RESEARCH ARTICLE

Mean Platelet Volume as an Independent Predictive Marker for Pathologic Complete Response after Neoadjuvant Chemotherapy in Patients with Locally Advanced Breast Cancer

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Abstract

Background: The impact of mean platelet volume (MPV) on prognosis, diagnosis and response to therapy in cancer patients has been widely investigated. In the present study, we evaluated whether MPV at diagnosis has predictive value for pathologic complete response (pCR) after neoadjuvant chemotherapy in patients with locally advanced breast cancer (LABC). **Materials and Methods:** A total of 109 patients with LABC from Akdeniz University and Antalya Research and Training Hospital were evaluated retrospectively. **Results:** ROC curve analysis suggested that the optimum MPV cut-off point for LABC patients with pCR (+) was 8.15 (AUC:0.378, 95%CI [0.256- 0.499], p=0.077). The patients with MPV <8.15 had higher pCR rates (29.2% vs. 13.1%, p=0.038). After binary logistic regression analysis, MPV and estrogen receptor absence were independent predictors for pCR. **Conclusions:** MPV has an independent predictive value for pCR after neoadjuvant chemotherapy in patients with LABC.

Keywords: Mean platelet volume - pathologic complete response - breast cancer - neoadjuvant chemotherapy

Introduction

Breast cancer (BC) is the most common type of malignancies in women (Ferlay et al., 2015). In order to improve the survival of patients with BC systemic therapies (chemotherapy or hormonal therapy) are suggested to the patients after surgery. Sometimes upfront systemic treatment (neoadjuvant chemotherapy (NACT)) may be suggested to the patients BC in whom a primary surgery is technically not feasible or breast conserving surgery is preferred in operable disease (Gralow et al., 2008). The pathologic complete response (pCR) is one of the most important outcomes after NACT because pCR have a predictive value for survival (Kong et al., 2011).

Thrombocytes play an important role in atherosclerotic complications and mean platelet volume (MPV) is accepted as an indicator of thrombocyte volume. Some studies were previously reported that there was wide platelets with dense granules, containing more thromboxane A2 resulted in tendency to thrombosis in the blood in the presence of increased MPV levels (Davi et al., 2007; Greisenegger et al., 2004).

In breast cancer like other cancer types, it is investigating whether MPV has a predictive or prognostic value (Yao et al., 2014). In the present study, we evaluated whether MPV has a predictive value for pCR after NACT in patients with LABC.

Materials and Methods

A total of 109 patients with LABC from Akdeniz University and Antalya Research and Training Hospital were evaluated retrospectively. The age, menopausal status, MPV, histological type, tumor and nodal stage, the presence of estrogen reseptor (ER), progesterone reseptor (PR) and human epidermal growth factor receptor 2 (HER2) status, lymphovascular invasion (LVI), perineural invasion (PNI) and grade were recorded into the Statistical Package for the Social Sciences version 16.0 (SPSS 16.0) from the medical archives retrospectively.

To determine the properties of patients with LABC, frequency analysis, two independent samples t test, and chi-square tests were performed. The capacity of MPV in predicting pCR (breast and axillary) to NACT in patients with BC was analyzed using receiver operating characteristic (ROC) curve analysis. Optimal cut-off

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values were determined. While evaluating the area under the curve, a5% type-I error level was used to accept a statistically significant predictive value of the test variables. After univariate analysis to identify associated with PCR, for the multivariate analysis, the possible factors were further entered into logistic regression analysis to determine independent predictors of PCR. Hosmer-Lemeshow goodness of fit statistics were used to assess model fit. A p value of < 0.05 was considered significant.

Results

A total of 109 were retrospectively evaluated for MPV. ROC curve analysis suggested that the optimum MPV cut-off point for LABC patients with PCR (+) was 8.15 (AUC:0.378, 95%CI [0.256- 0.499], p=0.077) with sensitivity, specificity, positive predictive value, and negative predictive value of $63,6\%, 60,9\%, 29,2\%$, and $86,9\%$, respectively (Figure 1).
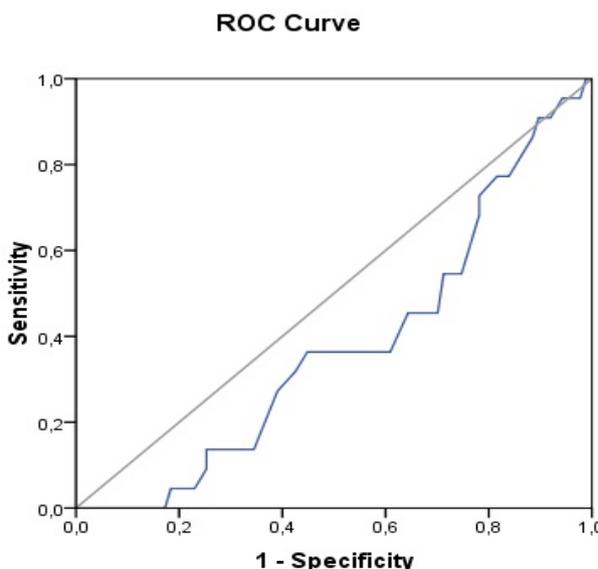

Figure 1. Receiver Operating Characteristic (ROC) Curves

Table 1. The characteristics of patients according to mean platelet volume <8.15 or >8.15

	Patients with MPV<8.15 (n:48)	Patients with MPV>8.15 (n:61)	P Value
Age(mean-years)	47,4±8,3	49,1±10,9	0.379
Menopausal Status			0.085
Premenopausal	68.80%	52.50%	
Postmenopausal	31.20%	47.50%	
Histologic type			0.603
Invazıv Ductal Carcinom	16.70%	13.10%	
Non-Invazıv Ductal Carcinom	83.30%	86.90%	
T stage (Clinic)			0.991
T0	2.10%	1.60%	
T1	4.20%	3.30%	
T2	45.80%	45.90%	
T3	18.80%	16.40%	
T4	29.20%	32.80%	
N stage (Clinic)			0.333
N0	14.60%	16.40%	
N1	45.80%	29.50%	
N2	33.30%	42.60%	
N3	6.20%	11.50%	
Estrogen Receptor			0.712
Positive	62.50%	59%	
Negative	37.50%	41%	
Progesteron Receptor			0.392
Positive	45.80%	54.10%	
Negative	54.20%	45.90%	
CerbB2 receptor			0.348
Positive	40%	41%	
Negative	50%	59%	
Lymphovasculer invasion			0.062
Positive	27.10%	42.60%	
Negative	60.40%	37.70%	
Unknown	12.50%	19.70%	
Perineural invasion			0.602
Positive	8.30%	8.20%	
Negative	79.20%	72.10%	
Unknown	12.50%	19.70%	
Grade			0.708
Grade1	4.20%	1.60%	
Grade2	64.60%	60.70%	
Grade3	29.20%	32.80%	
Unknown	2.10%	4.90%	

The patients were divided into two groups according MPV: MPV<8.15 (n:48) and MPV>8.15 (n:61). When we evaluated the patients with LABC according to MPV, there was no difference between MPV<8.15 and MPV>8.15 groups regarding the mean age, menopausal status, histological type, clinical T stage, clinical N stage (p=0.379, p=0.085, p=0.603, p=0.991, and p=0.333, respectively). The ratio of ER, PR and HER 2 positivity were similar between groups (p=0.712, p=0.392 and p=0.348, respectively). Also it was not found any significant difference regarding LVI, PNI and grade (p=0.062, p=0.602 and p=0.708, respectively). According to MPV<8.15 and >8.15, the properties of patients were given in Table 1.

When evaluating the factors had a independently predictive value for PCR, the absence ER positivity and MPV were found as independent predictors (p=0.004 and p=0.046, respectively).

Discussion

In the present study, we investigated whether MPV at diagnosis has a predictive value for pCR after NACT in patients with LABC. We found a significant difference between groups in terms of pCR according to MPV (<8.15 or >8.15). The patients with LABC in whom MPV<8.15 at diagnosis had higher pCR rates after NACT than other patients with MPV>8.15. To our knowledge, this is the first study to demonstrate the relationship between MPV and pCR after NACT in patients with LABC.

Generally, it is known that larger MPV is correlated thromboembolic events (Sansanayudh N et al., 2014; Han JS et al., 2013; Canan A et al., 2012). In previously presented studies, according to MPV, it was reported different outcomes in cancer patients in terms of prognosis (Dirican A et al., 2013; Tuncel T et al., 2014; Inagaki N et al., 2014; Aliustaoglu M et al., 2014). The cancer mortality is mostly dependent infection and thromboembolic events, therefore MPV be important a predictive and prognostic factor for cancer patients.

In patients with LABC, the pCR after NACT predict survival advantage especially HER2 like and triple negative groups (Berruti A et al., 2014; von Minckwitz G, 2013). In previously, some factors were reported as predictive factors of pCR to NACT. The breast cancer with grade 3 or higher Ki-67 expression is more responsive to NACT associated with higher pCR rates (Colleoni et al., 2004; Cristofanilli et al., 2005). Also, pCR are associated with absence of ER and PR expression (Cristofanilli et al., 2005). The histological type was one of them and when compared with invasive ductal carcinoma, pCR ratio was lower in invasive lobular carcinoma (Kim et al., 2014). Additionally, NACT agents are also important for the pCR. It has reported that taxan addition to an anthracycline-containing regimen, dose dens-intensified treatment and trastuzumab addition in HER2 positive tumors have increased the ratio of pCR (Berruti et al., 2014; Bear et al., 2006; Buzdar et al., 2005).

Inflammation based markers have investigated and been shown that they were a predictor for chemotherapy response (Krauthamer et al., 2013; Noble et al., 2013; Guthrie et al., 2013; Kobayashi et al., 2008). In the most of these studies, higher inflammation scores were associated with poorer outcomes (Yao et al., 2014; Pistelli et al., 2015). It was reported that the higher inflammation markers were associated with worst outcome or poorer survival in studies performed in patients with BC (Kobayashi et al., 2008; Pistelli et al., 2015). Also, lower PCR rates have been showed in patients with higher inflammation markers in neoadjuvant setting (Eryilmaz et al., 2014; Koh et al., 2014).

MPV is accepted one of the inflammatory markers, such as the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio, C-reactive protein and serum albumin levels (Sansanayudh et al., 2014). Higher MPV is associated with comorbidities (Madan et al., 2016). According to our study, lower MPV has predicted higher PCR rates and it was an independent predictor.

In conclusion, we speculate that MPV may be used as a predictor to decide NACT in the borderline patients with BC.

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