "severe" (Group S) in those scoring 3-4 points. Periorbital edema and ecchymosis of the patients in both groups were scored based on the digital photographs taken on the 1st postoperative day.

Results: There was no significant difference in the demographic and clinical characteristics of the patients grouped according to the degree of edema and ecchymosis. The optimal cut-off value of NLR was 2.1 (AUC = 0.747, Sensitivity = 0.666, Specificity = 0.707) for edema and 1.5 (AUC = 0.747, Sensitivity = 0.869, Specificity = 0.470) for ecchymosis. Multivariable analyzes for the development of edema and ecchymosis identified NLR (4.67 [2.38-9.40] and 6.54 [3.02-15.08; respectively) as a statistically significant independent prognostic factor.

Conclusion: This study identified preoperative NLR as a predictor value of severe postoperative edema and ecchymosis after open rhinoplasty.

Keywords:. Neutrophil/lymphocyte ratio, open rhinoplasty, edema, ecchymosis, predictive value.

Öz

Amaç: Çalışmamızda açık rinoplastilerde preoperatif nötrofil/lenfosit oranı (NLR) ile postoperatif şiddetli ödem ve ekimoz arasındaki ilişki araştırılmıştır.

Gereç ve Yöntem: Çalışma Plastik ve Rekonstrüktif Cerrahisi tarafından açık rinoplasti uygulanan 18-45 yaş, ASA I-II 165 hastada retrospektif olarak gerçekleştirildi. Hastalar ödem ve ekimoz skalalarına göre, ödem ve ekimoz skoru 0-2 olanlar "minimal" (Group M), 3-4 olanlar "severe" (Group S) olarak gruplara ayrıldı. Grupların postoperatif 1. günde digital ortamda gerçekleştirilen fotoğraflarından periorbital ödem ve ekimoz skorları incelendi.

Bulgular: Hastaların ödem ve ekimoz varlığına göre grupların karşılaştırılmasında demografik ve klinik veriler arasında anlamlı bir fark yoktu. NLR nin optimal cut-off değeri ödem için 2.1 (AUC = 0.747, Sensitivite = 0.666, Spesifisite = 0.707), ekimoz için 1.5 (AUC = 0.747, Sensitivite = 0.869, Spesifisite = 0.470) olarak bulundu. Ödem ve ekimoz gelişimi için yapılan multivariable analizlerde NLR (sırasıyla, 4.67 [2.38-9.40] and 6.54 [3.02-15.08]) istatistiksel olarak anlamlı bağımsız prognostik faktör olarak saptandı.

Sonuç: Bu çalışmada preoperatif NLR'nin açık rinoplasti operasyonlarından sonra görülen şiddetli ödem ve ekimoz için öngörücü bir değer olduğu sonucuna vardık.

Anahtar kelimeler: Nötrofil/lenfosit oranı, açık rinoplasti, ekimoz, tahmin edici değer.

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INTRODUCTION

Open rhinoplasty, which is one of the surgical interventions in the facial area, often causes postoperative periorbital edema and ecchymosis due to trauma in the soft and bone tissue. Visual field limitation and cosmetic problems associated with these complications are undesirable for the surgeon and the patient[1,2].

During rhinoplasty, edema occurs as a result of trauma to the bone and soft tissue, the consequent inflammation of the lymphatic and venous systems in the nose, and obstruction of the drainage of the interstitial fluid[3]. Ecchymosis, on the other hand, occurs as a result of the post-traumatic extravasation of damaged vessels and the consequent movement of blood from these broken vessels in deep tissues into the eyelids with loose and thin skin. Ecchymosis can often move in the direction of gravity. Ecchymosis seen on the eyelids after open rhinoplasty usually increases in the first two postoperative days[4].

Although the importance of systemic leukocytic changes as an indicator of inflammatory response is still unclear, neutrophil-to-lymphocyte ratio (NLR) has been defined as a prognostic factor, especially in cancer patients[5-7]. Excessive increases in neutrophils and decreases in lymphocytes have been associated with increased susceptibility to postoperative infection[8]. Indeed, lymphopenia, an indicator of immunosuppression, is a risk factor for increased susceptibility to wound infection, especially in surgical patients[8]. As an indicator of the suppression of cellular immunity by lymphocytes and the activation of the inflammatory response characterized by neutrophilia, elevated NLR is considered a valuable marker in evaluating the postoperative inflammatory response[9].

Besides, in contrast to the complex parameters for inflammatory and immune responses such as interleukin measurements, NLR obtained from peripheral blood is a simple and inexpensive test in clinical practice[9]. Previous studies have shown the association of NLR in peripheral blood with the morbidity and mortality of various carcinomas, cardiovasculat system, renal and respiratory diseases[5,6,10]. Studies have reported very different threshold values for NLR.

Many studies in the literature have focused on the prevention of postoperative edema and ecchymosis. However, there is no study on the prediction of severe postoperative edema and ecchymosis. This study aims to determine the predictive value of the preoperative inflammatory marker NLR for severe postoperative edema and ecchymosis in patients after open rhinoplasty.

The hypothesis of this study is to reveal the NLR is a preoperative inflammatory marker for severe postoperative edema and ecchymosis in patients after open rhinoplasty.

MATERIAL AND METHODS

Study design

This study was carried out retrospectively in 165 ASA I-II patients aged 18-45 years who underwent open rhinoplasty with osteotomy at Karadeniz Technical University Faculty of Medicine, Department of Plastic and Reconstructive Surgery (Karadeniz Teknik University, Local Ethics Committee Approval No. 2022/62) between January 1, 2017, and December 31, 2021. Due to the inaccessibility of laboratory data and patient records, 145 patients were excluded from the study.

Patient files were reviewed by the researchers after obtaining permission from the local ethics committee and archive department. Demographic data (age, gender, American Society of Anesthesiologists (ASA) score, body mass index (BMI)), laboratory variables, and operative data (operation duration, bleeding amounts) were analyzed. Laboratory variables were obtained from the patient's blood counts (absolute and relative values of leukocytes, neutrophils, lymphocytes, monocytes, basophils, and eosinophils) requested by the relevant surgical branch before the operation. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

Scoring system

The patients were grouped according to their scores on the edema and ecchymosis scales[11]. Periorbital edema and ecchymosis scores obtained digitally on the first postoperative day by the Department of Plastic and Reconstructive Surgery were analyzed from the records. Eyelid edema [Eyelid edema Scale: 0 (none), +1 (minimal), +2 (closed iris), +3 (extending to the pupil), +4 (massive edema)] and periorbital ecchymosis [Periorbital echimosis Scale: 0 (none), +1 (medial canthus), +2 (advanced to pupil level), +3 (exceeding pupil level), +4 (extended to

lateralantus)], were evaluated separately in each patient via digital photographs[11].

The degree of edema and ecchymosis was considered "minimal/moderate" (Group M) in those scoring 0-2 points and "severe" (Group S) in those scoring 3-4 points. The study included 165 patients aged 18-40 years, with ASA risk classification I and II, who underwent rhinoplasty based on the file records. Patients with cardiovascular, liver, kidney and hematological diseases, psychiatric disorders, chronic drug use, and drug allergy were excluded. Other exclusion criteria were the lack of laboratory tests and records at the time of admission to the hospital.

Anesthesia management

In our clinic, the method of anesthesia for all patients undergoing open rhinoplasty is general anesthesia, same surgical position (10 degree head elevation) and performed by the same surgical team. All patients included in the study received general anesthesia and the drugs used for induction and maintenance were standard. Anesthesia was induced with IV 3 mg/kg propofol, 1 μg/kg fentanyl, and 0.6 mg/kg rocuronium for muscle relaxation. Maintenance of anesthesia was provided with a minimum alveolar concentration of 1–1.5 with sevoflurane, 1:1 O_2/N_2O and bispectral index (BIS) values between 40 and 60.

Patients who received only paracetamol in the standard analgesia protocol during the first 24 postoperative hours were included in the study, whereas patients who received steroid and non-steroidal analgesics in the pre-postoperative period were excluded. In the postoperative period, ice packs and an approximately 45-degree head elevation were arranged for all patients.

Statistical analysis

Data were presented as mean ± standard deviation or median (1st–3rd quartiles) for continuous variables, and as frequencies (percentages) for categorical variables. NLR was assessed with receiver operating characteristics (ROC) curves and the area under curves (AUC). Logistic regression analysis was used to evaluate the prognostic effects of parameters. In addition to the common confounders such as age and sex, variables with a p-value <0.10 on univariable analysis were entered into the multivariable model. All continuous variables were assessed for definitive evidence of non-linear relationships using restricted cubic splines. Linear variables were used in the logistic regression models only as continuous parameter, and variables showing non-linear relationship were used in two different versions (continuous and binary which was dictothomized by using a cut-off value). The Youden's index (sensitivity + specificity -1) was used to determine the optimal cut-off value for continuous variables when required. P-values were two-sided and statistical significance was defined as a p-value <0.05 unless otherwise stated. Statistical analysis was performed using R software (R Foundation for Statistical Computing, Vienna, Austria)."

RESULTS

The study included 165 patients who underwent open rhinoplasty surgery and met the inclusion criteria. The mean age of all patients was 25 (21-30), and 118 (71.5%) patients were female. Demographic and clinical characteristics of patients grouped according to their degree of edema and ecchymosis are summarized in Table-1 (Table 1).

The median NLR of all patients was 1.9 (1.4-2.4). The distribution of patients' NLR values according to the degree of edema and ecchymosis is shown in Figure-1. The NLR value was evaluated separately as both continuous and binary variables to model the prognostic value of NLR in the development of edema and ecchymosis. The optimal cut-off value of NLR was determined as 2.1 (AUC = 0.747, Sensitivity = 0.666, Specificity = 0.707) for edema and 1.5 (AUC = 0.747, Sensitivity = 0.869, Specificity = 0.470) for ecchymosis. ROC curves for both outcomes are shown in Figure-2.

The univariate logistic regression analysis for edema development determined the NLR value to be a statistically significant factor in both continuous (2.78 [1.70-4.83], p<0.001) and binary (4.83 [2.50-9.59], p0.001) models. The multivariable analysis also identified NLR (Continuous NLR: 2.77 [1.68-4.87, p<0.001], binary NLR: 4.67 [2.38-9.40, p0.001]) as the only statistically significant independent prognostic factor. Logistic regression results for edema are given in Table-2.

The univariate logistic regression analysis determined the amount of intraoperative bleeding (1.01 [1.00-1.01], p=0.035) and NLR value (Continuous NLR: 1.77 [1.13-2.93, p=0.019], binary NLR: 5.86 [2.80-12.86, p<0.001]) as statistically significant factors for the development of ecchymosis.

Table 1. Demographic and clinical characteristics of the patients for edema and ecchymosis.

		Edema		Ecchymosis	
		No	Yes	No	Yes
		n = 99	n = 66	n = 66	n = 99
Age (years)		25 (21-30)	25 (20-30)	24 (20-29)	25 (21-31)
Sex	Male	31 (31.3)	16 (24.2)	18 (27.3)	29 (29.3)
	Female	68 (68.7)	50 (75.8)	48 (72.7)	70 (70.7)
ASA score	ASA-I	66 (66.7)	46 (69.7)	47 (71.2)	65 (65.7)
	ASA-II	33 (33.3)	20 (30.3)	19 (28.8)	34 (34.3)
Body mass index (kg/m2)		22.5 (20.8-25.5)	22.4 (21-25.6)	22.4 (20.6-25.7)	22.5 (20.9-25.4)
Operation duration (min)		75 (60-100)	65 (50.5-90)	69 (56-94.8)	75 (60-100)
Intraoperative bleeding (mL)		65 (50-150)	77.5 (50-145)	60 (50-120)	80 (50-150)
NLR		1.7 (1.3-2.1)	2.2 (1.9-2.6)	1.6 (1.3-2.1)	2.1 (1.7-2.5)

Group M; moderate, Group S; severe.

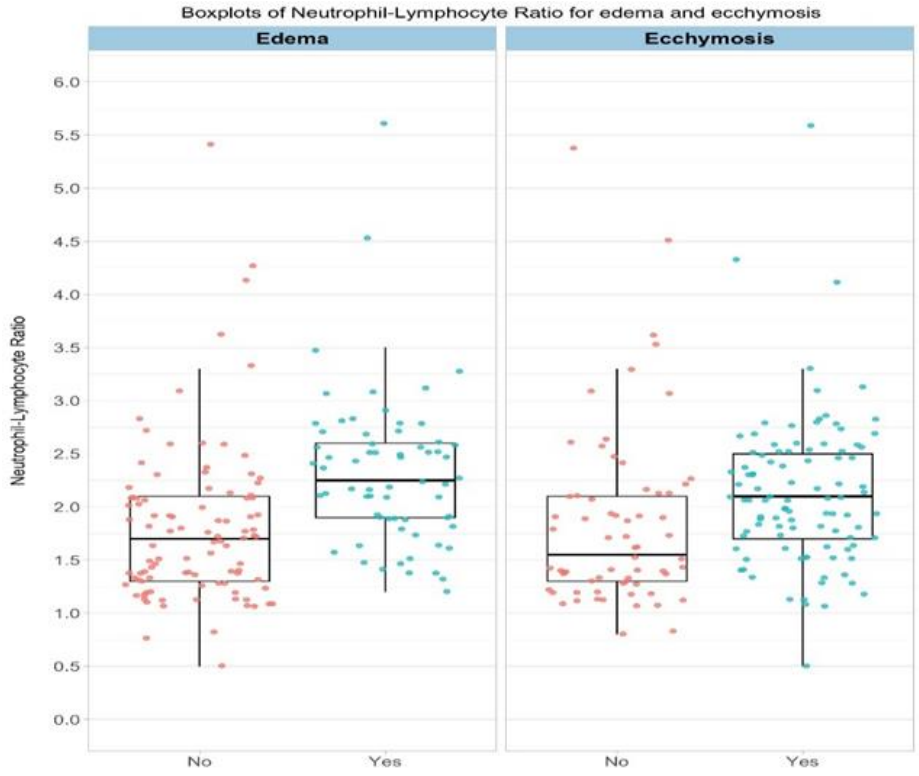

Figure 1. Box plots of the neutrophil-lymphocyte ratio for edema and ecchymosis.

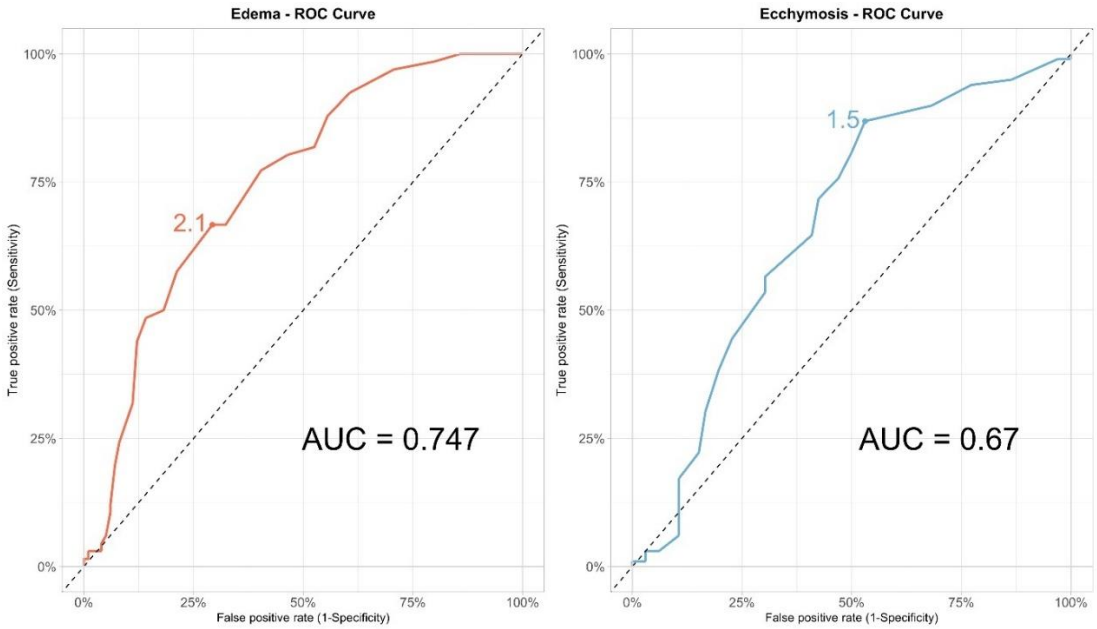

Figure 2. ROC Curves for edema and ecchymosis.

Table 2. Uni- and multivariable regression analysis for edema.

		OR (univariable)	OR (multivariable)†	OR (multivariable)‡
Age		1.00 (0.96-1.05, p=0.846)	1.00 (0.96-1.05, p=0.855)	1.00 (0.95-1.05, p=0.992)
Sex	Male	-	-	-
	Female	1.42 (0.71-2.93, p=0.325)	1.11 (0.52-2.39, p=0.791)	1.06 (0.49-2.33, p=0.883)
ASA score	ASA-I	-	-	-
	ASA-II	0.87 (0.44-1.69, p=0.683)	-	-
Body mass index		1.00 (0.91-1.10, p=0.945)	-	-
Operation duration		0.99 (0.98-1.00, p=0.079)	0.99 (0.98-1.00, p=0.111)	0.99 (0.98-1.00, p=0.159)
Intraoperative bleeding		1.00 (1.00-1.01, p=0.954)	-	-
NLR (Continuous)		2.78 (1.70-4.83, p<0.001)	2.77 (1.68-4.87, p<0.001)	-
NLR (Binary)	low-NLR	-	-	-
	high-NLR	4.83 (2.50-9.59, p<0.001)	-	4.67 (2.38-9.40, p<0.001)

Data were presented as Odds ratio (95% Confidence intervals, p value). OR: Odds ratio, ASA: American Society of Anesthesiology Score, NLR: Neutrophil-Lymphocyte Ratio
†NLR was entered to the model as a continuous variable
‡NLR was entered to the model as a binary variable

Table 3. Uni- and multivariable regression analysis for ecchymosis

		OR (univariable)	OR (multivariable)†	OR (multivariable)‡
Age		1.04 (0.99-1.09, p=0.131)	1.04 (0.99-1.09, p=0.106)	1.04 (0.99-1.10, p=0.100)
Sex	Male	-	-	-
	Female	0.91 (0.45-1.80, p=0.778)	1.13 (0.51-2.47, p=0.764)	1.17 (0.50-2.71, p=0.712)
ASA score	ASA-I	-	-	-
	ASA-II	1.29 (0.66-2.57, p=0.455)	-	-
Body mass index		0.99 (0.90-1.09, p=0.883)	-	-
Operation duration		1.00 (0.99-1.01, p=0.794)	-	-
Intraoperative bleeding		1.01 (1.00-1.01, p=0.035)	1.01 (1.00-1.01, p=0.026)	1.01 (1.00-1.01, p=0.014)
NLR (Continuous)		1.77 (1.13-2.93, p=0.019)	1.77 (1.12-2.98, p=0.022)	-
NLR (Binary)	low-NLR	-	-	-
	high-NLR	5.86 (2.80-12.86, p<0.001)	-	6.54 (3.02-15.08, p<0.001)

Data were presented as Odds ratio (95% Confidence intervals, p value). OR: Odds ratio, ASA: American Society of Anesthesiology Score, NLR: Neutrophil-Lymphocyte Ratio
†NLR was entered to the model as a continuous variable
‡NLR was entered to the model as a binary variable

In multivariable analysis, both the continuous and binary models determined intraoperative bleeding amount and NLR as statistically significant independent prognostic factors. In the continuous model, intraoperative bleeding amount was 1.01 (1.00-1.01, p=0.026) and NLR was 1.77 (1.12-2.98, p=0.022), while in the binary model, the intraoperative bleeding was 1.01 (1.00-1.01, p=0.014) and NLR was 6.54 (3.02-15.08, p<0.001). Logistic regression results for ecchymosis are given in Table-3.

DISCUSSION

This study identified NLR as a predictor for severe edema and ecchymosis seen after open rhinoplasty operations. We think that clinicians should be cautious about preoperative NLR > 2.1 for severe postoperative edema and NLR > 1.5 for severe postoperative ecchymosis in patients who will undergo open rhinoplasty. However, our findings need to be validated by prospective randomized controlled trials.

In open rhinoplasty, which is one of the frequently performed facial surgeries, in addition to cosmetic concerns, postoperative edema and ecchymosis negatively affect surgeon and patient satisfaction. Periorbital edema and ecchymosis, especially in the first 24 postoperative hours, are two common consequences of trauma-related inflammation and bleeding during the surgical procedure[11]. In addition, they may cause undesirable conditions such as temporary limitation of the visual field, increase in permanent pigmentation on the skin, patient dissatisfaction, and deterioration of scar tissue formation. All these cause prolongation of the postoperative recovery period, delay in returning to social life, and dissatisfaction of the patients[2,12,13].

As seen in the literature, pharmacological agents have been used frequently to reduce edema and ecchymosis after rhinoplasty. Despite the preventive effects of pharmacological agents on edema and ecchymosis, their possible side effects should not be overlooked. Recently, anesthesia methods and surgical positioning have also been shown effective in reducing postoperative complications[14]. However, studies in the literature are on the drugs and methodologies to be used during open rhinoplasty to reduce postoperative edema-ecchymosis. In this study, we investigated whether preoperative NLR, an inflammatory biomarker, could be a predictor of

postoperative edema and ecchymosis after open rhinoplasty.

Trauma-related nasal mucosa inflammation at the osteotomy site is a potentially important cause of intraoperative bleeding, periorbital edema, and ecchymosis in patients undergoing rhinoplasty[15]. Although a careful surgical approach during rhinoplasty can help reduce the destructive effect on blood vessels, it may not prevent it completely. Post-operative edema after rhinoplasty occurs as a result of inflammation of the venous and lymphatic systems in the nose due to trauma of the bone and soft tissue[16]. Ecchymosis occurs as a result of the extravasation of traumatized vessels and the movement of blood from these vessels in deep tissues into thin skin and eyelids[17].

NLR is a biomarker that provides information about inflammatory states in diseases with an inflammatory component, predicts clinical outcomes, and is easy to calculate and access[18]. This simple index shows the balance between lymphocytes, the "regulatory and protective" component, and neutrophils, the active inflammatory component[19]. In addition to being an indicator of chronic inflammation, NLR is also associated with the clinical outcomes of diseases with vascular involvement. NLR levels are positively correlated with vascular intima-media thickness. A relationship has also been established between high NLR levels and endothelial dysfunction[20,21].

While leukocytes play a key role in the severe inflammation seen in ischemic tissue damage, it is known that the increased damage in the endothelium results from the interaction between neutrophils and endothelial tissue[22]. Increased neutrophil infiltration in this region is the reason for the arterial wall inflammation-induced damage in vascular structure and various processes related to platelet adhesion[23]. Preoperative NLR is known to predict patients at increased risk of death due to major vascular surgery. Thus, higher NLR is associated with higher inflammation, arterial stiffness, and worse extremity survival after embolectomy[23,24]. Moreover, preoperative NLR is accepted as an independent predictor of saphenous vein graft patency after coronary artery bypass[25].

It has also been reported that NLR associated with endothelial dysfunction may reflect disease activity in Behçet's Disease, which is considered a chronic, multisystemic, and systemic immunoinflammatory vasculitis[18,26-28]. In addition, NLR is considered a potential predictor of the severity and complications of diseases that include vasculitis, such as Behçet's Disease and Henoch-Schonlein purpura[20,29].

To our knowledge, there is no study in the literature investigating the association of NLR levels with postoperative edema and ecchymosis often seen after open rhinoplasty, which is a frequently performed facial surgery. One of the intriguing findings of our study is the association of high preoperative NLR with the risk of severe edema and ecchymosis, determined in the multivariable regression analysis. Severe edema and ecchymosis in the early postoperative period after open rhinoplasty were associated with preoperative high NLR in our study (OR 4.67, 95% CI 2.38–9.40, $P < 0.001$ and OR 6.54, 95% CI 3.02–15.08, $P < 0.001$, respectively).

In an adult, non-geriatric, healthy population, normal NLR values are between 0.78 and 3.53[30]. The literature has reports of very different threshold values for NLR, which is an independent prognostic factor in determining morbidity and mortality in various cancers, major cardiovascular diseases, inflammatory and infectious conditions, and predicting postoperative complications[31-34].

A meta-analysis investigating the association of NLR with various tumor types and disease stages showed that NLR has a significant prognostic value, and an NLR value above certain threshold levels is associated with poor overall survival. In solid tumors, NLR > 4 is associated with poor overall survival, while in breast cancer, NLR has been reported to have a prognostic threshold between 3 and 3.3[35]. In pediatric patients diagnosed with acute appendicitis, the threshold NLR values vary between 3.2 and 10.5, depending on the occurrence of complications[36,37].

In patients with peripheral arterial disease, NLR >3 is accepted as an independent predictor of long-term cardiovascular mortality[38]. Hu Y et al. investigated patients with diabetic macular edema who received treatment and found that patients with NLR < 2.27 before treatment showed a better improvement in visual acuity score than those with NLR>2.27[39].

Animal studies on the development of cerebral edema have shown that there is a hyper-inflammatory period in which proinflammatory mediators increase within hours after acute brain injury[40,41]. Scarce human studies have reported that there is a relationship between the development of edema and inflammatory biomarkers such as NLR, and this

inflammatory process starts within hours and may continue for up to several days[42,43].

A predictive NLR threshold for severe postoperative edema-ecchymosis in open rhinoplasty with osteotomy has not yet been determined. Our study determined the optimal cut-off value of preoperative NLR as 2.1 for postoperative severe edema (AUC = 0.747, Sensitivity = 0.666, Specificity = 0.707) and 1.5 for severe ecchymosis (AUC = 0.747, Sensitivity = 0.869, Specificity = 0.470).

One of the intriguing findings of our study is the association of high preoperative NLR with the risk of severe edema and ecchymosis, determined in the multivariable regression analysis. Severe edema and ecchymosis in the early postoperative period after open rhinoplasty were associated with preoperative high NLR (OR 4.67, 95% CI 2.38–9.40, P < 0.001 and OR 6.54, 95% CI 3.02–15.08, P < 0.001, respectively). The mechanism underlying the association between elevated NLR and poor outcomes is unclear. However, it is known that NLR levels not only reflect the severity of conditions with an inflammatory component but also show a positive correlation with vessel intima-media thickness[20]. Therefore, we attribute the lower NLR levels to the fact that the affected vessels in open rhinoplasty are thinner and hence cause less endothelial dysfunction.

Our study suggests that the use of NLR may be an important predictor of severe edema and ecchymosis after open rhinoplasty cases and presents a clinical practice recommendation to the literature. However, further studies with larger case numbers are needed.

The study has some limitations. First, despite the inclusion of all consecutive patients during the study period, the retrospective design of the research may contain the potential for selection bias. Second, the limited number of patients in our study prevented comprehensive multivariate analyzes and drawing precise conclusions. Third, since our study was a retrospective study, there were problems in reaching other laboratory parameters of the patients.

In conclusion, this study identified NLR as a predictor for severe edema and ecchymosis seen after open rhinoplasty operations. We think that clinicians should be cautious about preoperative NLR > 2.1 for severe postoperative edema and NLR > 1.5 for severe postoperative ecchymosis in patients who will undergo open rhinoplasty. However, our findings need to be validated by prospective randomized controlled trials.

Yazar Katkıları: Çalışma konsepti/Tasarımı: AB,ET, AA, ML; Veri toplama: AB, ET, AA; Veri analizi ve yorumlama: AB, ET, AA; Yazı taslağı: AB, ET, AA; İçeriğin eleştirel incelenmesi: AB,ET, AA, ML; Son onay ve sorumluluk: AB,ET, AA, ML; Teknik ve malzeme desteği: AB, ML; Süpervizyon: AB,ET, AA, ML; Fon sağlama (mevcut ise): yok.
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