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Risk factors of breast cancer recurrence in pathologic complete response achieved patients following neoadjuvant chemotherapy

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Goals: Pathologic complete response (pCR) of breast cancer after neoadjuvant chemotherapy (NAC) is highly related to molecular subtypes. Patients who achieved tumor pCR after NAC have a better prognosis. However, despite of better prognosis, pCR patients have an opportunity of recurrence. There was little evidence of risk factors of recurrence who showed pCR. We aim to analyze factors associated with tumor recurrence in patients who achieved pCR.

Methods: This study retrospectively reviewed the data of patients diagnosed with breast cancer who achieved pCR after receiving NAC between January 2009 and December 2018 in Samsung Medical Center. pCR was defined as no residual invasive cancer in the breast and axillary nodes even if there is residual ductal carcinoma in situ (ypT0 or ypTis with ypN0). Breast cancers were classified into 4 subtypes based on hormone receptors (HR) and human epithelial growth factor receptor 2 (HER2) status. Patients who had bilateral breast cancer, inflammatory breast cancer, distant metastasis, unknown subtype, and histologically unique case were excluded.

Results: In total 483 patients were included in this study except for patients who corresponded to the exclusion criteria. The median follow-up duration was 59.0 months (range, 0.5–153.3 months). Breast cancer recurred in 4.1% (20 of 483). There was a significant difference at clinical T ($p=0.004$) and clinical N ($p=0.034$) stage at Kaplan-Meier curve for disease-free survival. Molecular subtypes ($p=0.573$), Ki67 ($p=1.000$), and breast surgery type ($p=0.574$) were not associated with tumor recurrence in patients who achieved pCR after NAC. In clinical T stage and clinical N stage, there was a significant difference between recurrence and no-recurrence groups (clinical T stage; $p=0.045$, clinical N stage; $p=0.002$). Univariable Cox regression revealed that clinical T ($p=0.049$), clinical N stage ($p=0.010$) was statistically significant, while multivariable Cox regression showed that these were not significant; clinical T stage ($p=0.320$) and clinical N stage ($p=0.073$).

Conclusion(s): Results in this study showed that clinical T, clinical N stage, and molecular subtypes were not statistically significant predictors of recurrence in patients who achieved pCR after NAC. However multicenter study would identify these factors as predictors of recurrence after achieving pCR.

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Clinical, pathological, and prognostic features of male breast cancer. A multicenter study

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Goals: Male breast cancer (MBC) represents less than 1% of male tumors. Due to its rarity, little is known about MBC characteristics, management, and survival, with many studies based on a small number of cases. Consequently, the treatment of MBC lacks specific guidelines. This study aims to compare male and female breast cancer (BC), analyzing clinical and anatomopathological features of the tumors and the treatment approach. The goal is to identify differences and possible impacts on disease management and survival.

Methods: Between January 1st, 2006, and December 31st, 2018 data regarding 49 male and 680 female patients with primary non-

metastatic BC who underwent breast surgery at Mauriziano Hospital in Turin and IRCCs Candiolo have been retrospectively acquired. Categorical variables have been confronted with X2-test. Disease free survival (DFS) and overall survival (OS) have been analyzed with Kaplan-Meier curves and log-rank tests. Cox multivariate regressions were also performed. Propensity Score Matching (PSM) has been performed to reduce bias due to the effects of confounding variables in the two cohorts. The patients have been matched 1:1 by age at diagnosis, nodal status (N), tumour size and molecular subtype.

Results: MBC in our series accounts for 6.7% of non-metastatic BC. The mean follow-up was 5.5 years.

Males developed BC at an older age than women. The majority of MBC patients had nodal involvement and received adjuvant endocrine therapy (tamoxifen) with a higher dropout rate due to side effects (17.3% vs 7.6% of females, $p=0.04$). Histological characteristics are reported in table 1. MBC were more frequently smaller at diagnosis compared to female BC (21.5 mm versus 17.3 mm, $p<0.05$). No differences have been identified between males and females in terms of DFS and OS with a similar 10 years-relapse rate (12% MBC vs 12.4% BC). N+, high grade (G3), and tumour size ≥ 20 mm were statistically related to worse DFS ($p<0.05$) in both groups. Multivariate Cox regression confirmed $pT\geq 2$ (HR 1.5 CI 1.15–1.94), N+ (HR 6.43; CI 3.55–1.67), and G3 (HR 1.94; CI 1.08–3.51) as independent negative prognostic factors in MBC (table 2). PSM had been performed to balance the two groups; after matching, no difference in OS was seen in the two groups ($p=0.09$).

Table 1.

Histological characteristics

Variables	Female BC N = 680	MBC N = 49	p-value
Mean tumour diameter (mm, SD)	21.5 (± 12.1)	17.3 (± 7.8)	< 0.05
pT			0.002
pT1	375 (54.3%)	26 (53.1%)	
pT2	251 (36.4%)	16 (32.7%)	
pT3	22 (3.2%)	0	
pT4	32 (6.1%)	7 (14.2%)	
Nodal status*			0.41
pN0	440 (66.1%)	33 (68.8%)	
pN+	215 (33.9%)	15 (31.2%)	
G3	324 (46.9%)	27 (55.1%)	0.31
Ki67 > 20%	372 (53.9%)	29 (59.1%)	0.3
Histological type			0.4
NST	500 (72.5%)	36 (73.5%)	
Lobular	69 (10%)	2 (4.1%)	
Other	121 (17.5%)	11 (22.4%)	
Molecular subtypes			0.08
Luminal A	300 (43.5%)	18 (36.7%)	
Luminal B	169 (24.5%)	26 (53.1%)	
Her2 positive	160 (23.1%)	5 (10.2%)	
Basal-like	51 (8.9%)	0 (0%)	

NST: Non Special Type; G3: High Grade; pT: tumor size sec. TNM

*in 25 women and 1 male no axillary surgery had been performed due to poor general conditions

Table 2.

MBC multivariate analysis Cox regression

Variables	HR	CI	p value
pT ≥ 2	1.50	1.15–1.94	0.02
Nodal involvement	6.43	3.55–11.67	< 0.05
G3	1.94	1.08–3.51	0.01
Ki67	1.11	0.59–2.11	0.7
Luminal B	1.22	0.66–1.201	0.4

G3: High Grade; pT: tumor size sec. TNM.

Conclusion(s): Prognostic factors for DFS were the same in both female and male populations. BC adjuvant endocrine therapy drop-out rate appears higher in MBC compared to females, although this does not seem to correlate with a worse prognosis.