PS4-10-17 - The Impact of Pre-Treatment Clinical, Pathological, and Radiological Parameters on Pathological Complete Response and Prognosis Following Neoadjuvant Therapy in Patients with Triple-Negative Breast Cancer

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Abstract

Triple Negative Breast Cancer (TNBC) accounts for approximately 15% of all breast cancers.The aim of this thesis is to investigate the sociodemographic, clinical, pathological, and radiological characteristics of patients with TNBC, their response to neoadjuvant chemotherapy (NACT) regimens, the factors influencing this response, and the disease-related variables affecting disease-free survival (DFS) and overall survival (OS). The study consisted of 90 female patients, age between 30–65 years, diagnosed with stage IIA- IIIB TNBC, between December 2012 and September 2017. Post-menopausal status and high ki-67 values at biopsy were found to be the strongest predictors of achieving a pathological complete response (pCR). Magnetic resonance imaging (MRI) performed after NACT and prior to surgery had the highest predictive value in assessing pCR (p=0.027, p=0.036, and p=0.0001, respectively). Pretreatment tumor size, presence of pCR, and post-surgical ki-67 values were statistically associated with 5-year OS. Presence of pCR, pathological nodal stage, necrosis, and post-surgical ki-67 values were significantly correlated with 5-year DFS. In patients with TNBC, achieving pCR after NACT and detecting low ki-67 values in residual tumors were associated with improved DFS and OS.

Introduction

Breast cancer is the most common cancer diagnosed in women worldwide, with more than 2 million new cases each year [1]. In this study, we aim to evaluate the sociodemographic characteristics and the clinical, pathological, and radiological features of patients with TNBC, characterized by the absence of both hormone receptor expression and HER-2/neu amplification, who represent a breast cancer subtype with high morbidity and mortality. We further sought to investigate their response to NACT regimens, the factors influencing this response, and the disease-related characteristics affecting DFS and OS.

Methods and Materials

The study population consisted of 84 female patients diagnosed with TNBC stages IIA- IIIB between December 2012 and September 2017 in Istanbul Medipol University. Inclusion criteria, in addition to confirmed TNBC, were: female gender, aged 30–65 years; no prior history of malignancy; and full compliance with the treatment and follow-up program. Exclusion criteria were: age outside the defined range; presence of distant metastasis at diagnosis; treatment or follow-up interruption or deviation from protocol; and death from causes unrelated to the disease within the study timeframe. The first part of the study investigated predictive factors associated with achieving pCR. The second part evaluated the impact of pCR on DFS and overall survival OS. A database was created for the 84 patients and extracted variables included: age, body mass index (BMI), smoking history, family history of breast/ovarian cancer, menopausal status, family history of breast cancer, BRCA 1/2 mutation status, cT, cN, tumor size, multicentricity, histologic grade and score, ki-67 (biopsy), ki-67 (surgical specimen), pT, pN, LVI, PNI, axillary involvement, necrosis, tumor type, Miller-Payne score, residual tumor size, tumor regression rate, and disease prognosis.

Table 1. Factors associated with pCR in logistic regression

Variable	B	SE	OR	95% CI	p
Menopausal status	-2.228	1.009	0.108	0.015–0.778	0.027
Clinical N (cN)	-0.819	1.033	0.441	0.058–3.339	0.428
LVI	-1.806	0.971	0.164	0.024–1.102	0.063
Ki-67 (biopsy)	0.004	0.019	1.004	—	0.036
MRI response	4.693	1.267	109.157	9.113–1307.461	<0.001
PET-CT response	0.313	1.207	1.367	0.128–14.567	0.796
Necrosis	-0.445	1.057	0.641	0.081–5.090	0.674

Results

In the multivariate logistic regression analysis evaluating factors associated with achieving pCR, menopausal status and MRI response were identified as significant independent predictors. Postmenopausal women were significantly less likely to achieve pCR compared with premenopausal women (B = −2.228, OR = 0.108, 95% CI = 0.015–0.778, $p = 0.027$). In contrast, a favorable MRI response was strongly associated with an increased likelihood of pCR (B = 4.693, OR = 109.157, 95% CI = 9.113–1307.461, $p < 0.001$). Although LVI and ki-67 index demonstrated trends toward association with pCR, these did not reach statistical significance in the final model (LVI: OR = 0.164, 95% CI = 0.024–1.102, $p = 0.063$; ki-67: OR = 1.004, $p = 0.036$). Other variables, including cN, PET-CT response, and tumor necrosis, showed no significant relationship with pCR ($p > 0.05$) (table1).

Figure 1. Predictive OS and pCR

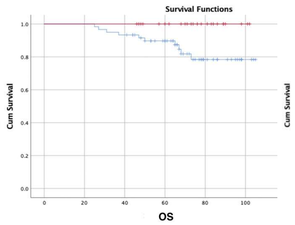
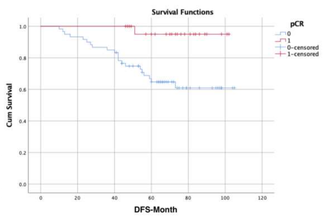


Figure 2. Predictive DFS and pCR



In the univariate analysis, BRCA mutation status, tumor type, clinical and pathological stage, treatment response, and histopathological features were significantly associated with 5-year OS and DFS. Patients with BRCA1/2 positivity, higher T or N stage, larger tumor size, presence of necrosis or LVI, and absence of pCR showed significantly worse OS and DFS ($p < 0.05$).

Discussion

The most notable finding in our dataset were that menopausal status and baseline ki-67 (biopsy) were the strongest predictors of pCR in TNBC. Postmenopausal status and higher baseline ki-67 were associated with the highest likelihood of pCR defined as no viable invasive tumor cells with only the tumor bed remaining on final pathology. These results agree with Masuda et al. (2010), who identified baseline ki-67 as a key predictor of NACT response in TNBC [2].
In the survival analyses many variables were associated with DFS and OS on univariate testing. On multivariable analysis, however, only pCR and Ki-67 levels in residual tumors remained prominent determinants of both DFS and OS (shown in Fig. 1 and 2). Prior work by Liedtke (2008) and Wu (2011) showed that TNBC patients achieving pCR after NACT have significantly better DFS and OS than those with residual disease [3,4], consistent with the notion that lack of chemoresistance translates into longer survival. Likewise, in our study, higher Ki-67 in residual tumors correlated negatively with survival. Gamucci et al., analyzing 213 patients, identified a residual-tumor Ki-67 cutoff of 13%, with values above this threshold associated with significantly worse DFS and OS [5].

Conclusions

When all data were considered together, postmenopausal patients with elevated initial ki-67 values achieved markedly higher DFS and OS, provided that pCR was obtained after NACT or that residual tumor ki-67 levels were ≤14.5%. In other words, while menopausal status and diagnostic ki-67 values alone are not independent prognostic factors, their predictive importance for achieving pCR indirectly links these groups to better survival outcomes.

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