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Does Platelet Mass Index Play a Role in Predicting Biochemical Recurrence in Localized Prostate Cancer?

Lokalize Prostat Kanserinde Trombosit Kitle İndeksinin Biyokimyasal Nüksü Öngörmede Yeri Var mıdır?

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What's known on the subject? and What does the study add?

The literature data used to predict early recurrence of localized prostate cancer need to be expanded, but studies should be continued.

Abstract

Objective: The aim of this study is to investigate the association of preoperative platelet mass index (PMI) with tumor pathologic features and postoperative biochemical recurrence in patients undergoing radical prostatectomy due to localized prostate cancer.

Materials and Methods: Data of 141 patients, who underwent radical prostatectomy for localized prostate cancer between April 2004 and April 2017, were retrospectively screened. Patient age, preoperative prostate-specific antigen (PSA) level, platelet count, mean platelet volume and PMI value, neutrophil-lymphocyte ratio (NLR), tumor grade, Gleason score, tumor volume, lymph node involvement, surgical margin positivity and biochemical recurrence at 3 months were all noted. The relationship of preoperative PMI value with age, PSA, pathologic parameters, surgical margin positivity and biochemical recurrence was evaluated.

Results: The mean age of the patients was 61.79±5.98 years, the mean PSA value was 9.50±6.69 ng/mL, mean PMI was 2003.91±486.69, and the mean NLR was 2.79±2.06. There was no correlation of PMI value with PSA, pathological stage, Gleason score, lymph node involvement, tumor volume, surgical margin positivity, and biochemical recurrence. There was statistically significant negative correlation between PMI and Gleason score.

Conclusion: In our study, we could not demonstrate preoperative PMI as a prognostic factor for early biochemical recurrence in patients undergoing radical prostatectomy for prostate cancer. To achieve a better conclusion that we can generalize, there is a need for prospective studies with larger patient series.

Keywords: Platelet mass index, Inflammation, Prostate cancer

Öz

Amaç: Bu çalışmanın amacı, lokalize prostat kanseri nedeniyle radikal prostatektomi yapılan hastalarda preoperatif trombosit kitle indeksi (PMI) ile tümörün patolojik özellikleri ve postoperatif biyokimyasal nüks arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: Nisan 2004 ile Nisan 2017 arasında lokalize prostat kanseri nedeniyle radikal prostatektomi yapılan 141 hastanın verileri retrospektif olarak tarandı. Hastaların yaş, preoperatif prostat spesifik antijen (PSA), trombosit sayısı, ortalama trombosit hacmi ve PMI değerleri, N/L oranı, tümör evresi, Gleason skoru, tümör hacmi, lenf nodu tutulumu, cerrahi sınır pozitifliği ve 3. ayda biyokimyasal nüks olup olmadığı kaydedildi. Ameliyat öncesi PMI değerinin yaş, PSA, patolojik parametreler, cerrahi sınır pozitifliği ve biyokimyasal nüks ile olan ilişkisi incelendi.

Bulgular: Hastaların yaş ortalaması 61,79±5,98 yıl, ortalama PSA değeri 9,50±6,69 ng/mL, ortalama PMI değeri 2003,91±486,69 ve ortalama N/L oranı 2,79±2,06 idi. PMI değeri ile PSA, patolojik evre, Gleason skoru, lenf nodu tutulumu, tümör hacmi, cerrahi sınır pozitifliği, biyokimyasal nüks arasında bir korelasyon izlenmedi. PMI ile Gleason skoru arasında istatistiksel olarak anlamlı negatif korelasyon izlendi.

Sonuç: Çalışmamızda prostat kanseri nedeniyle radikal prostatektomi uygulanmış hastalarda ameliyat öncesi PMI değerini, erken biyokimyasal nüks için prognostik bir faktör olarak gösteremedik. Genelleme yapabileceğimiz daha iyi bir sonuç elde etmek için, daha geniş hasta serileri ile prospektif olarak tasarlanmış çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Trombosit kitle indeksi, Enflamasyon, Prostat kanseri

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Introduction

Although prostate cancer is now accepted as an important cause of male deaths, the mystery over the behavior of cancer cells is still ongoing. Prostate-specific antigen (PSA) screening can be used in the diagnosis of early-stage prostate cancer, but the pathological features of cases undergoing radical surgery continue to be questioned. For this reason, there is still a need to update the information on prostate cancer. The relationship between cancer formation and inflammation has become a very interesting subject nowadays and the evidence about the link between these two conditions is increasing day by day. It has been shown that increased angiogenesis as a result of inflammation caused by infection, autoimmunity, chronic irritation, and tumor and resulting from treatments, contributes to carcinogenesis (1). The relationship between tumor survival and inflammation has been tried to be shown using neutrophil-lymphocyte ratio (NLR) in many cancer types. It is known that platelets play an important role not only in achieving hemostasis but also in inflammatory reactions and in immunological responses (2,3,4,5). Mean platelet volume (MPV) has been previously reported to be a marker of platelet activation, but, recently, platelet mass index (PMI) calculated by multiplying platelet count by MPV was claimed to be a better parameter of inflammation than MPV in a study (6,7).

In this retrospective study, we aimed to investigate the association of preoperative PMI with tumor pathologic features and postoperative biochemical recurrence in patients undergoing radical prostatectomy due to localized prostate cancer.

Materials and Methods

Data of patients, who underwent radical prostatectomy for localized prostate cancer at Zonguldak Bülent Ecevit University, Health Practice and Research Center, Clinic of Urology between April 2004 and April 2017 by four expert surgeons in urooncology, were retrospectively screened following the approval of Bülent Ecevit University Local Ethics Committee (protocol number: 2018-23-17/01). Using hospital records, patients' age, preoperative PSA, platelet count, MPV and PMI value, NLR, tumor grade, Gleason score, tumor volume, lymph node involvement, surgical margin positivity, and biochemical recurrence at 3 months were analyzed. A total of 141 patients with written consent and at least 6 months of follow-up were included in the study. PMI value was examined in relation to age, PSA, pathologic parameters, surgical margin positivity and biochemical recurrence. Biochemical recurrence was accepted when an additional treatment started at the third month control with an increase of PSA value or if there was a persistent increase in PSA value at the 6th month control.

Statistical Analysis

Mean, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of the variables was measured by the Kolmogorov-Smirnov test. The Kruskal-Wallis test and the Mann-Whitney U test were used in the analysis of quantitative independent data. In correlation analysis, the Spearman correlation coefficient was used. SPSS 18.0 program was used for statistical analysis.

Results

The mean age of the patients was 61.79±5.98 years, the mean PSA value was 9.50±6.69 ng/mL, the mean PMI was 2003.91±486.69, and mean NLR was 2.79±2.06. The preoperative data of the patients are summarized in Table 1. The mean tumor volume was 9.20±8.42 cm^3. Four (2.8%) patients had lymph node involvement, while 66 (47.6%) patients had positive surgical margin; 25 (17.5%) patients had biochemical recurrence at the third month control. The distribution of patients according to preoperative PSA levels and pathologic variables is shown in Table 2. The relationship between surgical margin involvement and histopathological findings is shown in Table 3. There was no correlation of PMI value with PSA, pathological stage, Gleason score, lymph node involvement, tumor volume, surgical margin positivity, and biochemical recurrence (Table 4). The correlation of NLR with PSA, pathological stage, Gleason score, lymph node involvement, tumor volume, surgical margin positivity, and biochemical recurrence is shown in Table 5. NLR was statistically significantly lower in lymph node-positive patients. Analysis of correlation between NLR and age, PSA, Gleason score and tumor volume and between PMI and age, PSA, Gleason score and tumor volume are shown in Table 6. There was a statistically significant negative correlation between PMI and Gleason score.

Table 1. Preoperative data of the patients

	Min	Max	Mean ± SD
Age (year)	42	74	61.79±5.98
Total PSA (ng/mL)	2.41	36.72	9.50±6.69
Platelet count (K/µL)	130	461	243.02±66.13
MPV (fL)	6.7	11.5	8.3±0.93
PMI	962	3558.3	2003.91±486.69
Neutrophil count (K/µL)	0.6	17.2	4.96±2.25
Lymphocyte count (K/µL)	0.5	4.6	2.07±0.72
NLR	0.31	17.20	2.79±2.06
Tumor volume (cm^3)	0.12	38.5	9.20±8.42

PSA: Prostate-specific antigen, MPV: Mean platelet volume, PMI: Platelet mass index, NLR: Neutrophil-lymphocyte ratio, Min: Minimum, Max: Maximum, SD: Standard deviation

Table 2. The distribution of patients according to preoperative prostate-specific antigen levels and pathologic variables

		n	%
PSA (ng/mL)			
	0-4	4	2.8
	4-10	95	66.4
	10-20	30	21.0
	20<	12	8.5
Clinical stage			
	T2a	21	14.7
	T2b	11	7.7
	T2c	42	29.4
	T3a	55	38.5
	T3b	12	8.4
Surgical margin			
	Negative	75	52.4
	Apex	29	20.3
	Basal	12	8.4
	Multifocal	25	17.5
Lymphovascular invasion			
	Negative	123	86.0
	Positive	17	11.9
Perineural invasion			
	Negative	51	35.7
	Positive	90	62.9
Seminal vesicle invasion			
	Negative	128	89.5
	Positive	13	9.1
Lymph node invasion			
	Negative	137	95.8
	Positive	4	2.8
Third month biochemical recurrence			
	No	116	81.1
	Yes	25	17.5

PSA: Prostate-specific antigen

Discussion

It is known that the development of tumor cells in our body activates an inflammatory response. Systemic inflammation also suppresses the anti-tumor immune system, thus facilitating cancer progression and metastasis (8,9,10,11,12,13). Previously, biomarkers of inflammation, such as NLR, platelet-lymphocyte ratio and C-reactive protein, have been shown to be valuable prognostic factors in many cancers (8,10,11,12,14,15,16,17). During the inflammatory process, many mediators that activate thrombocytes are released. Platelets secrete various growth factors that support angiogenesis, cell proliferation and metastasis (15,16,17,18,19). Tumor-associated thrombocyte aggregation forms a barrier against T-cells by forming a protective shield around the tumor cells (20,21).

While localized prostate cancer treatment and follow-up schemes are created, many biochemical and pathological data are benefited from. Prostate cancer may show differences between treatment strategies when cases become resistant to castration. Thus, the idea of using simple blood tests to guide the experts is available for a long time. NLR is the most studied parameter for this purpose. However, in the literature, we have not seen any study evaluating such a relationship with PMI in prostate cancer.

In our study comparing the NLR with preoperative PSA value, pathologic data and the presence of biochemical recurrence in patients with localized prostate cancer undergoing radical prostatectomy, NLR was lower in lymph node-positive patients and it was statistically significant. Unlike our work, a significant correlation was found between high NLR and lymph node positivity in a study with 1688 patients performed by Zhang et al. (22). However, in their study with 217 cases, Kwon et al. (23) found a positive relationship only between NLR and Gleason score. On the other hand, we did not observe a relationship with other parameters.

PMI is a biomarker that has recently attracted the attention of researchers. In the first study about PMI, it has been reported that unnecessary platelet transfusions in neonatal intensive care units could be prevented (24,25,26,27). There is an inverse

Table 3. Distribution of histopathological findings with surgical margin involvement

		Surgical margin involvement n (%)*				
		Non	Apex	Basal	Multifocal	p
Gleason score	5-6	51 (68.0)	13 (17.3)	5 (6.7)	6 (8.0)	0.003
	7	22 (40.0)	13 (23.6)	6 (10.9)	14 (25.6)	
	8 and above	2 (18.2)	3 (27.3)	1 (9.1)	5 (45.5)	

*Percentages are given in parentheses, p<0.05

Table 4. Correlation between platelet mass index value and biochemical and pathological variables

PMI					
		Min-max	Median	Mean ± SD	p*
PSA (ng/mL)	0-4	1579-2456	1789	1903±384	0.588
	4-10	962-3558	1923	1989±502	
	10-20	1340-2978	1899	1985±412	
	20<	1235-3091	2097	2202±571	
Clinical stage	T2	1047-3273	1938	2017±442	0.548
	T3	962-3558	1913	1990±534	
Gleason	5-6	962-3558	2049	2077±497	0.157
	7	1066-3091	1847	1922±476	
	8<	1322-2468	2009	1915±423	
Tumor volume (cm^3)	≤5	962-3273	1962	2013±459	0.533
	5<	1066-3558	1908	2007±509	
Surgical margin	(-)	1047-3273	1938	2003±432	0.968
	(+)	962-3558	1877	2005±546	
Lymph node invasion	(-)	962-3558	1932	2009±491	0.164
	(+)	1448-1883	1742	1704±186	
Biochemical recurrence	(-)	962-3558	1918	2005±492	0.929
	(+)	1235-3091	1998	2032±468	

PSA: Prostate-specific antigen, PMI: Platelet mass index, Min: Minimum, Max: Maximum, SD: Standard deviation
*p<0.05

Table 5. Correlation between neutrophil-lymphocyte ratio and biochemical and pathological variables

NLR					
		Min-max	Median	Mean ± SD	p*
PSA (ng/mL)	0-4	1.6-3.5	2.04	2.31±0.82	0.920
	4-10	0.32-17.2	2.25	2.87±2.33	
	10-20	0.87-7.22	2.09	2.61±1.49	
	20<	1.09-5.07	2.54	2.88±1.37	
Clinical stage	T2	0.32-9.6	2.43	2.89±1.98	0.444
	T3	0.91-17.2	2.07	2.7±2.17	
Gleason	5-6	0.88-9.6	2.41	2.81±1.66	0.433
	7	0.32-17.2	2	2.88±2.66	
	8<	1-4.18	2.09	2.31±0.95	
Tumor volume (cm^3)	≤5	0.91-9.6	2.17	2.76±1.71	0.835
	5<	0.32-17.2	2.22	3.03±2.3	
Surgical margin	(-)	0.78-9.6	2.33	2.73±1.73	0.882
	(+)	0.32-17.2	2.1	2.87±2.41	
Lymph node invasion	(-)	0.32-17.2	2.23	2.83±2.08	0.02
	(+)	1-1.96	1.24	1.36±0.44	
Biochemical recurrence	(-)	0.32-17.2	2.2	2.9±2.18	0.688
	(+)	1.09-6.56	2.11	2.84±1.48	

PSA: Prostate-specific antigen, NLR: Neutrophil-lymphocyte ratio, Min: Minimum, Max: Maximum, SD: Standard deviation
*p<0.05

Table 6. Analysis of correlation between neutrophil-lymphocyte ratio and platelet mass index value

		Age	PSA	Gleason	Tumor volume
NLR	r	-0.003	0.036	-0.99	-0.002
	p	0.972	0.674	0.242	0.985
		Age	**PSA**	**Gleason**	**Tumor volume**
PMI	r	-0.119	0.005	-0.16	-0.037
	p	0.158	0.95	0.049	0.667

PSA: Prostate-specific antigen, NLR: Neutrophil-lymphocyte ratio, PMI: Platelet mass index
Spearman correlation coefficient

relationship between platelet count and platelet volume in order to keep PMI stable, and therefore platelet activity at a constant value. Apart from PMI value, high MPV value and larger platelet diameter were found to be associated with increased platelet activity (28).

It is seen in the literature that MPV has different prognostic significance in different cancers. However, how MPV values affect prognosis remains to be discussed. High MPV value is significant in breast and hepatocellular carcinomas, but it gains significance when decreasing in lung cancer (29,30,31,32,33). It is not possible to reach a definite result with MPV today. Elevation in platelet count was found to be associated with metastasis development and poor prognosis in some solid cancers (34,35). This is being explained by the overproduction of megakaryocyte colony-stimulating cytokines (36). On the other hand, it has been also claimed that platelets act as a protective shield against circulating tumor cells (37). Takeuchi et al. (38,39) showed that the higher the platelet counts and platelet-lymphocyte ratio the poorer the prognosis of breast cancer. The prognostic value of increase in the number of platelets in renal cell carcinoma cases has also been investigated, but the results were different from each other (36).

In this pioneer study, a negative correlation between PMI and Gleason score was found which was to be statistically significant. We assume that the low number of patients may be misleading. We did not observe a statistically significant difference between PMI values and biochemical recurrence among patients.

Study Limitations

There were some limitations in this study. First, the retrospective nature of the study makes it difficult to obtain generalizable results. The lack of long-term follow-up results of patients was the other limitation of this study. The low number of patients treated at a single institution also weakens the power of influence of the study.

Conclusion

Our study demonstrates that preoperative PMI is not a prognostic factor for early biochemical recurrence in patients undergoing radical prostatectomy for prostate cancer. When the literature is examined, it is emphasized that platelet count and platelet volume may be prognostic factors in some advanced cancers. To achieve the same result for PMI values in prostate cancer, there is a need for prospective studies with larger patient series.

Ethics

Ethics Committee Approval: This study was approved by Bülent Ecevit University Local Ethics Committee (protocol number: 2018-23-17/01).

Informed Consent: Written consent was taken from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.G., E.B., Ö.Ç., Concept: R.G., Design: R.G., Data Collection or Processing: C.F.Ö., E.B., Analysis or Interpretation: R.G., E.B., Ö.Ç., Literature Search: C.F.Ö., Writing: R.G.

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