

Trombosit İndekslerinin Meme Kanseri Prognozuna Etkileri

Effects of Platelet Indices on Breast Cancer Prognosis

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Özet: Amaç: Trombosit sayısı (PLT), trombosit dağılım genişliği (PDW), ortalama trombosit hacmi (MPV) ve trombositkriti (PCT) içeren trombosit indekslerinin yaşa göre değerini değerlendirmek ve meme kanseri (MK) ile ilişkisini belirlemek. **Yöntem:** Etik Kurul'dan 05.07.2022 tarih ve 2022/95 sayılı izinler alındı. Çalışmaya 01/01/2015-10/06/2022 tarihleri arasında Şırnak devlet hastanesine başvuran meme kanserli 68 hasta dahil edildi. Hastaların Trombosit İndeks düzeyleri hastane kayıt sisteminden retrospektif olarak taranarak yapıldı. Hastalar 18-45 ve 46-90 yaş grubu olarak iki gruba ayrıldı. Verilerin analizinde SPSS 21.0 paket programı kullanıldı. $p < 0.05$ anlamlı kabul edildi. **Bulgular:** Yaşa göre trombosit sayısı, MPV, PDW ve PCT grupları arasında istatistiksel olarak farklılık göstermedi. Ancak MPV, PDW ve PCT ortalamalarının 18-45 yaş aralığında, ortalama trombosit sayısının ise 46-90 yaş aralığında daha yüksek olduğu belirlendi. PLT, MPV, PDW, PCT sırasıyla ($p=0,917$, $p=0,159$, $p=0,419$, $p=0,285$) bulundu. 18-45 yaş arası hastalarda PDW ile MPV arasında orta derecede güçlü pozitif korelasyon ($r=0.546$), PCT ile PLT arasında yüksek-güçlü pozitif korelasyon ($r=0.828$) ve zayıf-güçlü pozitif korelasyon ($r=0.370$) vardı. PCT ve MPV arasında 46-90 yaş arası hastalarda PCT ile PLT arasında anlamlı bir pozitif korelasyon ($r=0.872$) bulundu. **Sonuç:** MK'nin trombosit sayısı ve hacmi üzerinde etkisi olmadığı söylenemez; MK'ye bağlı inflamasyonun trombosit indeksleri üzerindeki zıt (hem artırıcı hem de azaltıcı) etkilerinin kombinasyonu nedeniyle, MK'li hastaların trombosit indekslerinde kantitatif olarak anlamlı bir değişiklik olmadığı şeklinde bir yorum yapmanın daha uygun olacağını düşünüyoruz.

Anahtar Kelimeler: Meme kanseri, MPV, PDW, Platelet, Yaş.

Abstract: Objective: To assess the importance of platelet indices such as platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) in connection to age and to ascertain their relationship to breast cancer (BC). **Methods:** Permissions dated 05.07.2022 and numbered 2022 /95 were obtained from the Ethics Committee. 68 patients with breast cancer who applied to Şırnak state Hospital between 01/01/2015 and 10/06/2022 were included in the study. The patients' Platelet Index levels were performed by retrospectively screening from the hospital registry system. The patients were split into two groups 18-45 and 46-90 age groups. SPSS 21.0 package program was used in the analysis of the data. $p < 0.05$ was considered significant. **Results:** Platelet count for age did not differ statistically between MPV, PDW and PCT groups. However, it was determined that the mean of MPV, PDW and PCT were higher in the 18-45 age range, and the mean platelet count was higher in the 46-90 age range. PLT, MPV, PDW, and PCT were found, respectively ($p=0.917$, $p=0.159$, $p=0.419$, $p=0.285$). Patients aged 18-45 years had a moderately strong positive correlation ($r=0.546$) between PDW and MPV, a high-strong positive interaction ($r=0.828$) between PCT and PLT, and a weak-strong positive correlation ($r=0.370$) between PCT and MPV. A substantial interaction ($r=0.872$) was found between PCT and PLT for patients aged 46-90 years. **Conclusion:** It's not that BC has no impact on platelet volume and number; We think that it would be more appropriate to interpret that there is no quantitatively important change in the platelet indices of patients with BC due to the combination of opposing (both increasing and decreasing) effects of inflammation due to BC on platelet indices.

Keywords: Breast cancer, MPV, PDW, Platelet, Age.

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INTRODUCTION

Breast cancer (BC) is the most common form of cancer diagnosed in women and the second greatest cause of death from cancer (Fahad,2019). BC is responsible for 18% of all deaths in women from cancer. Although BC is rarely seen in women under the age of 30, it is known that it increases more rapidly in the years following this age and this increase continues to increase slowly after menopause (Ozmen,2014; Çakır et al, 2016). When the results obtained from BC incidence and epidemiological studies are examined, it is seen that not a single factor is responsible for the formation of breast cancer, but there are many risk factors (Yıldız,2014; Rojas and Stuckey,2016).

When the results obtained from BC incidence and epidemiological studies are examined, it is seen that not a single factor is responsible for the formation of breast cancer, but there are many risk factors (Yıldız,2014; Rojas and Stuckey,2016). These risk variables include racial and ethnic diversity, age at first menstruation, number of live births, age at first live birth, age at menopause, and reproductive history. Family history has also been linked to an increased risk of BC (Koça et al., 2011). In addition to all these factors, studies are showing that inflammation might play an significant role in cancer progression and metastasis through platelets (Menter et al, 2017). This study's objective is to assess the significance of platelet indices such as platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) in relation to age and to ascertain their relationship to BC.

MATERIALS AND METHODS

Approval for this study, dated 05.07.2022 and numbered 2022/95, was obtained from a state university ethics committee. 68 breast cancer patients who applied to Şırnak state hospital between 01/01/2015-10/06/2022 were included in

the study. Data were collected retrospectively in the automation system of the hospital. Patients' Platelet Index levels were determined using a retrospective review of the hospital registration system. The patients were split into two age groups: 18–45 and 46–90. The relationship of platelet indices according to these two groups was investigated. Platelet indices were obtained by measuring PCT, PDW and MPV values using a hemogram device (Sysmex Corporation, Kobe, Japan).

Statistical analysis

SPSS 21.0 package program was used for statistical analysis. The conformity of the data to the normal distribution was examined with the Kolmogorov-Smirnov test. With the Student's t-test, statistical analysis was performed. The data were displayed as mean \pm standard error. To ascertain the correlation between the platelet indices, Pearson correlation analysis was used. A value of $P < 0.05$ was considered significant.

RESULTS

There was no statistical difference between PLT, MPV, PDW and PCT groups according to age, respectively ($p=0.917$, $p=0.159$, $p=0.419$, $p=0.285$). However, it was found that the mean of MPV, PDW, and PCT was higher in the 18-45 age range, and the mean PLT was higher in the 46-90 age range (Table 1). PDW and MPV were found to have a moderately strong positive association ($r=0.546$), PLT and PCT to have a high-strong high association ($r=0.828$), and PCT and MPV to have a weak-strong high association ($r=0.370$) in individuals between the ages of 18 and 45. (Table 2 and Figure 1). Significant correlation of patients aged between 46-90 years A high strong positive correlation ($r=0.872$) was found between PCT and PLT. (Table 3 and Figure 2).

Table 1: Mean platelet indices by age

Parameters	18-45 age	46-90 age	P
PLT(THSD/CU)	273,47±11,47	275,25±12,41	0,917
MPV(fL)	9,47±0,24	9,06±0,17	0,159
PDW(fL)	13,65±0,44	13,08±0,53	0,419
PCT(%)	0,27±0,01	0,25±0,01	0,285

PLT: Platelet count; MPV: Mean platelet volume; Pct: Plateletcrit; PDW: Platelet distribution width

Table 2: Correlation table for data between 18-45 years old

	MPV	PDW	PCT
PLT	,040	-,135	,828*
MPV		,546*	,370*
PDW			-,046

*Correlation is significant at the 0.05 level (2-tailed).

Table 3: Correlation table for 46-90 age data

	MPV	PDW	PCT
PLT	-,227	,035	,872*
MPV		,146	,112
PDW			-,092

*Correlation is significant at the 0.05 level (2-tailed).

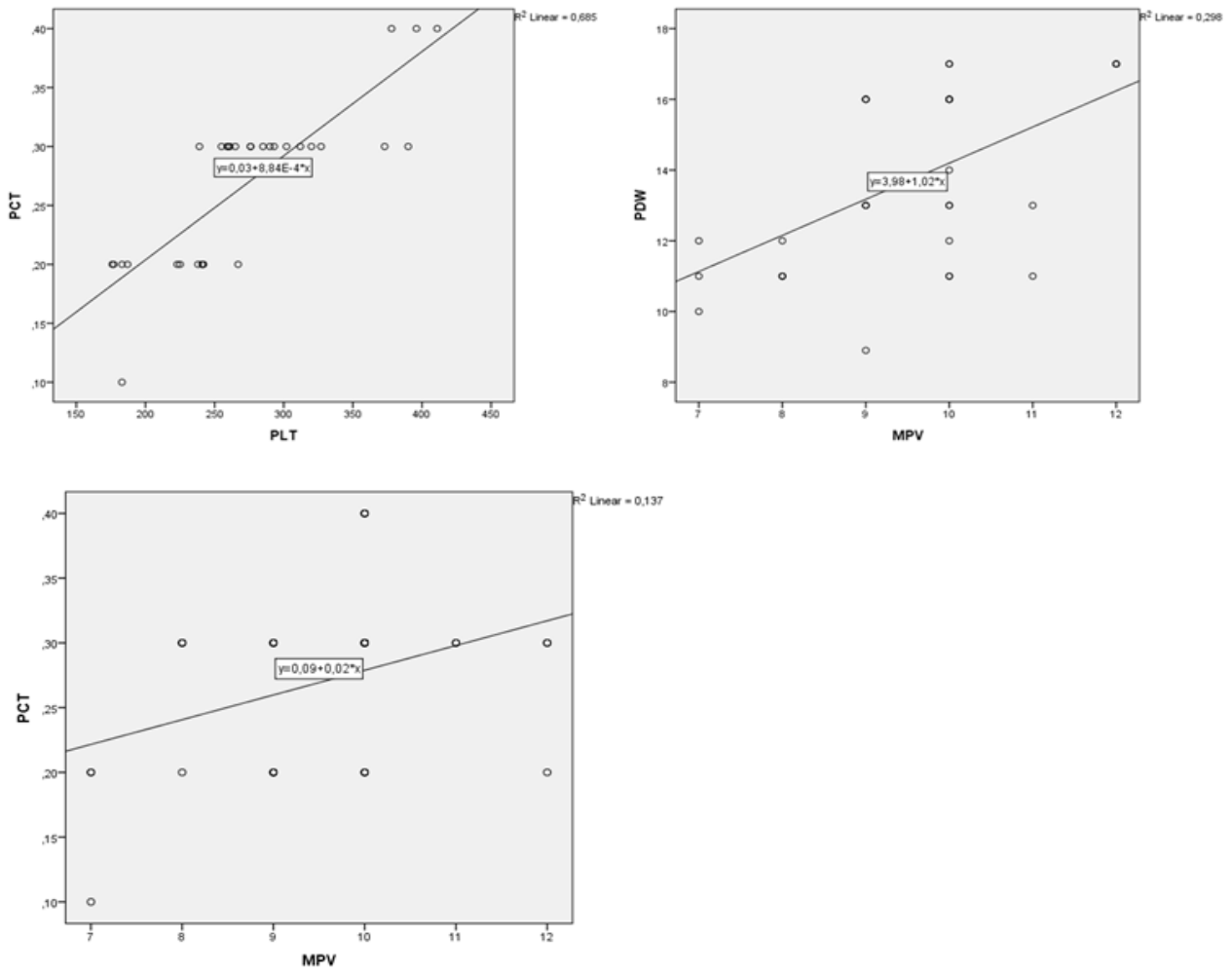


Figure 1: Correlation graphs for the 18-45 age range

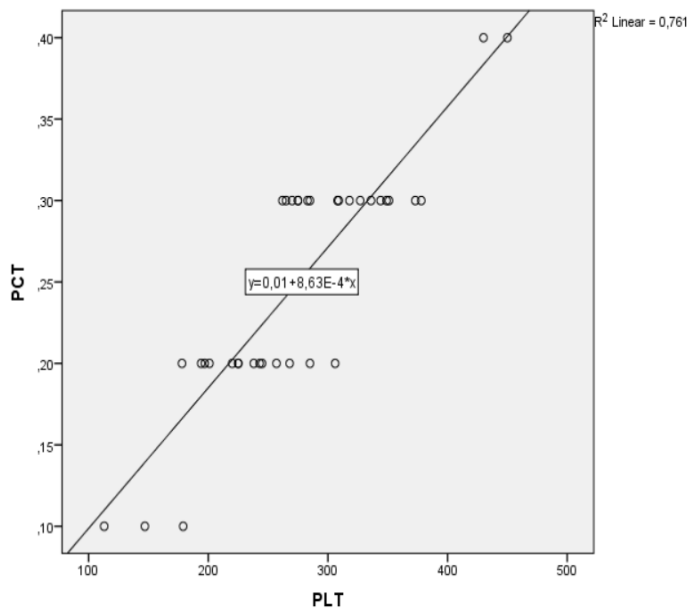


Figure 2: Correlation graph for the age range of 46-90

DISCUSSION

In this investigation, there was no discernible variation in platelet count, mean platelet volume, plateletcrit, or platelet distribution width between the age groups. Recently, it has been established that platelet indices are helpful indicators in several malignancies (Mezouar et al, 2016). It has been reported that there is a bidirectional interaction between platelets and cancer. The development of cancer is said to involve every stage, including platelet activation, aggregation, and activated platelets (Mezouar et al, 2016).

Long-term inflammation has been linked in studies to the growth and development of malignancies (Grivennikov et al, 2010; Wu et al, 2014). In our study, it is noteworthy that the tendency to decrease in platelet count in the 18-45 age group is more pronounced than in the 46-90 age group. However, there was no significant statistical change. In addition, the total platelet count in the 46-90 age group tended to be higher than in the 18-45 age group. The reason for this is also some platelet consumption occurs in the inflammatory area, and on the other hand, there may be an increase in production in the bone marrow that exceeds the consumption amount. Inflammation in breast cancer may partly explain the decreasing trend in

observed to cause heterogeneity in platelet volume (Paulus,1981). In our study, the mean PDW in the 18-45 age group was found to be higher than the average in the 46-90 age range. The reason for this may be that malignant rates are higher in patients between the ages of 18-45 compared to the rates of patients between the ages of 46-90.

The reason why we could not find a significant difference in PDW levels in the 18-45 age group compared to the 46-90 age group in our study may be due to the consumption of large-volume platelets in the inflammation area as well as the large-volume young platelets produced in the bone marrow. Looking at the literature, fu et al. reported that the PDW value of the malignant group was higher than the benign group (Fu et al, 2017). In

thrombopoietin (TPO) levels. Because more platelets can internalize TPO in plasma and lower blood levels of TPO (Kaushansky, 2015).

Hematological parameters, and noninvasive routine blood test, have also been used as markers for systemic inflammatory response for a long time (Bozan et al, 2016). Sun et al. conducted on the clinical importance of the inflammatory index related to routine blood test in MC patients, the mean platelet count in groups aged below 50 years and above was 207.50 ± 54.24 for those under 50 years of age, 205.20 ± 52.43 for those above 50 years of age, and for those below 50 years of age for MPV. They reported 9.12 ± 1.20 for those over 50 years of age as 9.10 ± 1.35 (Sun et, 2017). In our study, we found a mean platelet count of 273.47 ± 11.47 in the 18-45 age group, and 275.25 ± 12.41 in the 46-90 age group.

For MPV, it was found 9.47 ± 0.24 in the 18-45 age group and 9.06 ± 0.17 in the 46-90 age group. We think that the reason for the difference in the number of platelets will depend on the stages. There is yet no established mechanism to explain how PDW functions in MC. Affected PDW may be caused by the dysregulation of bone marrow cells, especially megakaryocytes. Platelet heterogeneity is quantified by platelet distribution width. Megakaryocyte heterogeneous limitation has been another study, it was reported that PDW is an effective and appropriate indicator of cancer prognosis. In the same study, they also pointed out that PDW differs in young and old individuals (Xia et al, 2018). PCT is the total volume occupied by platelets in the blood and is expressed as a percentage (%).

It is known that in cases affecting platelet count and MPV, plateletcrit will change (Budak et al,2016; Sirois ,2014). In our study, the mean PCT in the 18-45 age group was found to be higher than the average in the 46-90 age group. We think that this situation is due to the relationship between cancer stages, as we have stated above. In our study, there was a moderately strong positive correlation ($r=0.546$) between PDW and MPV in patients aged

18-45 years. In recent studies, it has been found that MPV and PDW levels increase with platelet activation; however, PDW has been shown to be a more specific marker of platelet activation than MPV (Akarsu et al,2006 Vagdatli et al,2010; Jindal et al,2011). The reason for this is thought to be a more specific indicator of platelet activation than MPV, since the PDW value does not increase in single platelet distension caused by platelet volume increase (Vagdatli et al, 2010). There was a strong positive connection ($r=0.828$) between PCT and PLT, and a weak strong positive connection ($r=0.370$) between PCT and MPV. Correlation of patients aged 46-90 years A strong positive connection ($r=0.872$) was found between PCT and PLT. It has been reported that in cases affecting platelet count and MPV, plateletcrit will change in the same direction (Budak et al,2016; Sirois ,2014).

Limitations of the Study

Our study's retrospective design, limited patient population, and undetermined lag time between

blood collection and analysis are all drawbacks. Had the prospective study method been used, different results could have been obtained.

CONCLUSION

As a result; It was determined that BC did not cause a clear change in the platelet indices (platelet count, MPV, PDW and plateletcrit) of the patients examined. When this finding is evaluated in the light of information obtained from previous scientific studies, it is not that BC does not affect the number and volume of platelets; It seems that it would be more appropriate to interpret that there is no quantitatively significant change in the platelet indices of patients with BC, due to the combination of opposing (both increasing and decreasing) effects of inflammation because of BC on platelet indices. Especially this study is very important in terms of addressing age levels. Greater research is required to comprehend the function of platelets in the pathogenesis and diagnosis of BC disease.

REFERENCES

- Akarsu, S., Kurt, N. Ç., Kurt, A., Varol, İ. & Şen, Y. (2006). Değişik hastalık gruplarında trombosit hacim değişkenleri Orijinal Araştırma . *Türk Pediatri Arşivi* ,41 (4) , 208-213 .
- Bozan, N., Alpaycı, M., Aslan, M., Cankaya ,H., Kiroglu, A.F., Turan, M., Ayril, A., Senkoy, E., & Ilter S.(2016) Mean platelet volume, red cell distribution width, platelet-to-lymphocyte and neutrophil-to-lymphocyte ratios in patients with ankylosing spondylitis and their relationships with high-frequency hearing thresholds. *Eur Arch Otorhinolaryngol*, 273(11),3663-3672.
- Budak, Y.U, Polat ,M., & Huysal, K.(2016). The use of platelet indices, plateletcrit, mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: a systematic review. *Biochem Med (Zagreb)*, 26(2),178-193.
- Çakır, S., Kafadar, M.T., Arslan, Ş.N., Türkan, A., Kara, B., & İnan A. (2016). Meme kanseri tanısı konmuş kadınlarda risk faktörlerinin güncel veriler ışığında gözden geçirilmesi, *İstanbul Bilim Üniversitesi Florence Nightingale Tıp Dergisi*, 2(3), 186-194.
- Fahad Ullah, M.(2019). Breast Cancer: Current Perspectives on the Disease Status. *Adv Exp Med Biol*. 1152,51-64.
- Fu, S., Yun, Z.Y., Cui, M.M., Meng, H., Qian, C., Liu, T., Liu, ZP., Wang ,R.T., & Yu, K.J.(2017). Cancer antigen 15-3, platelet distribution width, and fibrinogen in combination to distinguish breast cancer from benign breast disease in non-conclusive mammography patients. *Oncotarget*. 8(40),67829-67836.
- Grivennikov, S.I., & Greten, F.R., Karin M. (2010) Immunity, inflammation, and cancer. *Cell*, 140(6), 883–99.
- Jindal, S., Gupta, S., Gupta, R., Kakkar, A., Singh, H.V., Gupta, K., & Singh S.(2011). Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. *Hematology*,16(2),86-89.
- Kaushansky, K.(2015). Thrombopoiesis. *Semin Hematol*. 52(1),4-11.
- Koça, S., Çelik, L., Özbaş, S., Sak, S.D., Tükün, A., & Yalçın, B. (2011): Meme kanserinde risk faktörleri, riskin değerlendirilmesi ve prevansiyon: İstanbul 2010 Konsensus Raporu. *Meme Sağlığı Dergisi/Journal of Breast Health*, 7(2),47-67.
- Menter, D.G., Kopetz, S., Hawk, E., Sood, A.K., Loree, J.M., Gresele, P., & Honn, K.V. (2017).Platelet “first responders” in wound response, cancer,and metastasis. *Cancer Metastasis Rev* 36(2),199-213.
- Mezouar, S., Frere, C., Darbousset R., Mege, D., Crescence, L., Dignat-George F., Panicot-Dubois, L., & Dubois, C. (2016).Role of platelets in cancer and cancer-associated thrombosis: Experimental and clinical evidences. *Thromb Res* 139, 65-76.
- Ozmen, V.(2014). Breast Cancer in Turkey: Clinical and Histopathological Characteristics (Analysis of 13.240 Patients). *J Breast Health*. 10(2),98-105.
- Paulus, J.M. (1981). Recent advances in the story of megakaryocyte physiology. *Pathol Biol (Paris)*. 29: 133-5.
- Rojas, K., & Stuckey, A.(2016). Breast Cancer Epidemiology and Risk Factors. *Clin Obstet Gynecol*. 59(4),651-672.
- Sirois M.(2014). *Laboratory Procedures for Veterinary Technicians*. 6th edition, Elsevier Health Sciences, ABD.
- Sun, H., Yin, C.Q., Liu, Q., Wang, F., & Yuan, C.H.(2017). Clinical Significance of Routine Blood Test-Associated Inflammatory Index in Breast Cancer Patients. *Med Sci Monit*. 23,5090-5095.
- Vagdatli, E., Gounari, E., Lazaridou, E., Katsibourlia,E., Tsikopoulou, F., & Labrianou, I. (2010). Platelet distribution width: a simple , practical and specific marker of activation of coagulation. *HIPPOKRATIA*.14(1),28-32.
- Wu, Y., Antony, S., Meitzler, J.L.,& Doroshov, J,H. (2014). Molecular mechanisms underlying chronic inflammation-associated cancers. *Cancer Lett*. 345(2), 164–173.
- Xia, W., Chen, W., Tu, J., Ni, C., & Meng, K.(2018). Prognostic Value and Clinicopathologic Features of Platelet Distribution Width in Cancer: A Meta-Analysis. *Med Sci Monit*. 24,7130-7136.
- Yıldız, E. (2014). *Meme Kanseri*. Tuzlalı S., Güllüoğlu M., Çevikbaş U. (Çeviri Ed), Robbins Temel Patoloji. 9th ed. 723-739.