Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1092191
J Health Sci Med 2022; 5(4): 1170-1175

The role of red cell distribution width in predicting the prognosis of patients with breast cancer

Dursun Burak Özdemir[1], Ahmet Karayiğit[2], Hayrettin Dizen[3], Bülent Ünal[4]

[1]Samsun Education and Research Hospital, Department of Surgical Oncology, Samsun, Turkey
[2]Adana City Training and Research Hospital, Department of Surgical Oncology, Adana, Turkey
[3]Acıbadem Eskisehir Hospital, Department of General Surgery, Eskisehir, Turkey
[4]İstanbul Aydın University, Medical Park Florya Hospital, Faculty of Medicine, Department of Organ Transplantation, İstanbul, Turkey

Cite this article as: Özdemir DB, Karayiğit A, Dizen H, Ünal B. The role of red cell distribution width in predicting the prognosis of patients with breast cancer. J Health Sci Med 2022; 5(4): 1170-1175.

ABSTRACT

Objective: In this study, we aimed to assess the relationship between preoperative red cell distribution width (RDW) and the clinicopathological stage and prognosis of disease in patients operated for invasive epithelial breast cancer (BC).

Material and Method: This retrospective cross-sectional study was conducted between January 2010 and January 2015 at a tertiary hospital in Turkey. A total of 280 patients who underwent surgery for histologically diagnosed invasive epithelial BC were included in the study.

Results: The mean age of the patients was 53.31±12.58 years. The median follow-up time was 83 (IQR: 56.5–102) months. According to the results we found, there was a statistically significant positive correlation between progesterone receptor (PR) negativity and RDW values (p=0.015). In addition, the RDW values of patients with perineural invasion (PNI) were found to be significantly higher than those without (p=0.036).

Conclusion: When the results of our study are evaluated together with prior reports, it can be said that higher preoperative RDW is associated with poor prognosis. When RDW is evaluated together with other possible prognostic factors, such as PNI and PR status, it has the potential to be a new, easily applicable and accurate marker to assess prognosis in patients with invasive epithelial BC.

Keywords: Breast cancer, red cell distribution width (RDW), progesterone receptor, perineural invasion, overall survival

INTRODUCTION

Breast cancer (BC) is the most common cancer and the main cause of cancer-related death in women (1). Its mortality and morbidity are increasing gradually (2). In addition to frequent local relapses and distant metastases, about 20% of patients with BC are diagnosed at advanced stages and experience either recurrence or distant metastasis within 5 years (1). Recognition of prognostic features are of critical importance (3). Despite significant improvements in treatment with advances in surgical treatments, prognosis still needs to be improved (4). Early diagnosis of cancer and prediction of prognosis are important for decision-making both before and after surgery. This shows the importance of identifying simple, useful and sensitive biomarkers that can be utilized for diagnostic, clinical and prognostic evaluation of BC (2).

Red cell distribution width (RDW) is a laboratory parameter commonly used in the measurement of erythrocyte anisocytosis (variability of the volume of circulating erythrocytes), and can be easily acquired from routine blood tests (5). In addition to its usual roles in the diagnosis of iron deficiency anemia or thalassemia (6), RDW elevation has been associated with ischemic heart disease, heart failure, atherosclerosis, vascular occlusive disease, hypertension, inflammatory bowel disease, and rheumatoid arthritis (7-10). Today, RDW is also employed as an inflammatory biomarker which may be important for cancers, since cancer presence has been associated with chronic inflammation (10,11). For instance, recent studies have established that RDW levels are associated with carcinogenesis, tumor progression and cancer prognosis (12-14). More specifically, RDW is demonstrated to be associated with poor prognosis in various tumor types such as lung cancer, malignant mesothelioma, and multiple myeloma (15-17). There

Corresponding Author: Dursun Burak Özdemir, dursun_burak@yahoo.com
Received: 29.03.2022 **Accepted:** 28.06.2022

has been an increase in the number of studies examining possible relationships between the stage and prognosis of BC and RDW, and it has been suggested that RDW has a prognostic value in BC in the majority of these studies (2,18-20). However, considering that complete blood count parameters may demonstrate considerable variations based on measurement devices and demographic characteristics, it is clear that more studies are needed to assess the prognostic value of RDW in women with BC.

In this study, we aimed to assess the relationship between preoperative RDW values and the clinic-pathological stage and prognosis of disease in patients operated for invasive epithelial BC.

MATERIAL AND METHOD

Study Design

This cross-sectional study was conducted from January 2010 to January 2015 at the Department of General Surgery, Osmangazi University Faculty of Medicine, Eskişehir, Turkey. The study was initiated with the approval of the Ethics Committee of Osmangazi University Faculty of Medicine (Date: 15.06.2021, Decision No: 02). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Written informed consent for study participation was not deemed to be necessary by the Osmangazi University Medical Ethics Committee, since the study was retrospective. All data were recorded anonymously.

Study Population

A total of 280 patients who underwent surgery for histologically diagnosed invasive epithelial BC were included in the study. Male patients, subjects who had received neoadjuvant chemotherapy and/or radiotherapy, those with second primary cancers, subjects with autoimmune diseases, those with hematological malignancies, patients who used corticosteroids in the last 6 months, cases with active infection, patients who could not be followed, and subjects with incomplete data were excluded from the study.

Data Collection

The following information about each patient was obtained from hospital records: demographic characteristics, menopause status, tumor localization, biopsy method, type of surgery, axillary management, laboratory results, pathological and immunohistochemical results, whether adjuvant chemotherapy and/or adjuvant radiotherapy was received, use of hormonal therapy, presence of recurrence, follow-up time (months), final status (mortality).

Laboratory Analysis

Preoperative blood samples were drawn from the antecubital vein for measurement of complete blood count (CBC), cancer antigen 15-3 (CA15-3), carcinoembryonic antigen (CEA). CBC including neutrophil count ($\times 10^3$) lymphocyte count ($\times 10^3$), platelet count ($\times 10^3$) and RDW; CA15-3 and CEA values were measured using routine devices 2 weeks before surgery at the Clinical Biochemistry Department of Osmangazi University Faculty of Medicine.

Pathological and Immunohistochemical Analysis

All of the specimens acquired from fully resected tumors had been sent to the pathology unit of Osmangazi University Faculty of Medicine for pathological examinations. Pathological diagnosis, surgical margin, tumor grade, estrogen receptor (ER) status, progesterone receptor (PR) status, c-erbB-2 positivity, ki-67 score, presence/absence of perineural invasion (PNI), lymphovascular invasion (LVI), extracapsular invasion (ECI), multifocality, multicentricity, T and N stages, and clinical stage (reported according to the pathological classification criteria of the 8th Edition of the American Joint Committee on Cancer guidelines for BC), number of lymph nodes, number of metastatic lymph nodes were reported by qualified pathologists. Immunohistochemical evaluations were performed by the same pathologists using the same routine techniques and devices.

Statistical Analysis

All analyses, with a significance threshold of 0.05, were performed on SPSS v25 (SPSS Inc., Chicago, IL, USA). Q-Q and histogram plots were evaluated to determine presence/absence of normal distribution. Data are given as mean ± standard deviation or median (interquartile range; IQR) according to normality results, and as frequency (percentage) for categorical variables. Comparison of RDW levels were performed with the Mann-Whitney U or the Kruskal-Wallis test depending on the number of groups being compared. Spearman correlation coefficients were calculated to evaluate relationships between RDW and other continuous variables.

RESULTS

Two hundred and eighty female patients were included in our study, and the mean age of the patients was 53.31 ± 12.58 (range: 27–89) years. Median follow-up time was 83 months (IQR: 56.5–102). Clinic and demographic characteristics of the patients, surgical features, pathological results and laboratory findings are summarized in **Table 1**.

Table 1. Summary of patients and tumor characteristics	
Age	53.31 ± 12.58
Sex, female	280 (100.0%)
Menopause status	
Premenopausal	104 (37.1%)
Postmenopausal	176 (62.9%)
Side	
Right	143 (51.1%)
Left	137 (48.9%)
Bilateral	0 (0.0%)
Diagnosis	
Invasive ductal carcinoma	233 (83.2%)
Invasive lobular carcinoma	17 (6.1%)
Other invasive tumors	30 (10.7%)
Biopsy method	
Tru-cut	190 (67.9%)
Excisional	40 (14.3%)
Incisional	50 (17.9%)
Surgery	
Mastectomy	213 (76.1%)
Breast-conserving	67 (23.9%)
Surgical margin	
Negative	261 (93.2%)
Positive & Re-excision	5 (1.8%)
Positive & Mastectomy	14 (5.0%)
Axillary management	
SLNB (-)	114 (40.7%)
SLNB (+) & ALND	103 (36.8%)
ALND	63 (22.5%)
Grade	
Grade 1	75 (26.8%)
Grade 2	147 (52.5%)
Grade 3	58 (20.7%)
Estrogen receptor positivity	245 (87.5%)
Progesterone receptor positivity	216 (77.1%)
cerbB2 positivity	108 (38.6%)
ki-67 score	
0-15	131 (46.8%)
16-30	83 (29.6%)
>30	66 (23.6%)
Perineural invasion	65 (23.2%)
Lymphovascular invasion	86 (30.7%)
Extracapsular invasion	93 (33.2%)
Multifocal	59 (21.1%)
Multicentric	39 (13.9%)
T stage	
T1	77 (27.5%)
T2	169 (60.4%)
T3	25 (8.9%)
T4	9 (3.2%)
N stage	
N0	115 (41.1%)
N1	85 (30.4%)
N2	45 (16.1%)
N3	35 (12.5%)
M stage	
M0	278 (99.3%)
M1	2 (0.7%)
Stage	
Stage I	51 (18.2%)
Stage II	137 (48.9%)
Stage III	90 (32.1%)
Stage IV	2 (0.7%)
Number of lymph nodes	12 (3-21)
Number of metastatic lymph nodes	1 (0-4)
Adjuvant chemotherapy	255 (91.1%)
Adjuvant radiotherapy	183 (65.4%)
Hormonotherapy	253 (90.4%)
Recurrence	41 (14.6%)
Follow-up time, months	83 (56.5-102)
Final status	
Exitus	66 (23.6%)
Alive	214 (76.4%)
Neutrophil ($\times 10^3$)	4.45 (3.60-5.56)
Lymphocyte ($\times 10^3$)	2.0 (1.6-2.5)
Platelet ($\times 10^3$)	254 (218-296.5)
RDW	13.9 (13.1-15.0)
CA15-3	22.4 (15.7-30.76)
CEA	1.86 (1.18-2.86)

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables. SLNB: Sentinel lymph node biopsy, ALND: Axillary lymph node dissection

There was a significant positive correlation between PR negativity and RDW values (p=0.015). In addition, RDW values of cases with PNI were found to be significantly higher than those without PNI (p=0.036). When the relationship of RDW with continuous variables was examined, it was seen that there was a significant negative correlation only between CA15-3 and RDW, but the correlation coefficient was very weak (r=-0.135, p=0.024). There were no significant relationships between RDW value and age (p=0.455), menopause status (p=0.663), pathological diagnosis (p=0.943), tumor grade (p=0.783), ER positivity (p=0.141), c-erbB-2 (p=0.792), Ki-67 score (p=0.908), LVI (p=0.614), extracapsular invasion (p=0.810), tumor multifocality (p=0.091), tumor multicentricity (p=0.810), T stage (p=0.641), N stage (p=0.286), clinical stage (p=0.947), number of lymph nodes (p=0.831), number of metastatic lymph nodes (p=0.826), CEA (p=0.248), presence of recurrence (p=0.326), or death status (p=0.900) (**Table 2 and 3**).

DISCUSSION

Breast cancer currently accounts for almost 1 in 3 cancers and is considered the most common cancer worldwide. Most importantly, BC is currently the main cause of cancer-related death in women (18). Although the overall mortality rate from BC decreased by 36% from 1989 to 2012 due to advances in early detection and systemic treatments, to our current knowledge, about 20% of BC patients are diagnosed in advanced stages and experience recurrence or distant metastasis within 5 years (18,21) Therefore, outcome evaluation in patients with BC is very important because it influences treatment decisions.

Table 2. RDW levels with regard to patients and tumor characteristics

	RDW	p
Menopause status		
Premenopausal	13.85 (12.95-15.5)	0.663
Postmenopausal	13.9 (13.1-14.8)	
Diagnosis		
Invasive ductal carcinoma	13.9 (13.1-14.9)	0.943
Others	13.9 (12.9-15.5)	
Grade		
Grade 1	13.8 (13.1-14.8)	
Grade 2	14.0 (13.0-15.3)	0.783
Grade 3	13.55 (13.2-14.9)	
Estrogen receptor		
Negative	14.5 (13.2-15.8)	0.141
Positive	13.8 (13.1-14.9)	
Progesterone receptor		
Negative	14.3 (13.25-15.75)	0.015
Positive	13.7 (13.05-14.8)	
cerbB2		
Negative	13.9 (13.1-15.0)	0.792
Positive	13.9 (13.2-14.9)	
ki-67 score		
0-15	14.0 (13.1-15.1)	
16-30	13.9 (13.1-14.9)	0.908
>30	13.75 (13.0-14.9)	
Perineural invasion		
No	13.7 (13.0-14.9)	0.036
Yes	14.2 (13.4-15.8)	
Lymphovascular invasion		
No	13.9 (13.1-15.0)	0.614
Yes	13.85 (13.2-15.1)	
Extracapsular invasion		
No	13.8 (13.1-15.0)	0.810
Yes	13.9 (13.1-14.9)	
Multifocal		
No	13.7 (13.0-14.9)	0.091
Yes	14.2 (13.3-15.1)	
Multicentric		
No	13.9 (13.1-14.9)	0.810
Yes	13.8 (13.1-15.1)	
T stage		
T1	13.9 (13.2-14.8)	
T2	13.9 (13.1-15.1)	0.641
T3 & T4	13.45 (13.0-14.8)	
N stage		
N0	13.7 (13.2-15.0)	
N1	14.0 (13.0-14.9)	0.286
N2	14.5 (13.1-15.6)	
N3	13.6 (13.1-14.2)	
Stage		
Stage I	13.7 (13.2-14.8)	
Stage II	14.0 (13.1-15.1)	0.947
Stage III & IV	13.9 (13.05-15.2)	
Recurrence		
No	13.9 (13.1-15.1)	0.326
Yes	13.6 (13.0-14.6)	
Final status		
Exitus	13.8 (13.1-14.8)	0.900
Alive	13.9 (13.1-15.0)	

Data are given as median (1st quartile-3rd quartile) according to normality of distribution.

Table 3. Correlations between RDW and other continuous variables

	r	p
Age	-0.045	0.455
Number of lymph nodes	-0.013	0.831
Number of metastatic lymph nodes	-0.013	0.826
CA15-3	-0.135	0.024
CEA	-0.069	0.248

Inflammation in the tumor microenvironment triggers tumor growth, invasion, angiogenesis, and metastasis (2). Cancer-related systemic inflammation has been shown to play an important role in the development and progression of many neoplastic diseases, including BC. In addition to clinicodemographic data, many new hematological prognostic markers have been discovered and defined (19). RDW describes the size variability of circulating red blood cells and has recently gained use as an inflammatory biomarker (18). It has been suggested that RDW is associated with the poor prognosis of different cancer types, such as non-small cell lung cancer, prostate cancer, colorectal cancer, and gastric cancer (22-25). The reason for the relationship between RDW and survival and prognosis of cancer has not been clearly explained. However, high RDW is thought to be associated with malnutrition, oxidative stress and age-related diseases as well as inflammation (26). In a retrospective cohort study including 825 patients, a significant positive correlation was found between RDW elevation and tumor size, lymph node metastasis number, and tumor stage in patients with BC. In the multivariable analysis of the same study, it was suggested that RDW was an independent predictor for local recurrence/distant metastasis. It was also found that the group with high RDW demonstrated poorer prognosis compared to patients with low RDW. Again in this study, no significant relationship was found between RDW and ER positivity, PR positivity and c-erbB-2 positivity (2). In a study of several preoperative routine laboratory markers that could be used to predict postoperative recurrence and death in patients with BC, RDW value demonstrated the highest predictive power

for postoperative mortality and survival (18). RDW elevation has also been shown to be an independent prognostic factor for both OS and disease-free survival (DFS). In this study, a significant correlation was found between RDW and peritumoral vascular invasion, ER status, PR status, c-erbB-2 status, and Ki-67 score (19). Another retrospective study showed that RDW is one of the most effective indicators in distinguishing BC from healthy individuals and, when combined with other tests, RDW can enable early detection of BC (20). In a pilot study focused on this topic, RDW was found to be significantly elevated in patients with BC and it was suggested that RDW could be helpful in differentiating benign or malignant tumors (27). An interesting result of the same study was that RDW was significantly correlated with primary tumor diameter and the number of infiltrating axillary lymph nodes. The study also emphasized that there was a close relationship between RDW elevation and c-erbB-2 overexpression. As a result, it has been said that RDW can be used to monitor response recipients of anti-c-erbB-2 agents (27). In the present study, we did not find a significant relationship between RDW and OS. However, RDW values were higher in BC patients with PR negativity. In addition, there was a significant relationship between RDW level and PNI presence.

In addition to being critical regulators of transcription, PRs also function to activate the signal transduction pathways of proliferation (28). The ER is a nuclear hormone receptor that acts as a transcription factor, and PR is involved in ER signaling. Both ER and PR are important triggers of BC development, and it is well known that positivity for ER and PR improve response to endocrine therapy but not cytotoxic chemotherapy. Consequently, the presence/absence of these receptors play an important role in disease recurrence and OS (29). Huang et al. (30) found positive PR status as an independent prognostic for OS and DFS. Similarly, multivariable analyses of another study confirmed the independent association between PR expression and survival (31), similar to other studies (32). Although RDW was not found to be associated with OS in our study, this indirect relationship between RDW and PR status and the fact that PR negativity was associated with poor OS in previous studies may suggest that RDW may be indirectly associated with OS.

Perineural invasion is a relatively rare histological feature that occurs 10 times less frequently than LVI in patients with invasive BC. It has been established that PNI may be associated with some tumor features, such as higher T stage, higher tumor grade, and LVI, but its role as an independent poor prognostic factor is controversial (33). In one study, vascular invasion, axillary lymph node and PR positivity ratios were found to be significantly higher in PNI-positive patients than in PNI-negative ones. In the same study, no difference was found between PNI-positive and PNI-negative patients in terms of DFS in patients with BC (1). Cox regression analysis of another study also found PNI to be significantly associated with DFS (34). These discrepancies between studies examining relationships between PNI and survival reveal the need for more comprehensive studies on this subject. To our knowledge, there is no other study examining the relationship between RDW and PNI in BC.

There are some limitations of our study. First, the current study is single-center which limits the generalizability. Secondly, the research was performed in a retrospective manner, so the data obtained should be supported by prospective studies due to possible biases. Third, we did not investigate the molecular mechanisms, and therefore, our results only show associations which may have emerged in relation with various other factors or parameters. Finally, imbalances in the distribution of the patient numbers in the subgroups of some factors may have adversely affected statistical evaluations. Therefore, there is a need for collaborative, multicenter, prospective studies with larger numbers of patients in which molecular mechanisms are also examined to confirm our results.

CONCLUSION

In this study in which we investigated the prognostic role of RDW in BC, we did not find a direct significant relationship between RDW and survival, contrary to most published literature. There was a positive correlation between RDW and PNI only, and a negative correlation only with PR positivity. When the results of our study and previous studies are evaluated together, it can be said that patients with relatively higher preoperative RDW may require closer follow-up. Also, if RDW is evaluated together with other possible prognostic factors (such as PNI and PR status), it may be more likely to obtain potential benefits with its assessment.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Ethics Committee of Osmangazi University Faculty of Medicine (Date: 15.06.2021, Decision No: 02).

Informed Consent: Written informed consent for study participation was not deemed to be necessary by the Osmangazi University Medical Ethics Committee, since the study was retrospective. All data were recorded anonymously.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: The author declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Duraker N, Caynak Z, Türköz K. Perineural invasion has no prognostic value in patients with invasive breast carcinoma. The Breast 2006; 15: 629-34.
2. Yao D, Wang Z, Cai H, et al. Relationship between red cell distribution width and prognosis in patients with breast cancer after operation: a retrospective cohort study. Biosci Rep 2019; 39: BSR20190740.
3. Tungsukruthai S, Petpiroon N, Chanvorachote P. Molecular mechanisms of breast cancer metastasis and potential anti-metastatic compounds. Anticancer Res 2018; 38: 2607-18.
4. Raghunath A, Desai K, Ahluwalia MS. Current treatment options for breast cancer brain metastases. Curr Treat Options Oncol 2019; 20: 1-18.
5. Förhécz Z, Gombos T, Borgulya G, et al. Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. Am Heart J 2009; 158: 659-66.
6. Demir A, Yarali N, Fisgin T, et al. Most reliable indices in differentiation between thalassemia trait and iron deficiency anemia. Pediatr Int 2002; 44: 612-6.
7. Gunebakmaz O, Kaya MG, Duran M, et al. Red blood cell distribution width in 'non-dippers' versus 'dippers'. Cardiology 2012; 123: 154-9.
8. Nishizaki Y, Yamagami S, Suzuki H, et al. Red blood cell distribution width as an effective tool for detecting fatal heart failure in super-elderly patients. Intern Med 2012; 51: 2271-6.
9. Karabulut A, Uzunlar B. Correlation between red cell distribution width and coronary ectasia in the acute myocardial infarction. SAGE Publications Sage CA: Los Angeles, CA; 2012.
10. Chiba T, Marusawa H, Ushijima T. Inflammation-associated cancer development in digestive organs: mechanisms and roles for genetic and epigenetic modulation. Gastroenterology 2012; 143: 550-63.
11. Mladenova D, Kohonen-Corish MR. Mouse models of inflammatory bowel disease-insights into the mechanisms of inflammation-associated colorectal cancer. In Vivo 2012; 26: 627-46.
12. Periša V, Zibar L, Sinčić-Petričević J, et al. Red blood cell distribution width as a simple negative prognostic factor in patients with diffuse large B-cell lymphoma: a retrospective study. Croat Med J 2015; 56: 334-43.
13. Ay S, Eryilmaz MA, Aksoy N, et al. Is early detection of colon cancer possible with red blood cell distribution width? Asian Pac J Cancer Prev 2015; 16: 753-6.
14. Riedl J, Posch F, Königsbrügge O, et al. Red cell distribution width and other red blood cell parameters in patients with cancer: association with risk of venous thromboembolism and mortality. PLoS One 2014; 9: e111440.
15. Koma Y, Onishi A, Matsuoka H, et al. Increased red blood cell distribution width associates with cancer stage and prognosis in patients with lung cancer. PLoS One 2013; 8: e80240.
16. Abakay O, Tanrikulu AC, Palanci Y, et al. The value of inflammatory parameters in the prognosis of malignant mesothelioma. J Int Med Res 2014; 42: 554-65.
17. Lee H, Kong S-Y, Sohn JY, et al. Elevated red blood cell distribution width as a simple prognostic factor in patients with symptomatic multiple myeloma. Biomed Res Int 2014; 2014: 145619.
18. Yoo Y-C, Park S, Kim H-J, et al. Preoperative routine laboratory markers for predicting postoperative recurrence and death in patients with breast cancer. J Clin Med 2021; 10: 2610.
19. Koh C, Bhoo-Pathy N, Ng K, et al. Utility of pre-treatment neutrophil–lymphocyte ratio and platelet–lymphocyte ratio as prognostic factors in breast cancer. Br J Cancer 2015; 113: 150-8.
20. Sun H, Yin C-Q, Liu Q, et al. Clinical significance of routine blood test-associated inflammatory index in breast cancer patients. Med Sci Monit 2017; 23: 5090-5.
21. Wang H, Naghavi M, Allen C, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016; 388: 1459-544.
22. Warwick R, Mediratta N, Shackcloth M, et al. Preoperative red cell distribution width in patients undergoing pulmonary resections for non-small-cell lung cancer. Eur J Cardiothorac Surg 2014; 45: 108-13.
23. Albayrak S, Zengin K, Tanik S, et al. Red cell distribution width as a predictor of prostate cancer progression. Asian Pac J Cancer Prev 2014; 15: 7781-4.
24. Kust D, Lucijanic M, Urch K, et al. Clinical and prognostic significance of anisocytosis measured as a red cell distribution width in patients with colorectal cancer. Int J Med 2017; 110: 361-7.
25. Yazici P, Demir U, Bozkurt E, et al. The role of red cell distribution width in the prognosis of patients with gastric cancer. Cancer Biomark 2017; 18: 19-25.
26. Sousa R, Gonçalves C, Guerra IC, et al. Increased red cell distribution width in Fanconi anemia: a novel marker of stress erythropoiesis. Orphanet J Rare Dis 2016; 11: 1-10.
27. Seretis C, Seretis F, Lagoudianakis E, et al. Is red cell distribution width a novel biomarker of breast cancer activity? Data from a pilot study. J Clin Med Res 2013; 5: 121-6.
28. Daniel AR, Hagan CR, Lange CA. Progesterone receptor action: defining a role in breast cancer. Expert Rev Endocrinol Metab 2011; 6: 359-69.
29. Jafari SH, Jahanmir A, Bahramvand Y, et al. Association of Estrogen Receptor, Progesterone Receptor, and Human Epidermal Growth Factor Receptor 2 Expression with Breast Cancer Metastasis in Iran. Iran J Med Sci 2022; 47: 40-47.
30. Huang D-P, Ma R-M, Xiang Y-Q. Utility of red cell distribution width as a prognostic factor in young breast cancer patients. Medicine 2016; 95: e3430.
31. Prat A, Cheang MCU, Martín M, et al. Prognostic significance of progesterone receptor–positive tumor cells within immunohistochemically defined luminal A breast cancer. J Clin Oncol 2013; 31: 203-9.
32. Purdie C, Quinlan P, Jordan L, et al. Progesterone receptor expression is an independent prognostic variable in early breast cancer: a population-based study. Br J Cancer 2014; 110: 565-72.
33. Karak SG, Quatrano N, Buckley J, et al. Prevalence and significance of perineural invasion in invasive breast carcinoma. Conn Med 2010; 74: 17-21.
34. Koca E, Kuzan TY, Dizdar O, et al. Outcomes of locally advanced breast cancer patients with≥ 10 positive axillary lymph nodes. Med Oncol 2013; 30: 615.