

Can The Monocyte-To-Lymphocyte Ratio Be Another Predictor Of Prostate Cancer?

Monosit-Lenfosit Oranı, Prostat Kanserinin Başka Bir Göstergesi Olabilir Mi?

Gökçe DÜNDAR¹, Anıl ERKAN¹

¹University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital

Yazışma Adresi / Correspondence:


Gökçe DÜNDAR

Altınşehir M. 208. S. No:16 Nilüfer/Bursa

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 Gökçe DÜNDAR <https://orcid.org/0000-0001-9799-9700> dr@gokcedundar.com

 Anıl ERKAN <https://orcid.org/0000-0003-3130-9046> dr.anilerkan@hotmail.com

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Abstract

Introduction This study aimed to evaluate whether monocyte-lymphocyte-ratio (MLR) had a potential role as a biomarker of prostate cancer (PCa).

Materials and Methods For patients who underwent a prostate biopsy between January 1, 2017, and December 31, 2021, age, hemogram parameters, free-total PSA values, and pathology results were recorded. Patients with a pathology result of PCa and those with a Gleason score of 3+4 and above were defined as having clinically significant PCa (csPCa), while other PCa cases were defined as having clinically non-significant PCa (non-csPCa).

Results The pathology result was reported as PCa in 164 of the 510 patients included in the study and non-PCa in 346. The monocyte count was found to be higher in the PCa group than in the non-PCa group (0.61 ± 0.33 and 0.53 ± 0.19 , respectively; $p=0.002$). MLR was also significantly higher in the PCa group (0.35 ± 0.29 and 0.26 ± 0.13 , respectively; $p<0.001$). Of 164 patients whose pathology was reported as PCa, 69 (39%) had csPCa and 95 (61%) had non-csPCa. When these PCa subgroups were analyzed, age at diagnosis, free PSA, and total PSA were found to be statistically significantly higher in the csPCa group, while the f/tPSA value was statistically significantly lower in this group. There was no statistically significant difference between the csPCa and non-csPCa groups in terms of the lymphocyte and monocyte counts, and MLR.

Conclusion In patients undergoing a biopsy, an MLR value above 0.3 can predict the pathology result being reported as PCa at a sensitivity of 27.4% and specificity of 85.3%.

Keywords monocyte-to-lymphocyte ratio, monocyte, prostate cancer, prostate biopsy

Özet

Amaç PSA'nın nispeten düşük duyarlılığı ve özgüllüğü nedeniyle tanı verimliliğini artırmak için ucuz, invaziv olmayan ve özellikle klinik önemli prostat kanserini tanıyabilen belirteçlere ihtiyaç vardır. MLR'nin prostat kanserinin bir biyobelirteci olarak potansiyel rolü olup olmadığının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem 1 Ocak 2017 ile 31 Aralık 2021 tarihleri arasında prostat biyopsisi alınan hastaların yaşı, işlem öncesinde lenfosit, monosit sayısı gibi hemogram parametreleri, free-total PSA değerleri, patoloji sonuçları kayıt altına alındı. Patoloji sonucu prostat kanseri (PCa) gelenlerin, Gleason Skoru 3+4 ve üzeri olan hastalar klinik anlamlı prostat kanseri (csPCa) olarak tanımlanırken, diğer PCa'li hastalar klinik anlamlı olmayan prostat kanseri (non-csPCa) olarak tanımlandı.

Bulgular Çalışmaya dahil edilen 510 hastanın 164'ünün patolojisi PCa, 346'sının sonucu non-PCa olarak raporlandı. Monosit sayıları PCa'li grupta non-PCa gruptan daha yüksek bulundu. (sırasıyla; $0,61 \pm 0,33$ ve $0,53 \pm 0,19$, $p=0,002$) MLR de PCa grubunda daha yüksek bulundu. (sırasıyla; $0,35 \pm 0,29$ ve $0,26 \pm 0,13$, $p<0,001$) Tanı anındaki yaş, total PSA, monosit sayısı, MLR, PCa grubunda istatistiksel anlamlı olarak daha yüksek bulunurken, free/total PSA oranı (f/tPSA) bu grupta istatistiksel anlamlı daha düşük izlendi. Patolojisi PCa olarak raporlanan 164 hastalardan 69'unda (39%) csPCa bulunurken, 95'inde (61%) non-csPCa mevcuttu. Bu sub-grupların analizi yapıldığında tanı anındaki yaş, free PSA, total PSA csPCa grubunda istatistiksel anlamlı olarak daha yüksek bulunurken bu grupta f/tPSA değeri istatistiksel olarak anlamlı daha düşük bulundu. Lenfosit, monosit, MLR değerleri açısından csPCa ve non-csPCa grupları arasında istatistiksel olarak anlamlı bir fark bulunamadı.

Sonuç Biyopsi yapılan hastalarda 0.3'ün üzerindeki MLR değeri olması halinde patolojinin PCa olarak sonuçlanması %27,4 duyarlılık ve %85,3 özgüllük ile öngörülebilir.

Anahtar Kelimeler monosit-lenfosit oranı, monosit, prostat kanseri, prostat biyopsisi

INTRODUCTION

Due to the relatively low sensitivity and specificity of PSA, it is often used together with its derivatives, such as free PSA, PSA density, and PSA velocity to increase diagnostic efficiency.(1) However, due to the low specificity of these parameters, many unnecessary biopsies are still performed. In some centers, the urinary prostate cancer antigen 3 test has proven helpful in detecting PCa, and the United States Food and Drug Administration has approved it for repeat biopsies.(2) Another tool used to reduce unnecessary prostate biopsies is multi-parametric magnetic resonance imaging (mpMRI). When a suspicious lesion is detected, a targeted biopsy can be performed with mpMRI. However, the performance of this diagnostic tool may be affected by the characteristics of the patient population, quality of MRI scans, and experience of the radiologist.(3) In addition, the high cost of such additional approaches is the greatest obstacle to their widespread use in clinical practice.(4) It is known that low IPSS score and positive rectal examination (stiffness) increase the probability of being diagnosed with cancer in patients with PSA

levels in the gray zone.(5) But there is still a need for markers that can be measured with a low cost in a non-invasive manner, especially to identify clinically significant PCa (csPCa).

PCa is the most common urological malignancy in men and is the second leading cause of cancer-related death after lung cancer.(6) Tumor-associated inflammation and microenvironment are known to be key factors for neoplasia, proliferation, and metastasis.(7, 8) It has also been reported that systemic inflammatory responses play a role in the initiation and progression of PCa.(9) Inflammation has been considered to increase the risk of PCa, similar to some other types of cancer.(8) Oxidative substances released by inflammatory cells cause cell and gene damage, as well as cellular changes and genetic mutations that may lead to PCa.(10)

Considering that appropriate biomarkers were needed for the detection of csPCa before a needle biopsy, some authors investigated the number of serum monocytes in patients with PCa and found it to be significantly increased in those with a high GS.(11) Another study showed that in addition to PSA and f/tPSA, the diagnostic value of MLR

Assessed for eligibility	Patients who underwent prostate biopsy: 1611
Exclusion*	Patients without pathological examination results: 105 Patients without PSA values: 252 Patients without hemogram results before procedure: 862 Patients with anemia: 113 Patients with acute or chronic prostatitis, prostatic intraepithelial neoplasia according to the pathology result : 238 Patients taking antibiotics, non-steroidal anti-inflammatory drugs, or 5-alpha reductase inhibitors: 102 Patients with malignancy other than prostate cancer: 3
Grouping	Prostate cancer group (Pca): 164 non-Prostate cancer group (non-Pca): 346
Cancer grouping	Clinically significant prostate cancer group (csPca): 69 Clinically non-significant prostate cancer group (non-csPca): 95

Figure 1. Flowchart for patient selection

Table 1. Clinical characteristics and blood parameters of the PCa and non-PCa groups

		PCa Group	Non-PCa Group	P value
Cases (n)		164	346	
Age of diagnosis (years)		67 ± 7 (62-79)	63 ± 7 (59-73)	<0.001*
Free PSA (ng/mL)		3.78 ± 7.08 (0.88-19.68)	1.73 ± 2.00 (0.90-3.68)	0.121
Total PSA (ng/mL)		34.19 ± 109.59 (6.47-100)	8.54 ± 7.79 (4.78-21.27)	<0.001*
f/tPSA		0.17 ± 0.10 (0.10-0.37)	0.22 ± 0.09 (0.15-0.38)	<0.001*
Hgb (g/dL)		14.73 ± 1.13 (13.90-16.40)	14.84 ± 1.01 (14.00-16.5)	0.144
Hct (%)		43.91 ± 3.27 (41.90-48.60)	44.06 ± 3.59 (41.80-49.30)	0.287
MCV (fL)		88.78 ± 5.13 (85.60-96.80)	88.19 ± 4.68 (85.60-95.10)	0.331
WBC (n, x10 ³ /mL)		8.12 ± 2.29 (6.60-12.68)	8.32 ± 3.52 (6.29-12.90)	0.807
Lym (n, x10 ³ /mL)		2.08 ± 0.81 (1.50-3.70)	2.22 ± 1.04 (1.64-3.40)	0.077
Mono (n, x10 ³ /mL)		0.61 ± 0.33 (0.44-0.92)	0.53 ± 0.19 (0.40-0.90)	0.002*
MLR		0.35 ± 0.29 (0.20-0.80)	0.26 ± 0.13 (0.20-0.50)	<0.001*
Hypertension	Absent	107 (65.2)	238 (68.8)	0.424
	Present	57 (34.8)	108 (31.2)	
Cardiovascular disease	Absent	128 (78.0)	275 (79.5)	0.711
	Present	36 (22.0)	71 (20.5)	
Hyperlipidemia	Absent	137 (83.5)	296 (85.5)	0.553
	Present	27 (16.5)	50 (14.5)	
Diabetes	Absent	150 ^a (91.5)	288 ^b (83.2)	0.013*
	Present	14 ^a (8.5)	58 ^b (16.8)	

Data in the table are given as mean value ± standard deviation (interquartile range) for values and number (percentage) for comorbidities. Abbreviations and explanations: PCa, prostate cancer; PSA, prostate-specific antigen; f/tPSA, ratio of free/total serum prostate-specific antigen; Hgb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; WBC, white blood cell; Lym, lymphocyte; Mono, monocyte; MLR, monocyte-to-lymphocyte ratio. *Statistically significant at $p < 0.05$

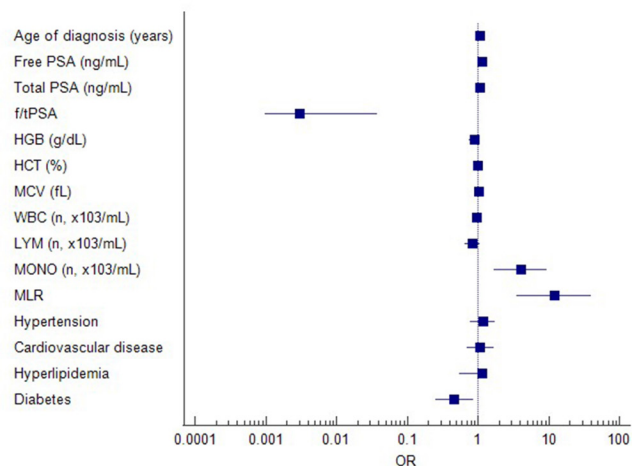


Figure 2. Forest plot graphic of risk factors on PCa

Table 2. Clinical characteristics and blood parameter of the PCa subgroups

		csPCa Group	Non-csPCa Group	P value
Cases (n)		69	95	
Age of diagnosis (years)		68 ± 7 (63-74)	66 ± 7 (61-70)	0.044*
Free PSA (ng/mL)		6.50 ± 10.20 (1.00-6.15)	1.86 ± 2.01 (0.83-2.13)	0.005*
Total PSA (ng/mL)		65.73 ± 164.01 (7.69-42.29)	11.28 ± 10.27 (6.24-11.88)	<0.001*
f/tPSA		0.16 ± 0.11 (0.09-0.20)	0.18 ± 0.09 (0.11-0.22)	0.049*
Hgb (g/dL)		14.55 ± 0.92 (13.80-15.10)	14.86 ± 1.25 (14.00-15.40)	0.092
Hct (%)		43.57 ± 2.72 (42.10-45.30)	44.15 ± 3.62 (41.3-45.80)	0.511
MCV (fL)		88.45 ± 5.19 (85.30-91.70)	89.01 ± 5.09 (85.80-91.50)	0.458
WBC (n, x10 ³ /mL)		8.21 ± 2.19 (6.59-9.30)	8.06 ± 2.37 (6.60-9.02)	0.520
Lym (n, x10 ³ /mL)		2.11 ± 0.91 (1.50-2.49)	2.07 ± 0.74 (1.50-2.50)	0.882
Mono (n, x10 ³ /mL)		0.63 ± 0.41 (0.45-0.70)	0.60 ± 0.25 (0.43-0.70)	0.745
MLR		0.34 ± 0.26 (0.20-0.40)	0.36 ± 0.31 (0.20-0.40)	0.854
Hypertension	Absent	45 (65.2)	62 (65.3)	1.000
	Present	24 (34.8)	33 (34.7)	
Cardiovascular disease	Absent	58 (84.1)	70 (73.7)	0.129
	Present	11 (15.9)	25 (26.3)	
Hyperlipidemia	Absent	60 (87.0)	77 (81.1)	0.395
	Present	9 (13)	18 (18.9)	
Diabetes	Absent	64 (92.8)	86 (90.5)	0.779
	Present	5 (7.2)	9 (9.5)	

Data in the table are given as mean value ± standard deviation (interquartile range) for values and number (percentage) for comorbidities. Abbreviations and explanations: PCa, prostate cancer; csPCa, clinically significant prostate cancer; non-csPCa, clinically non-significant PCa; PSA, prostate-specific antigen; f/tPSA, ratio of free/total serum prostate-specific antigen; Hgb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; WBC, white blood cell; Lym, lymphocyte; Mono, monocyte; MLR, monocyte-to-lymphocyte ratio. *Statistically significant at p<0.05.

was also higher than that of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), and concluded that MLR could be a good helpful indicator for the diagnosis of PCa.(12)

In a previous study, it was suggested that the total number of white blood cells (WBC), their fractions, C-reactive protein (CRP) level, or their ratio over each other could be good candidates as biomarkers to predict aggressive cancer as indicators of systemic inflammation and immune responses.(11) Monocytes, a fraction of WBC, can suppress lymphocyte activation and increase tumor prog-

ression.(13) A high monocyte count can promote tumorigenesis and angiogenesis by suppressing local immunity and stimulating tumor neovasculogenesis.(14) The monocyte-lymphocyte ratio (MLR), which is calculated by dividing the absolute monocyte count by the absolute lymphocyte count, is a frequently used and easily accessible hematological and inflammatory parameter for this purpose. It has been reported that MLR predicts a poor prognosis in primary pulmonary lymphoepithelioma-like carcinoma.(15) In addition, it has been suggested that a high MLR value, a simple biomarker of the host immu-

Table 3. Results of the univariate and multivariate analyses for the effect of MLR on PCa detection

	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age of diagnosis (years)	1.088	1.056-1.121	<0.001*	1.088	1.052-1.125	<0.001*
Free PSA (ng/mL)	1.148	1.061-1.242	0.001*			
Total PSA (ng/mL)	1.060	1.037-1.083	<0.001*			
f/tPSA	0.003	0.000-0.038	<0.001*	0.001	0.000-0.019	<0.001*
Hgb (g/dL)	0.901	0.751-1.080	0.261			
Hct (%)	0.987	0.937-1.041	0.640			
MCV (fL)	1.026	0.987-1.066	0.200			
WBC (n, x10 ³ /mL)	0.979	0.920-1.042	0.504			
Lym (n, x10 ³ /mL)	0.833	0.652-1.064	0.143			
Mono (n, x10 ³ /mL)	4.019	1.696-9.525	0.002*			
MLR	12.047	3.571-40.640	<0.001*	7.076	1.879-26.645	0.004*
Hypertension	1.174	0.792-1.740	0.425			
Cardiovascular disease	1.089	0.693-1.713	0.711			
Hyperlipidemia	1.167	0.553-1.167	0.553			
Diabetes	0.463	0.250-0.858	0.014*			

Abbreviations and explanations: PCa, prostate cancer; SD, standard deviation; OR, odds ratio; CI, confidence interval; PSA, prostate-specific antigen; f/tPSA, ratio of free/total serum prostate-specific antigen; Hgb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; WBC, white blood cell; Lym, lymphocyte; Mono, monocyte; MLR, monocyte-to-lymphocyte ratio. *Statistically significant at p<0.05.

ne system, is associated with a poor prognosis in various cancers.(16)

There are few studies in the literature that draw attention to the role of MLR in the prediction of PCa.(4, 11, 12) In this retrospective study, we evaluated whether MLR had a potential role as a biomarker of PCa activity based on clinicopathological data.

MATERIAL and METHODS

Patients who underwent a transrectal prostate biopsy at our urology clinic between January 01, 2017, and December 31, 2021, were included in the study. The pathology results of the prostate biopsies performed in the clinic, patients' history, and results of routine examinations performed before the biopsy procedure were obtained from the Hospital Information Management System (HIMS). Patients with urinary tract infections, active or previous

malignancies, or anemia, those that used antibiotics or non-steroidal anti-inflammatory drugs before the biopsy, and those with pathology results being reported as prostatic intraepithelial neoplasia, and acute or chronic prostatitis were not included in the study.

For all the patients included in the study, age, hemogram parameters [hemoglobin (Hgb), lymphocyte and monocyte counts], free PSA-total PSA, biopsy pathologies, and presence of comorbidities (hypertension, diabetes, cardiovascular disease, and hyperlipidemia) were recorded. The Gleason score (GS) of the patients with PCa according to the pathology results was determined by the pathologists of our hospital based on the 2005 International Society of Urological Pathology Consensus Conference. Patients with a GS of 3+4 and above were defined as having csPCa while other PCa cases were defined as having clinically non-significant PCa (non-csPCa).

Statistical analysis:

The data were examined with the Shapiro-Wilk test to determine whether they represented a normal distribution. The results were presented as mean \pm standard deviation, interquartile range (IQR) median (minimum-maximum), or frequency and percentages. Normally distributed data were compared with the independent-samples t-test or the Mann Whitney U test for non-normally distributed data. Categorical variables were compared between groups using Pearson's chi-square test and Fisher's exact test. The logistic regression analysis was performed, and the crude odds ratios (ORs) along with their 95% confidence intervals (CIs) were reported. The multivariate binary logistic regression analysis was also undertaken, and the adjusted ORs and 95% CIs were obtained. $p < 0.05$ was considered as the statistical significance level. Statistical analyses were performed using IBM SPSS ver. 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

RESULTS

When the data of the 1,611 patients who underwent a transrectal prostate biopsy were examined, 510 patients were found to be eligible for the study. The flowchart of the study is shown in Figure 1.

The pathology result was reported as PCa in 164 of the 510 patients included in the study and non-PCa in the remaining 346. The monocyte count was significantly higher in the PCa group than in the non-PCa group (0.61 ± 0.33 and 0.53 ± 0.19 , respectively; $p = 0.002$). MLR was also found to be significantly higher in the PCa group than in the non-PCa group (0.35 ± 0.29 and 0.26 ± 0.13 , respectively; $p < 0.001$). In the PCa group, age at diagnosis, total PSA, were statistically significantly higher and f/tPSA was statistically significantly lower compared to the non-PCa group. There was no statistically significant difference between the PCa and non-PCa groups in terms of Hgb, hematocrit (Hct), mean corpuscular volume (MCV), WBC, and lymphocyte values. The percentage of patients with diabetes was significantly higher in the non-PCa group, but there

was no other statistically significant difference in relation to the remaining comorbidities. The clinical characteristics and blood parameters of the PCa and non-PCa groups are shown in Table 1.

Of the 164 patients whose pathology result was reported as PCa, 69 (39%) had csPCa and 95 (61%) had non-csPCa. When these subgroups were analyzed, age at diagnosis, free PSA, and total PSA were found to be statistically significantly higher in the csPCa group, while the f/tPSA value was statistically significantly lower in this group. The subgroup analysis of the patients with PCa revealed no statistically significant difference between the csPCa and non-csPCa groups in terms of the Hgb, Hct, MCV, WBC, lymphocyte, monocyte, and MLR values. Table 2 shows the clinical characteristics and blood parameter of the PCa subgroups (csPCa and non-csPCa). The statistically significant difference observed in the monocyte count and MLR, which were higher in the PCa group compared to the non-PCa group, was not detected in the PCa subgroup analysis.

The receiver-operating characteristic (ROC)-derived area under the curve (AUC) analysis was performed to evaluate the predictive accuracy, and Youden's index was used to determine the optimal cut-off values. The ROC-derived AUC analysis was performed to evaluate the predictive accuracy of the investigated parameters, and Youden's index was used to determine their optimal cut-off values. In the ROC analysis, it was observed that an MLR value of 0.3 provided the maximum Youden index. Therefore, the cut-off value for MLR was set as 0.3. For the likelihood of f/tPSA to predict PCa, the AUC value was determined as 0.665 (95% CI: 0.620-0.709), and at a cut-off value of ≤ 0.15 , it had 55.1% sensitivity and 74.8% specificity. For MLR, the AUC value was calculated as 0.593 (95% confidence interval [CI] 0.549-0.636) for the likelihood of this parameter to predict PCa in all men. When the cut-off value of MLR was taken as > 0.3 , it had a sensitivity of 27.4% and specificity of 85.3%. Lastly, the AUC value of the combination of age, f/tPSA, and MLR in this prediction was determined to be 0.727 (95% CI: 0.684-0.768, sensitivity:

63.0%, specificity: 73.9%).

The logistic regression analysis showed a positive correlation between PCa and age, free PSA, total PSA, monocyte count, and MLR. A negative correlation was found between the presence of diabetes and *f/t*PSA. The remaining hemogram parameters examined in the study (Hgb, Hct, MCV, WBC, and lymphocyte) were not predictors of PCa (Figure 2). According to the multivariate logistic regression analysis, MLR was a significant predictor of PCa, when used together with *f/t*PSA and age ($p < 0.001$). Table 3 presents the results of the univariate and multivariate analyses of the effects of the investigated parameters on PCa detection.

DISCUSSION

The reason for the increased monocyte fraction in PCa cases with a high GS has not yet been clearly defined. In vitro studies of PCa have reported that monocyte-induced cancer cell invasion mediates chemokine ligand 2 (monocyte chemotactic protein-1) and nuclear factor- κ B activity and that tumor stroma-derived factors skew monocyte to dendritic cell differentiation toward a suppressive phenotype.(17) One study showed that tumor-associated macrophages (TAMs), which are putatively derived from serum monocytes, could interact with tumor cells to promote cancer progression by producing a variety of cytokines and chemokines.(18) Another study reported that the infiltration of TAMs in prostate biopsy specimens predicted disease progression in PCa after hormonal therapy.(19) The formation of TAMs in the tumor microenvironment can be accelerated by a high number of monocytes. Conversely, a wide variety of cytokines and chemokines produced by cancer cells can affect the serum monocyte count.(11)

Currently, leukocyte subpopulation tests are frequently used to detect inflammation.(20) Although varying physiological conditions may result in changes in the absolute value of each test, this has little effect on MLR, NLR, and PLR.(21) Based on this idea, a previous study showed that among WBC fraction ratios, NLR was a potential marker to predict PCa.(22) NLR has been widely investigated in

other urological malignancies such as bladder cancer or testicular cancer.(23, 24) A decrease in NLR with BCG treatment was found to be an indicative of the decreased likelihood of recurrence and progression for non-muscle invasive bladder cancer.(24) In a study investigating the role of NLR, PLR, and MLR in predicting PCa, MLR was shown to be the best indicator among the three values.(12) In our study, consistent with the literature, in addition to the monocyte fraction, we found MLR to be statistically higher in the patients with PCa compared to those without cancer. We determined that in the prediction of PCa among patients with high PSA values, rather than using *f/t*PSA (AUC:0.665) alone, the combination of *f/t*PSA with age and MLR increased the likelihood of this prediction (AUC:0.727).

It has been shown that the monocyte ratio in peripheral blood is correlated with GS, and the monocyte ratio is significantly increased in patients with PCa with a high GS, but the underlying mechanism has not yet been clearly revealed.(11) In another recent large series, it was suggested that the lymphocyte-to-monocyte ratio might play an independent predictive role in the detection of csPCa.(4) In the current study, of the patients whose pathology result was reported as PCa, those with a GS of 3+4 and above were accepted as having csPCa, and unlike the literature no statistically significant difference was found between the csPCa group and the non-csPCa group in terms of the monocyte fraction and MLR.

MLR can be expected to become one of the candidate biomarkers for PCa when used together with age and *f/t*PSA. However, further research and validation are still needed to determine whether the serum monocyte fraction is one of the useful biomarkers of PCa and elucidate the association of serum monocytes with the progression of PCa. In addition, future studies should investigate whether it is associated with the stages and prognosis of PCa.

There are some limitations to our study. Due to the retrospective design, hemogram parameters, which were of great importance for this study, could not be accessed in almost half of the patients who underwent a biopsy. Furthermore,

due to our hospital being a reference hospital, the examinations of many patients had been undertaken in another center from which they were referred, but they were not recorded in HIMS. In addition, PSA density, which is a frequently used PSA derivative in the literature, could not be calculated because the prostatic volumes of the patients were not recorded in the form used during the biopsy procedure. Another limitation of our study is that it evaluated data from a single center. In the literature, it is known that there is a statistically significant mismatch between the prostate needle biopsy and radical prostatectomy materials in relation to GS and tumor volume, but this agreement increases as GS and tumor volume increase.(25) Further studies evaluating patients who have undergone radical prostatectomy can contribute to the literature by better presenting the difference between the patients with csPCa and non-csPCa.

CONCLUSION

We determined that the serum monocyte fraction and MLR were significantly increased in patients with PCa compared to patients with benign prostate pathologies. However, the monocyte fraction and MLR were not adequate in the differentiation between the csPCa and non-csPCa subgroups. In patients undergoing a biopsy, an MLR value above 0.3 can predict the pathology result being reported as PCa at a sensitivity of 27.4% and specificity of 85.3%.

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References

1. Huang TB, Zhu LY, Zhou GC, Ding XF. Pre-treatment red blood cell distribution width as a predictor of clinically significant prostate cancer. *International urology and nephrology*. 2021;53(9):1765-71.
2. Fujita K, Nonomura N. Urinary biomarkers of prostate cancer. *International journal of urology : official journal of the Japanese Urological Association*. 2018;25(9):770-9.
3. Stabile A, Giganti F, Rosenkrantz AB, Taneja SS, Villeirs G, Gill IS, et al. Multiparametric MRI for prostate cancer diagnosis: current status and future directions. *Nature reviews Urology*. 2020;17(1):41-61.
4. Cho MC, Yoo S, Choo MS, Son H, Jeong H. Lymphocyte-to-monocyte ratio is a predictor of clinically significant prostate cancer at prostate biopsy. *The Prostate*. 2021;81(16):1278-86.
5. Başer A, Aydın C, Çelikörs B, Başer HY, Baykam MM, Alkış O. PSA seviyesi 4-10 ng/mL olan hastalarda alt üriner sistem semptomları patoloji sonucunu ön görebilir mi? *Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi*. 2020;53(2):81-4.
6. Siegel RL, Miller KD, Jemal A. *Cancer statistics, 2018*. CA: a cancer journal for clinicians. 2018;68(1):7-30.
7. Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? *Lancet (London, England)*. 2001;357(9255):539-45.
8. Coussens LM, Werb Z. *Inflammation and cancer*. *Nature*. 2002;420(6917):860-7.
9. Fujita K, Imamura R, Tanigawa G, Nakagawa M, Hayashi T, Kishimoto N, et al. Low serum neutrophil count predicts a positive prostate biopsy. *Prostate cancer and prostatic diseases*. 2012;15(4):386-90.
10. Caruso C, Balistreri CR, Candore G, Carruba G, Colonna-Romano G, Di Bona D, et al. Polymorphisms of pro-inflammatory genes and prostate cancer risk: a pharmacogenomic approach. *Cancer immunology, immunotherapy : CII*. 2009;58(12):1919-33.
11. Hayashi T, Fujita K, Tanigawa G, Kawashima A, Nagahara A, Ujike T, et al. Serum monocyte fraction of white blood cells is increased in patients with high Gleason score prostate cancer. *Oncotarget*. 2017;8(21):35255-61.
12. Xu Z, Zhang J, Zhong Y, Mai Y, Huang D, Wei W, et al. Predictive value of the monocyte-to-lymphocyte ratio in the diagnosis of prostate cancer. *Medicine*. 2021;100(38):e27244.
13. Augier S, Ciucci T, Luci C, Carle GF, Blin-Wakkach C, Wakkach A. Inflammatory blood monocytes contribute to tumor development and represent a privileged target to improve host immunosurveillance. *Journal of immunology (Baltimore, Md : 1950)*. 2010;185(12):7165-73.
14. Gabrilovich DI, Nagaraj S. Myeloid-derived suppressor cells as regulators of the immune system. *Nature reviews Immunology*. 2009;9(3):162-74.
15. Wang L, Long W, Li PF, Lin YB, Liang Y. An Elevated Peripheral Blood Monocyte-to-Lymphocyte Ratio Predicts Poor Prognosis in Patients with Primary Pulmonary Lymphoepithelioma-Like Carcinoma. *PLoS one*. 2015;10(5):e0126269.
16. Nishijima TF, Muss HB, Shachar SS, Tamura K, Takamatsu Y. Prognostic value of lymphocyte-to-monocyte ratio in patients with solid tumors: A systematic review and meta-analysis. *Cancer treatment reviews*. 2015;41(10):971-8.
17. Lindholm PF, Sivapurapu N, Jovanovic B, Kajdacsy-Balla A. Monocyte-Induced Prostate Cancer Cell Invasion is Mediated by Chemokine ligand 2 and Nuclear Factor-kappaB Activity. *Journal of clinical & cellular immunology*. 2015;6(2).
18. Mantovani A, Bottazzi B, Colotta F, Sozzani S, Ruco L. The origin and function of tumor-associated macrophages. *Immunology today*. 1992;13(7):265-70.
19. Nonomura N, Takayama H, Nakayama M, Nakai Y, Kawashima A, Mukai M, et al. Infiltration of tumour-associated macrophages in prostate biopsy specimens is predictive of disease progression after hormonal therapy for prostate cancer. *BJU international*. 2011;107(12):1918-22.
20. Weitzmann MN, Ofotokun I. Physiological and pathophysiological bone turnover - role of the immune system. *Nature reviews Endocrinology*. 2016;12(9):518-32.
21. Huang Y, Liu A, Liang L, Jiang J, Luo H, Deng W, et al. Diagnostic value of blood parameters for community-acquired pneumonia. *International immunopharmacology*. 2018;64:10-5.
22. Kawahara T, Fukui S, Sakamaki K, Ito Y, Ito H, Kobayashi N, et al. Neutrophil-to-lymphocyte ratio predicts prostatic carcinoma in men undergoing needle biopsy. *Oncotarget*. 2015;6(31):32169-76.
23. Gokcen K, Dunder G, Gulbahar H, Gokce G, Gultekin EY. Can routine peripheral blood counts like neutrophil-to-lymphocyte ratio be beneficial in prediagnosis of testicular cancer and its stages? *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences*. 2018;23:64.
24. Baser A. Does the Decrease in Neutrophil-lymphocyte Ratio after BCG Treatment Be a Prognostic Marker for NMIBC? *Journal of Urological Surgery*. 2020;7(4):271-6.
25. Yeldir N, Yildiz E, DüNDAR G. Gleason score correlation between prostate needle biopsy and radical prostatectomy materials. *Turkish Journal of Pathology*. 2019;35(3):185-92.