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ORIGINAL ARTICLE / ÖZGÜN MAKALE

The change of systemic inflammation response index in the treatment of patients with myasthenia gravis undergoing thymectomy: A retrospective, follow-up study

Timektomi yapılan myastenia gravis hastalarının tedavisinde sistemik inflamatuvar yanıt indeksinin değişimi: Retrospektif takip çalışması

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ABSTRACT

Background: This study aims to investigate the role of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, and systemic inflammation response index in patients with myasthenia gravis, thymomas and thymic hyperplasia and to identify the relationship between the inflammation response and disease activity.

Methods: Between January 2010 and December 2018, a total of 97 patients (71 males, 26 females; mean age: 36.7±16.3 years; range, 15 to 76 years) who underwent extended thymectomy with the diagnosis of myasthenia gravis were retrospectively analyzed. The patients were divided into two groups as the patient group (n=42) and the control group (n=55). Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, and systemic inflammation response index were measured one day prior to and one month after surgery.

Results: The patients with thymoma were older with a higher mean pre-systemic inflammation response index value. Preoperative systemic inflammation response index, neutrophil-to-lymphocyte ratio, and monocyte-to-lymphocyte ratio were significantly higher in patients with thymoma. A preoperative systemic inflammation response index value of less than 0.62 was accepted to indicate thymic hyperplasia and a postoperative systemic inflammation response index value higher than 2.94 was indicative of thymoma. In myasthenic patients whose steroid dose was increased and/or remained the same at the first month after surgery, postoperative monocyte-to-lymphocyte ratio and systemic inflammation response index values were found to be higher compared to preoperative values (p=0.006 and p=0.032, respectively). Patients whose pyridostigmine dose was increased and/or remained the same had significantly higher systemic inflammation response index values postoperatively (p=0.029).

Conclusion: The precise cut-off values of systemic inflammation response index may be helpful for the surgeon to predict the surgical outcome and post-systemic inflammation response index may be a predictive marker for estimating postoperative treatment changes.

Keywords: Inflammation, thymectomy, thymic hyperplasia, thymoma.

ÖZ

Amaç: Bu çalışmada myastenia gravis, timoma ve timik hiperplazili hastalarda nötrofil-lenfosit oranı, trombosit-lenfosit oranı, monosit-lenfosit oranı ve sistemik inflamatuvar yanıt indeksinin rolü incelendi ve inflamatuvar yanıt ve hastalık aktivitesi arasındaki ilişki belirlendi.

Çalışma planı: Ocak 2010 - Aralık 2018 tarihleri arasında myastenia gravis tanısı ile genişletilmiş timektomi yapılan toplam 97 hasta (71 erkek, 26 kadın; ort. yaş: 36.7±16.3 yıl; dağılım, 15-76 yıl) retrospektif olarak incelendi. Hastalar hasta grubu (n=42) ve kontrol grubu (n=55) olmak üzere iki gruba ayrıldı. Nötrofil-lenfosit oranı, trombosit-lenfosit oranı, monosit-lenfosit oranı ve sistemik inflamatuvar yanıt indeksi ameliyattan bir gün önce ve bir ay sonra ölçüldü.

Bulgular: Timomalı hastalar daha ileri yaş olup, ortalama pre-sistemik inflamatuvar yanıt indeks değerleri daha yüksekti. Ameliyat öncesi sistemik inflamatuvar yanıt indeksi, nötrofil-lenfosit oranı ve monosit-lenfosit oranı timomalı hastalarda anlamlı düzeyde daha yüksekti. Ameliyat öncesi sistemik inflamatuvar yanıt indeks değerinin 0.62'den düşük olması, timik hiperplazi göstergesi olarak kabul edildi ve ameliyat sonrası sistemik inflamatuvar yanıt indeks değerinin 2.94'ün üzerinde olması timoma göstergesi idi. Ameliyat sonrası birinci ayda steroid dozu artırılan ve/veya aynı kalan myastenia hastalarında ameliyat sonrası monosit-lenfosit oranı ve sistemik inflamatuvar yanıt indeks değerleri ameliyat öncesi değerlere kıyasla daha yüksek izlendi (sırasıyla p=0.006 ve p=0.032). Piridostigmin dozu artırılan ve/veya aynı kalan hastalarda ameliyat sonrası sistemik inflamatuvar yanıt indeks değerleri anlamlı olarak daha yüksekti (p=0.029).

Sonuç: Sistemik inflamatuvar yanıt indeksinin kesin sınır değerleri, cerrahın cerrahi sonucu tahmin etmesine yardımcı olabilir ve ameliyat sonrası sistemik inflamatuvar yanıt indeksi tedavi değişikliklerini tahmin etmek için öngördürücü bir belirteç olabilir.

Anahtar sözcükler: İnflamasyon, timektomi, timik hiperplazi, timoma.

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Thymomas are the most common primary neoplasm of the anterior mediastinum[1] and myasthenia gravis (MG) is the most common disease presented in patients with thymomas with an average prevalence of 20 to 40%. It is an organ-specific autoimmune disease characterized by muscle fatigability[2] and its pathogenesis is not fully known, but inflammation is a consistent key factor in the disease.[3] Likewise, inflammation is an accepted sign of cancer and it is reported that not only local inflammation, but also systemic inflammation plays a central role in the development and progression of the tumor, as well as in the process of the patient survival.[4] All these facts substantially contribute to the opportunity to predict the patient outcomes via looking for these inflammatory responses.[4] Recently, the neutrophil-to-lymphocyte ratio (NLR), a ratio which can easily be calculated with the count of white blood cells (WBC), has been reported as a potential mark of systemic inflammation.[5] Other types of WBC such as neutrophils, lymphocytes, and monocytes, are also recognized players in the systemic inflammation. Thus, additional ratios including the NLR, platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), and the systemic inflammation response index (SIRI), which is mainly defined based on peripheral neutrophil, lymphocyte, and monocyte counts have also been demonstrated as valid indicators.[6,7] Moreover, NLR has been recently reported to indicate the status of the inflammation and to predict the activity of the disease.[8] Obviously, there is a need to objectively evaluate the inflammatory status in the patients undergoing surgery for thymectomy and thymothymectomy as MG is a heterogeneous fluctuating condition.[9] Therefore, in the present study, we aimed to investigate the role of SIRI, NLR, PLR, and MLR in patients with MG, thymomas and thymic hyperplasia and to identify the relationship between the inflammatory response and disease activity.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Dokuz Eylül University Faculty of Medicine, Department of Chest Surgery between January 2010 and December 2018. A total of 97 patients (71 males, 26 females; mean age: 36.7±16.3 years; range, 15 to 76 years) who underwent extended thymectomy with the diagnosis of MG were included. The patients were divided into two groups as the MG group (n=42) and the control group (n=55). The control group consisted of patients presenting with acute cardiac problems, cancer and immunological diseases such as diabetes mellitus, rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis, who underwent thoracic drainage due to primary spontaneous pneumothorax and had no comorbidity. Patients with secondary causes of spontaneous pneumothorax were excluded. Patients were also excluded, if they did not undergo extended thymectomy, had missing data, thymic carcinoma or neuroendocrine tumors, and/or previously received chemotherapy or radiotherapy. Data including age, sex, Masaoka stage, histology according to the World Health Organization (WHO) classification, presence of MG, and the surgical approach implemented were recorded. Myasthenic crisis was defined as respiratory failure arising from muscle weakness requiring mechanical ventilation with intubation or non-invasive ventilatory support (continuous or bi-level positive airway pressure).[10] The preoperative work-up included a routine physical examination, standard blood tests and contrast-enhanced thoracic computed tomography (CT) scan. Histopathological reports were reviewed. Surgery was performed using either median sternotomy, thoracotomy, or video-assisted thoracic surgery (VATS).

Data collection

Data were obtained from medical records of the patients. Samples of venous blood collected one day prior to and one month following surgery were also analyzed; the WBC, including neutrophils, lymphocytes and monocytes, and platelets in the samples were measured. The NLR was calculated by dividing the relative neutrophil counts by the relative lymphocyte counts, while the MLR was calculated by dividing the relative monocyte counts by the relative lymphocyte counts. The PLR was calculated by dividing the absolute platelet numbers by the absolute lymphocyte numbers. The SIRI was calculated according to the following formula: SIRI=monocyte × neutrophil/ lymphocyte.

Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 17.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were presented in mean ± standard deviation (SD), median (min-max) or number and frequency, where applicable. The Kolmogorov-Smirnov test was performed to test the normality of continuous variables. The differences in categorical variables between the groups were tested using the chi-square test, or Fisher exact test when the assumptions for

Table 1. Demographic and laboratory characteristics of patients and preoperative systemic inflammation response markers

	MG (n=42)			Thymoma (n=21)			Non thymoma (thymic hyperplasia) (n=21)			Control (n=55)						
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p**	*p*1	*p*2	*p*3
Age (year) (median)			44.3±16.0 (43)			50.9±13.4			37.7±16			30.8±13.9 (24)	<0.001	0.0211	<0.001	NS
Sex													<0.001	NS	<0.001	<0.001
Female	24	57.1		10	47.6		14	66.7		2	3.6					
Pre neutrophil count (10*3/µL) (median)			4.90±2.98 (4.6)			7.35±2.21 (6.55)			2.43±0.74 (2.30)			2.82±1.05 (2.3)	<0.001	<0.001	<.0.001	NS
Pre lymphocyte count (10*3/µL) (median)			1.49±0.71 (1.3)			1.31±0.52 (1.30)			1.65±0.83 (1.30)			2.41±0.84 (2.2)	<0.001	NS	<0.001	<0.001
Pre platelet count (10*3/µL) (median)			278.24±77.67 (262)			291.23±65.69 (264)			265.23±87.72 (246)			225.27±50.88 (225)	>0.05	-	-	-
Pre monocyte count (10*3/µL) (median)			0.68±0.26 (0.7)			0.83±0.21 (0.80)			0.51±0.20 (0.50)			0.39±0.12 (0.4)	<0.001	0.002	<0.001	NS
Pre-SIRI (median)			3.01±2.78 (1.79)			5.17±2.41 (4.61)			0.84±0.42 (0.73)			0.48±0.23 (0.4)	<0.001	0.001	<0.001	0.004
Pre-NLR (median)			3.92±2.79 (3.43)			6.18±2.16 (5.90)			1.65±0.68 (1.61)			1.33±1.00 (1.22)	<0.001	<0.001	<.0.001	NS
Pre-MLR (median)			0.54±0.33 (0.47)			0.72±0.34 (0.61)			0.36±0.18 (0.28)			0.18±0.08 (0.17)	<0.001	0.031	<0.001	<.0.001
Pre-PLR (median)			218.35±95.80 (193.19)			250.46±98.06 (224.11)			186.22±83.85 (183.00)			113.18±118.15 (96.5)	<0.001	NS	<0.001	<0.001

MG: Myasthenia gravis; SD: Standard deviation; SIRI: Systemic inflammation response index; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; *Post-hoc* Kruskal-Wallis K test; p*: Myasthenia gravis *vs*. control; p1: Thymic hyperplasia *vs*. thymoma; p2: Control *vs*. thymoma; p3: Control *vs*. thymic hyperplasia; NS: Non-significant; * Statistically significant (p<0.05).

chi-square test were unmet. The Mann-Whitney U test was applied while evaluating non-normally distributed (non-parametric) variables between the two groups. The Kruskal-Wallis test was used to determine the differences of distributional characteristics among three groups of patients with MG consisting of those with thymic hyperplasia, and with thymoma and controls. Changes in the measured values were made by implementing the Wilcoxon test within the group and the repeated measures analysis between the groups. To test the predictive accuracy of the SIRI for detecting MG and to calculate an optimal cut-off value for the test, the area under the curves (AUC) of receiver operating characteristic (ROC) analysis were used. A *p* value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics of study patients

Of a total of 97 patients, 42 (43.30%) were in the MG group and 55 (56.70%) were in the control group. Regarding the mean age and sex, patients with MG were older than the control group (44 *vs*. 33.8 years, respectively; p<0.001), and there were more females in the MG group (57.14%) than in the control group (3.64%) (p<0.001) (Table 1). Patients with MG consisted of those with thymic hyperplasia (n=21) and with thymoma (n=21). Comparing patients with thymoma, those with thymic hyperplasia, and controls, patients with thymoma were older and had a higher mean pre-SIRI. In addition, there were fewer females among the controls. Demographic and laboratory characteristics of the patients are shown in Table 1.

In patients with MG, the surgery method was sternotomy in 37 (88.10%), VATS in two (4.76%), and thoracotomy in three (7.14%) patients. There were 18 (42.86%) patients with myasthenic crisis of which three occurring during follow-up after discharge. The presence of MG crisis was similar in patients with thymic hyperplasia and thymoma (p=0.533). The changes in pre- and postoperative measurements in the MG group are compared in Table 2. Accordingly, neutrophil and platelet counts decreased, while monocyte and MLR values increased.

Systemic inflammation response markers and their associations with the treatment

The NLR, MLR, PLR, SIRI values, and changes in treatment including pyridostigmine and steroid doses are compared in Table 3. In myasthenic patients whose steroid dose was increased and/or the same after the first month of surgery, post-MLR and post-SIRI values

Table 2. Pre- and postoperative measurements in the MG group

	Preoperative	Postoperative	
	Mean±SD	Mean±SD	*p*
Neutrophil (10*3/μL) (median)	4.90±2.98 (4.60)	4.22±2.37 (3.90)	**0.013**
Lymphocyte (10*3/μL) (median)	1.49±0.71 (1.30)	1.34±0.64 (1.25)	0.297
Platelet (10*3/μL) (median)	278.24±77.67 (262.0)	253.31±77.62 (258.00)	**0.003**
Monocyte (10*3/μL) (median)	0.68±0.26 (0.70)	0.86±0.38 (0.80)	**0.007**
NLR (median)	3.92±2.79 (3.43)	4.35±4.44 (2.87)	0.925
MLR (median)	0.54±0.33 (0.47)	0.81±0.56 (0.67)	**0.006**
PLR (median)	218.35±95.80 (193.19)	249.59±173.96 (205.00)	0.595
SIRI (median)	3.01±2.78 (1.79)	3.81±4.33 (1.93)	0.183

MG: Myasthenia gravis; SD: Standard deviation; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SIRI: Systemic inflammation response index; * Statistically significant (p<0.05); Wilcoxon t-test.

were found to be higher compared to preoperative values (p=0.006 and p=0.032, respectively). In patients whose pyridostigmine dose was increased and/or the same, patients had significantly higher post-SIRI values (p=0.029).

Cut-off values of pre- and postoperative SIRI

We attempted to establish the optimal thresholds for SIRI for our study population pre-and postoperatively with the ROC curve. The optimal cut-off values for pre-SIRI and post-SIRI were 0.62 and 2.94, respectively. Pre-SIRI with a cut-off value of 0.62 had a sensitivity of 85% and a specificity of 80%, while post-SIRI with a cut-off value of 2.94 had a sensitivity of 67% and a specificity of 81% for patients with MG.

The relationship between pre-SIRI, post-SIRI, and clinicopathological characteristics such as disease duration, treatment, thymus histology, Masaoka stage and myasthenic crisis is presented in Table 4. The patients with a value of pre-SIRI below 0.62 had thymic hyperplasia (p=0.021). In addition, most of the patients with a value of post-SIRI higher than 2.94 had thymoma (p=0.002).

DISCUSSION

In the present study, we demonstrated that pre-SIRI, pre-NLR, and pre-MLR values were higher in MG patients with thymoma than in those with thymic hyperplasia. In addition, in MG patients whose steroid doses were increased and/or the same at the first month following surgery, post-MLR and post-SIRI values were found to be higher compared to preoperative values. Similarly, in patients whose pyridostigmine dose was increased and/or the same, the patients were found to have a higher post-SIRI value. Moreover, patients with a pre-SIRI value less than 0.62 were had thymic hyperplasia and nearly three quarters of the patients having a value of post-SIRI higher than 2.94 had thymoma.

Myasthenia gravis is a severe autoimmune disease characterized by loss of acetylcholine receptor (AChR) on the postsynaptic membrane of the neuromuscular junction and results in impaired neuromuscular transmission and muscle weakness.[11,12] Accumulated evidence has recently demonstrated that the chronic inflammation response can be heavily implicated in the pathogenesis of MG.[13] Inflammation also affects each step of tumorigenesis, including tumor initiation, promotion, and metastatic progression,[14] which may be the case in thymoma. Biomarkers including neutrophil,

Table 3. Pre- and postoperative steroid and pyridostigmine dose change

	Steroid					Pyridostigmine				
	Dose same and/or increased		Dose cut			Dose same and/or increased		Dose cut		
	Mean±SD	Median	Mean±SD	Median	*p*	Mean±SD	Median	Mean±SD	Median	*p*
Pre-NLR	3.74±2.60	2.96	4.50±3.42	3.44	0.149	3.27±1.92	3.45	4.70±3.46	3.41	0.120
Post-NLR	4.68±4.82	3.29	3.30±2.83	2.02		4.60±5.25	2.87	4.05±3.32	2.86	
Pre-MLR	0.49±0.28	0.42	0.72±0.44	0.59	**0.006**	0.46±0.19	0.47	0.64±0.43	0.58	0.053
Post-MLR	0.91±0.60	0.75	0.49±0.20	0.46		0.90±0.61	0.71	0.69±0.48	0.57	
Pre-PLR	208.55±90.66	185.35	249.69±109.86	222.25	0.086	202.93±83.05	183.00	237.01±108.64	215.83	0.939
Post-PLR	263.59±179.50	212.50	204.77±154.75	153.77		232.42±182.30	182.00	270.37±165.77	247.69	
Pre-SIRI	2.80±2.65	1.68	3.70±3.21	2.75	**0.032**	2.49±1.93	1.88	3.64±3.50	1.70	**0.029**
Post-SIRI	4.42±4.73	3.10	1.86±1.68	1.73		4.66±5.08	3.02	2.78±3.01	1.71	

SD: Standard deviation; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SIRI: Systemic inflammation response index; Repeated measures test.

Table 4. Associations between SIRI and clinicopathological characteristics

	Pre-SIRI <0.62 (n=6)				Pre-SIRI >0.62 (n=36)					Post-SIRI <2.94 (n=24)				Post-SIRI >2.94 (n=18)				
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	*p*	n	%	Mean±SD	Median	n	%	Mean±SD	Median	*p*
Age (year)			43±19.4	41.5			44.5±15.7	43.5	0.843			43±16.2	40.5			48.6±15.4	52	0.268
Sex										8	33.3							
Male	3	50			15	41.7			0.704					10	55.6			0.150
Disease duration (month)			58.8±18.8	59			58.9±38.9	59.5	0.760			57.2±34	59.5			64.2±53.6	48	0.461
Follow up (month)			36.6±26.0	35			42.0±32.2	32	0.719			42.4±31.1	35			40.7±37.2	29.5	0.712
Thymus histology							**0.021**											**0.002**
Thymic hyperplasia	6	100			15	41.7				17	70.8			4	22.2			
Thymoma	0	0			21	58.3				7	29.2			14	77.8			
Masaoka stage (n=21)									NS									0.149
I+II	0	0			15	71.4				9	90			6	54.5			
III+IV	0	0			6	28.6				1	10			5	45.5			
Myasthenic crisis									0.685									0.280
With	2	33.3			16	44.4				12	50.0			6	33.3			
Without	4	66.7			20	55.6				12	50.0			12	66.7			
Steroid									NS									0.068
Dose same and increase	5	83.3			27	75.0				18	66.7			14	93.3			
Dose cut	1	16.7			9	25.0)				9	33.3			1	6.7			
Pyridostigmine									NS									0.248
Dose same and increase	3	50.0			20	55.6				13	48.1			10	66.7			
Dose decrease and cut	3	50.0			16	44.4				14	51.9			5	33.3			

SIRI: Systemic inflammation response index; SD: Standard deviation; NS: Non-significant.

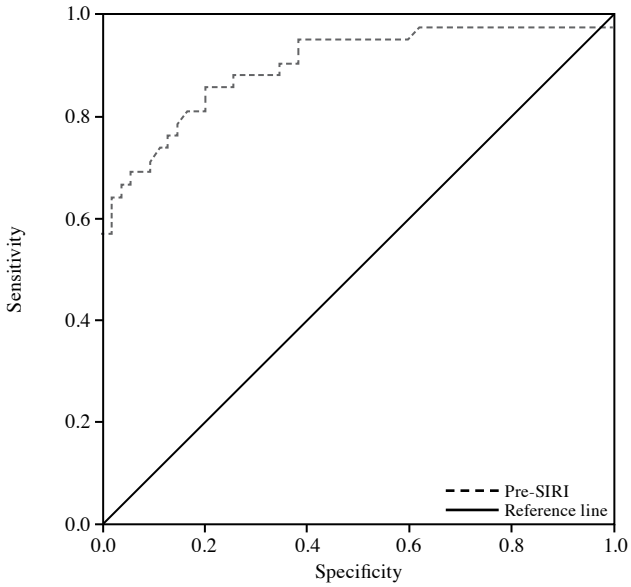

Figure 1. Receiver operating characteristic analysis of the preoperative SIRI value in the cohort of myasthenic patients surgically treated for thymoma and thymic hyperplasia.
SIRI: Systemic inflammation response index.

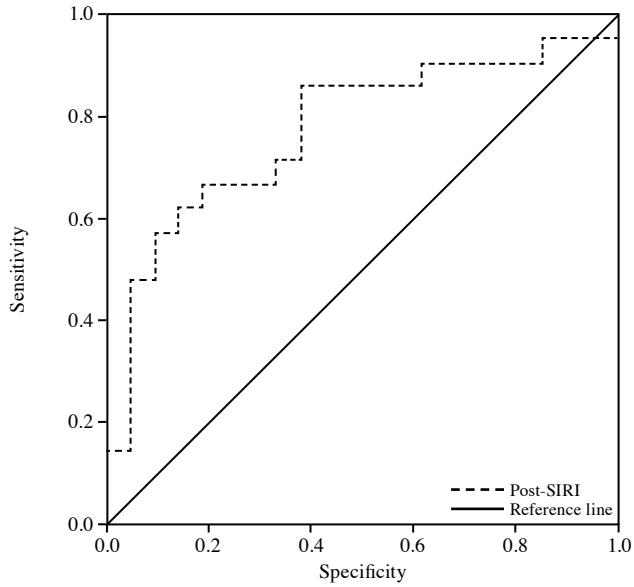

Figure 2. Receiver operating characteristic analysis of the postoperative SIRI value in the cohort of myasthenic patients surgically treated for thymoma and thymic hyperplasia.
SIRI: Systemic inflammation response index.

lymphocyte, and platelet counts, as well as the NLR, PLR, MLR, and SIRI, are indices of inflammation.[15] Similarly, we observed a significant difference in serum NLR, MLR, PLR, and SIRI values between MG patients (with thymoma or thymic hyperplasia) and the control group in our study. Yang et al.[5] showed a higher NLR level in patients with MG than in healthy controls ($p<0.0001$). In our study, in addition to pre-NLR, pre-MLR and pre-PLR, pre-SIRI values were also found to be significantly higher in MG patients than in healthy controls ($p<0.001$). This confirms that MG is associated with increased inflammation. When the pre- and postoperative NLR, MLR, PLR, and SIRI values were compared in the MG group, a significant increase was observed in postoperative monocyte and MLR values, which may indicate ongoing chronic inflammation in the postoperative period. Likewise, the fact that preoperative NLR, MLR, and SIRI values in our patients with thymomas were significantly different than those with thymic hyperplasia may result from cancer-related inflammation in thymomas,[15] since neutrophils and monocytes are two important myeloid compartments in humans involved in various inflammatory and immunological disease processes, including cancer.[16]

Furthermore, SIRI was higher postoperatively in MG patients whose pyridostigmine or steroid dose remained the same and/or was increased. Also, MLR was observed to be higher postoperatively, when the steroid dose was the same and/or increased. For the SIRI value to increase, the monocyte and/or neutrophil counts must increase, and/or the lymphocyte count must remain the same or decrease. Current evidence indicates that steroids suppress the leukocyte flow in the inflamed area[17] and increase monocyte production. In addition, since we observed no significant increase in the postoperative NLR values, but a significant increase in the MLR values, this may have led to an increase in the SIRI values. Nevertheless, there is not yet sufficient evidence regarding the effect of pyridostigmine on blood cells.

In our clinical setting, a cut-off value of 0.62 for pre-SIRI values and a cut-off value of 2.94 for post-SIRI were found to have satisfying sensitivity and specificity values (Figures 1 and 2). Accordingly, as a lower value of SIRI is expected for such a benign lesion, a preoperative SIRI value under 0.62 was related to indicate thymic hyperplasia. Additionally, nearly three quarters of patients having a postoperative SIRI value higher than 2.94 were found to suffer from thymoma. We believe that a precise cut-off value can provide an opportunity for the surgeon to predict the outcome of the operation, particularly for male patients. In addition, we could not determine a relationship

between pre- or postoperative SIRI cut-off and clinical variables such as disease duration, follow-up duration, Masaoka stage and presence of myasthenic crisis and this might be due to our small sample size.

The present study has certain strengths. To the best of our knowledge, this is the first study to compare pre- and postoperative inflammation indices in completely resected myasthenic patients with thymoma and thymic hyperplasia. In addition, multiple inflammation parameters were evaluated simultaneously. Moreover, this is the first study to compare inflammation parameters with pre- and postoperative steroid and pyridostigmine dose changes. Finally, unlike previous studies, SIRI values were analyzed in myasthenic patients who underwent complete resection.

Nonetheless, our study has several limitations. First, it has a retrospective design and, therefore, the cause-effect relationship was unable to be displayed. Second, it was limited by its relatively small size; the data were obtained from a single tertiary care center and, thus, cannot be generalized to other settings. Our findings require confirmation in multi-center, large-scale studies before the NLR, MLR, PLR and SIRI can be confidently applied to clinical decisions.

In conclusion, to the best of our knowledge, this is the first study to assess the relationship between neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, and the systemic inflammation response index, newly-emerging inflammatory markers, and myasthenia gravis and its activity not only preoperatively, but also at one month after surgery.

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Ethics Committee Approval: The study protocol was approved by the Dokuz Eylul University Non-Interventional Research Ethics Committee (date: 08.05.2019, no: 2019/12-36). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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