RESIDUAL CANCER BURDEN IN ER+/HER2- EARLY BREAST CANCER: PREDICTIVE ROLE OF ESTROGEN RECEPTOR EXPRESSION AND CLINICAL STAGE

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Introduction

Neoadjuvant chemotherapy (NACT) reduces tumor size and enables early systemic treatment in ER+/HER2 - locally advanced breast cancer. However, ER+/HER2− tumors show limited and variable response. Identifying predictive factors such as body mass index (BMI) and tumor characteristics is essential to personalize therapy and optimize patient management. The aim of this study is to identify clinicopathological factors associated with residual cancer burden (RCB) and to assess the impact of BMI and surgical outcomes.

Methods and Materials

Retrospective single-center study at the Catalan Institute of Oncology, Girona, including 111 cases, in stage I–III ER+/HER2− breast cancer patients treated with anthracycline- and/or taxane-based NACT (2010–2023). Clinical and pathological variables (age, BMI, ER/PR status, nodal stage, surgery) were analyzed, and associations with RCB were assessed using chi-square, Fisher's F-Test and regression analyses.

Results

Among 111 patients included (Table 1), only 13 achieved a favorable pathological response (RCB 0-1) (Figure 1). Tumors with ER-low expression were significantly more likely to respond to NACT. High Nodal Burden (cN3) was associated with chemo-resistant tumors. In contrast, age, BMI, menopausal status, tumor size, PR, HER2 and Ki67 expression were not significantly associated with RCB in this cohort (Table 2). Mastectomy was performed in 52.3% of patients, and axillary lymph node dissection in 74.8%, with 17.5% of patients converting to mastectomy after NACT (Figure 2).

Conclusions

This findings highlight ER-low expression and low nodal burden as predictive biomarkers of improved response to NACT in ER+/HER2− breast cancer. Given the low response rate, our results support a more tailored therapeutic approach and highlight the need for predictive tools to optimize patient selection within this biologically heterogeneous subgroup.

Table 1. Clinicopathological features

Variables	Cohort (N=111)	RCB 0-1 (N=13)	RCB 2-3 (N=98)	p-value
Age, mean (SD) years	47.6 (11.4)	43.5 (6.9)	48.2 (11.8)	0.169
BMI, mean (SD) kg/m²	25.8 (5.3)	26.3 (5.3)	25.7 (5.4)	0.696
Menopausal status, n (%)				0.033
Premenopausal	73 (65.8)	12 (92.3)	61 (62.2)	
Postmenopausal	38 (34.2)	1 (7.7)	37 (37.8)	
Tumor size (T), n (%)				0.166
cT0	1 (0.9)	1 (7.7)	0 (0.0)	
cT1	4 (3.6)	0 (0.0)	4 (4.1)	
cT2	34 (30.6)	5 (38.5)	29 (29.6)	
cT3	60 (54.1)	7 (53.8)	53 (54.1)	
cT4	12 (10.8)	0 (0.0)	12 (12.2)	
Nodal status (N), n (%) (N=110)				0.234
cN0	31 (28.2)	7 (53.8)	24 (24.7)	
cN1	50 (45.5)	4 (30.8)	46 (47.4)	
cN2	14 (12.7)	1 (7.7)	13 (13.4)	
cN3	15 (13.6)	1 (7.7)	14 (14.4)	
Estrogen receptor, n (%)				1.000
Negative	0 (0.0)	0 (0.0)	0 (0.0)	
Positive	111 (100.0)	13 (100.0)	98 (100.0)	
Progesterone receptor, n (%)				0.093
Negative	10 (9.0)	3 (23.1)	7 (7.1)	
Positive	101 (91.0)	10 (76.9)	91 (92.9)	
Ki67, n (%) (N=109)				0.104
<15%	8 (7.4)	0 (0.0)	8 (8.2)	
15-30%	43 (39.4)	2 (16.7)	41 (42.3)	
≥30%	58 (53.2)	10 (83.3)	48 (49.5)	
HER2 IHQ, n (%)				0.254
HER2-	51 (45.9)	6 (46.2)	45 (45.9)	
HER2 1+	35 (31.5)	2 (15.4)	33 (33.7)	
HER2 2+/FISH non-amp	25 (22.5)	5 (38.5)	20 (20.4)	

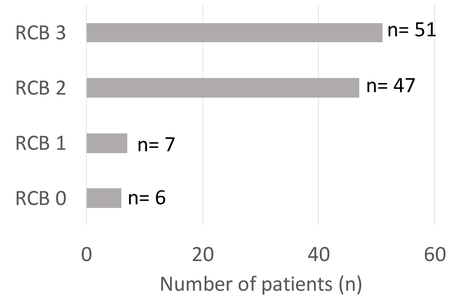


Figure 1. RCB in patients following NACT

Table 2. Factors associated with RCB

Variable	Comparation	OR (IC 95%)	p-value
Age		1.0 (0.9-1.1)	0.058
BMI		0.8 (0.7-1.0)	0.050
Postmenopausal	Premenopausal	5.5 (0.6-46.5)	0.118
ER 1-10%	ER 68-100%	0.1 (0.0-0.8)	**0.034**
RP +	RP -	3.9 (0.9-17.5)	0.076
HER2 2+	HER2-	0.8 (0.3-2.1)	0.681
Ki67 15-30%	Ki67 >30%	4.3 (0.9-20.6)	0.071
cN3	cN0	4.6 (1.2-18.5)	**0.030**
cT4	cT2	4.2 (0.8-21.8)	0.089

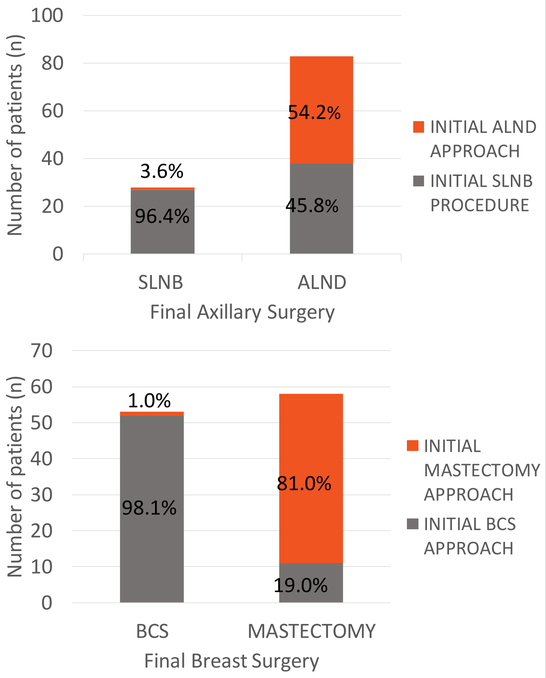


Figure 2. Rate of conversion axilary and breast surgery

ALND – Axillary lymph node dissection
SLNB – Sentinel lymph node biopsy
BCS – Breast conserving surgery

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