Original Article

Correlation of Androgen Receptor Expression with HER2 Status and Treatment Response in Breast Cancer

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Abstract

Background: Human epidermal growth factor receptor 2 (HER2) expression and androgen receptor (AR) status may influence breast cancer biology and response to neoadjuvant chemotherapy (NACT). The clinical significance of AR expression across Her2 negative, HER2-low, and HER2-positive tumors remains incompletely understood. The objective is to evaluate the association of HER2 status with AR expression and residual cancer burden (RCB) following NACT in patients with breast carcinoma. **Material and Methods:** This prospective observational study included 268 patients with histologically confirmed invasive breast carcinoma. HER2 status was classified as Her2 negative (IHC 0), HER2-low (IHC 1+ or IHC 2+/FISH-negative), and HER2-positive (IHC 3+ or IHC 2+/FISH-positive). AR expression was assessed by immunohistochemistry, and pathological response following NACT was evaluated using the RCB classification. **Results:** AR positivity was observed in 168 (62.7%) patients. Of 268 tumors, 115 (42.9%) were Her2 negative, 66 (24.6%) HER2-low, and 87 (32.5%) HER2-positive. AR positivity was significantly more frequent in HER2-low (72.7%) and HER2-positive (72.4%) tumors than in Her2 negative tumors (49.6%; p<0.001). RCB distribution differed significantly according to HER2 status (p=0.024); HER2-low tumors had the lowest RCB-0 rate (10.6%) and highest RCB-III rate (48.5%). AR-negative tumors had a higher RCB-0 rate than AR-positive tumors (31.0% vs 16.7%; p=0.019). Notably, among HER2-low/AR-positive tumors, only 4.2% achieved RCB-0, while 93.8% had RCB-II/III disease. **Conclusion:** HER2 status was significantly associated with AR expression and pathological response following NACT. The HER2-low/AR-positive phenotype demonstrated particularly high residual disease burden, suggesting that combined assessment of HER2 and AR may identify biologically distinct breast cancer subgroups with differential response to neoadjuvant therapy.

Keywords: Androgen receptor, HER2-low, breast cancer, neoadjuvant chemotherapy, residual cancer burden, HER2, pathological response.

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Introduction

Breast cancer (BC) is one of the most commonly diagnosed malignancies among women and remains a major cause of cancer-related morbidity and mortality worldwide. It is a biologically heterogeneous disease comprising multiple tumor subtypes that differ considerably in their molecular characteristics, hormonal dependence, clinical behaviour, therapeutic response, and prognosis.[1] A substantial proportion of patients, particularly in developing countries, present with locally advanced breast cancer, for which neoadjuvant chemotherapy (NACT) forms an important component of multidisciplinary management.[1] NACT provides early systemic treatment, reduces tumor burden, may facilitate breast-conserving surgery, and enables direct assessment of tumor response to systemic therapy. Advances in molecular biology and gene-expression profiling have classified breast cancer into major intrinsic subtypes, including luminal A, luminal B, HER2-enriched, basal-like, and normal-like tumors.[2,3] As gene-expression profiling may not be routinely feasible, immunohistochemistry (IHC) using estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67 provides a practical surrogate for molecular classification.[4,5] These biomarkers have important prognostic and therapeutic implications. However, considerable heterogeneity in clinical behaviour and treatment response persists even among tumors within the same conventional subtype.[6,7] The androgen receptor (AR), a member of the nuclear steroid hormone receptor family, has emerged as a potentially important biomarker in breast carcinoma. AR is expressed in normal breast epithelium as well as across different molecular subtypes of breast cancer and may influence cellular proliferation, differentiation, apoptosis, and interactions with other hormone-dependent signaling pathways.[8] AR expression is particularly frequent in luminal A and luminal B tumors and has often been associated with

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favorable clinicopathological features. Importantly, AR expression has also been reported in a subset of triple-negative breast cancers (TNBC), with approximately one-third demonstrating AR positivity.[9–11] AR expression has additionally been observed in ER-negative breast cancers and may occasionally represent the only detectable steroid hormone receptor.[12-14] The significance of AR is particularly relevant in TNBC, which lacks ER, PR, and HER2 expression and therefore cannot benefit from conventional endocrine or HER2-targeted therapies. Identification of an AR-positive subgroup may provide additional prognostic information and potentially offer opportunities for androgen-directed therapy.[12,13] However, the relationship of AR expression with tumor size, histological type and grade, lymph-node status, ER/PR/HER2 expression, Ki-67 index, molecular subtype, and treatment response remains inconsistent across studies. Furthermore, although pathological response to NACT provides valuable information regarding tumor chemosensitivity and prognosis, the predictive role of AR in determining response to NACT remains incompletely established. Data addressing these associations in Indian patients are comparatively limited. Therefore, the present prospective observational study was undertaken to Correlation of Androgen Receptor Expression with HER2 Status and Treatment Response in Breast Cancer.

Materials and Methods

Study Design and Setting: The present study was conducted as a prospective observational study among patients diagnosed with breast carcinoma. The study included patients with histologically confirmed invasive breast carcinoma who attended the study centre during the study period and fulfilled the predefined eligibility criteria. A total of 268 patients were enrolled in the study. A prospective observational study was conducted in the Department of Medical Oncology over a period of 18 months, from January 2024 to June 2025.

Inclusion Criteria

Patients with histologically confirmed invasive breast carcinoma who were planned for treatment and clinicopathological evaluation at the study centre were included. Patients for whom adequate tumor tissue was available for histopathological and immunohistochemical evaluation, including androgen receptor (AR) assessment, were considered eligible. For assessment of response to neoadjuvant chemotherapy (NACT), patients who received NACT followed by definitive surgical treatment and had adequate post-treatment specimens for pathological assessment were evaluated.

Exclusion Criteria

Patients with inadequate or poorly preserved tissue for immunohistochemical assessment, recurrent breast carcinoma, or incomplete clinicopathological or treatment-related information were excluded. Patients who did not complete the planned NACT or for whom post-NACT pathological assessment was unavailable were excluded from the analysis of response to NACT.

Data Collection: After enrolment, relevant demographic and clinical information was recorded using a predesigned data collection form. The variables included age, menopausal status, clinical presentation, tumor laterality, tumor size, clinical tumor stage, regional lymph-node status, and other relevant clinical characteristics. Details regarding NACT, surgical procedure, and treatment response were also recorded wherever applicable.

Histopathological Examination: Tumor specimens obtained by core needle biopsy and/or surgical resection were fixed in 10% neutral buffered formalin and processed according to standard histopathological procedures. Paraffin-embedded tissue sections were prepared and stained with hematoxylin and eosin. Each case was evaluated for histological type, tumor size, histological grade, lymphovascular invasion, and lymph-node involvement, wherever applicable. Histological classification and grading were performed according to accepted standard criteria.

Immunohistochemical Evaluation: Immunohistochemistry was performed on representative formalin-fixed, paraffin-embedded tumor tissue sections. The immunohistochemical panel included ER, PR, HER2, Ki-67, and AR. Appropriate positive and negative controls were used during each staining procedure.ER and PR expression was assessed on the basis of nuclear staining in tumor cells and interpreted according to the recommended guidelines. HER2 status was evaluated by membranous staining intensity and completeness in invasive tumor cells according to established criteria. Equivocal HER2 results were further evaluated by in-situ hybridization, wherever available and clinically indicated. The Ki-67 proliferation index was calculated as the percentage of positively stained tumor cell nuclei in representative areas of the tumor.

Assessment of Androgen Receptor Expression: AR expression was evaluated immunohistochemically using representative tumor sections. Nuclear staining of invasive tumor cells was considered specific for AR expression. The percentage of tumor cells demonstrating nuclear staining was recorded for each case. Cases were subsequently categorized as AR-positive or AR-negative according to the predefined immunohistochemical cut-off used in the study. The intensity and/or percentage of AR-positive tumor cells was also documented, wherever applicable, to evaluate its relationship with clinicopathological variables and other established breast cancer biomarkers.

Molecular Surrogate Classification: Based on the immunohistochemical expression of HER2, tumors were categorized into appropriate surrogate molecular subtypes, including luminal A-like, luminal B-like, HER2-positive/HER2-enriched, and triple-negative breast cancer. The distribution of AR expression across these molecular subtypes was subsequently assessed.

Neoadjuvant Chemotherapy: Patients for whom NACT was clinically indicated received chemotherapy according to the institutional treatment protocol and prevailing standard-of-care recommendations. The type and number of chemotherapy cycles administered were documented. Following completion of NACT, patients underwent definitive breast surgery with appropriate axillary management according to clinical indications.

Assessment of Response to Neoadjuvant Chemotherapy: Clinical response to NACT was assessed using clinical and radiological findings before and after completion of

chemotherapy, wherever applicable. Pathological response was assessed in the post-NACT surgical specimens by evaluating residual invasive carcinoma in the breast and regional lymph nodes. Pathological complete response (pCR) was defined as the absence of residual invasive carcinoma in the breast and regional lymph nodes after completion of NACT, according to the criteria adopted in the study. Patients with residual invasive carcinoma were categorized as having residual disease/non-pCR. The association between AR expression and response to NACT was evaluated by comparing the proportion of patients achieving pCR between AR-positive and AR-negative tumors. Response was also assessed in relation to conventional clinicopathological characteristics and molecular subtypes.

Outcome Measures: The primary outcomes of the study were the frequency of AR expression in invasive breast carcinoma and its association with clinicopathological characteristics.

Statistical Analysis: Data were entered into a computerized database and analysed using IBM SPSS Statistics version 26.0. Continuous variables were summarized as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate, while categorical variables were expressed as frequencies and percentages. HER2 status was categorized as Her2 negative, HER2-low, and HER2-positive after incorporating FISH results for IHC 2+ tumors. Associations between HER2 status, androgen receptor (AR) expression, and residual cancer burden (RCB) categories were assessed using the Pearson Chi-square test or Fisher's exact test, as appropriate. Subgroup analyses were performed to evaluate RCB distribution according to combined HER2 and AR status. All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

Results

A total of 268 patients with invasive breast carcinoma were included in the study. The mean age was 50.97 ± 10.27 years, with a median age of 51 years (IQR: 44–58 years). Most patients were aged 50–59 years (32.1%), and 55.2% were postmenopausal. The mean duration of breast lump at presentation was 3.84 ± 3.28 months. Hypertension (13.1%) and type 2 diabetes mellitus (11.2%) were the most frequently recorded comorbidities [Table 1].

Table 1: Demographic and Baseline Characteristics of the Study Population (N=268)

Characteristic	n (%) / Value
Age (years)	
Mean ± SD	50.97 ± 10.27
Median (IQR)	51 (44–58)
Range	27–80
Age group	
<40 years	45 (16.8)
40–49 years	76 (28.4)
50–59 years	86 (32.1)
≥60 years	61 (22.8)
Sex	
Female	267 (99.6)
Male	1 (0.4)
Menopausal status	
Premenopausal	120 (44.8)
Postmenopausal	148 (55.2)
Duration of breast lump (months)	
Mean ± SD	3.84 ± 3.28
Median (IQR)	3 (2–5)
Comorbidities	
Hypertension	35 (13.1)
Type 2 diabetes mellitus	30 (11.2)
Hypothyroidism	4 (1.5)
PLHIV	4 (1.5)
Ischemic heart disease	2 (0.7)

AR positivity was identified in 168 (62.7%) patients, whereas 100 (37.3%) were AR-negative [Table 2]. Thus, nearly two-thirds of the study population demonstrated AR expression.

Table 2: Distribution of Androgen Receptor Expression (N=268)

AR status	n (%)
AR positive	168 (62.7)
AR negative	100 (37.3)
Total	268 (100)

HER2 status was reclassified by incorporating FISH results for IHC 2+ tumors. Her2 negative was defined as IHC 0, HER2-low as IHC 1+ or IHC 2+/FISH-negative, and HER2-positive as IHC 3+ or IHC 2+/FISH-positive. Following reclassification, 115 (42.9%) tumors were Her2 negative, 66 (24.6%) were HER2-low, and 87 (32.5%) were HER2-positive [Table 3].

Table 3: Distribution of HER2 Status Following Incorporation of FISH Results (N=268)

HER2 status	Definition	n (%)
Her2 negative	IHC 0	115 (42.9)
HER2-low	IHC 1+ or IHC 2+/FISH-negative	66 (24.6)
HER2-positive	IHC 3+ or IHC 2+/FISH-positive	87 (32.5)
Total		268 (100)

A significant association was observed between the reclassified HER2 status and AR expression [Table 4]. Among Her2 negative tumors, 57/115 (49.6%) were AR-positive, compared with 48/66 (72.7%) HER2-low tumors and 63/87 (72.4%) HER2-positive tumors. Conversely, AR negativity was most frequent in Her2 negative disease (50.4%) and substantially lower in HER2-low (27.3%) and HER2-positive (27.6%) disease. The difference in AR expression across the three HER2 categories was statistically significant ($p<0.001$), demonstrating that AR expression was considerably more frequent in both HER2-low and HER2-positive tumors than in Her2 negative tumors.

Table 4: Association Between HER2 Status and Androgen Receptor Expression (N=268)

HER2 status	AR positive, n (%)	AR negative, n (%)	Total, n (%)	p-value*
Her2 negative	57 (49.6)	58 (50.4)	115 (100)	
HER2-low	48 (72.7)	18 (27.3)	66 (100)	
HER2-positive	63 (72.4)	24 (27.6)	87 (100)	<0.001
Total	168 (62.7)	100 (37.3)	268 (100)	

*Pearson Chi-square test; calculated p=0.0006.

The pathological response following NACT differed significantly according to HER2 status (Table 5). Overall, 59 (22.0%) patients achieved RCB-0, while 16 (6.0%), 91 (34.0%), and 102 (38.1%) were classified as RCB-I, RCB-II, and RCB-III, respectively. HER2-low tumors demonstrated the lowest RCB-0 rate, with only 7/66 (10.6%) achieving pathological complete response, compared with 29/115 (25.2%) Her2 negative and 23/87 (26.4%) HER2-positive tumors. Conversely, RCB-III was observed in 48.5% of HER2-low tumors, compared with 33.9% of Her2 negative and 35.6% of HER2-positive tumors. The overall distribution of RCB classes differed significantly across HER2 categories (p=0.024).

Table 5: Association Between HER2 Status and Residual Cancer Burden Following NACT (N=268)

HER2 status	RCB-0, n (%)	RCB-I, n (%)	RCB-II, n (%)	RCB-III, n (%)	Total	p-value*
Her2 negative	29 (25.2)	6 (5.2)	41 (35.7)	39 (33.9)	115	
HER2-low	7 (10.6)	1 (1.5)	26 (39.4)	32 (48.5)	66	
HER2-positive	23 (26.4)	9 (10.3)	24 (27.6)	31 (35.6)	87	0.024
Total	59 (22.0)	16 (6.0)	91 (34.0)	102 (38.1)	268	

*Pearson Chi-square test.

To determine whether AR expression further modified treatment response within the different HER2 phenotypes, RCB distribution was examined after stratification simultaneously by HER2 and AR status [Table 6]. Among Her2 negative tumors, RCB-0 was achieved in 15.8% of AR-positive tumors compared with 34.5% of AR-negative tumors. AR-positive/Her2 negative tumors were more frequently classified as RCB-II (49.1%) than AR-negative/Her2 negative tumors (22. 4%).The most pronounced difference was observed in the HER2-low subgroup. Among HER2-low/AR-positive tumors, only 2/48 (4.2%) achieved RCB-0, whereas 22 (45.8%) were RCB-II and 23 (47.9%) were RCB-III. Consequently, 93.8% of HER2-low/AR-positive tumors had RCB-II/III residual disease. In comparison, RCB-0 was observed in 5/18 (27.8%) HER2-low/AR-negative tumors.Among HER2-positive tumors, RCB-0 rates were relatively similar between AR-positive and AR-negative tumors (27.0% vs 25.0%). However, RCB-III was more frequent among HER2-positive/AR-negative tumors (54.2%) than HER2-positive/AR-positive tumors (28. 6%).Overall, the distribution of RCB classes differed significantly across the combined HER2/AR phenotypes (p<0.001).

Table 6: Combined Association of HER2 Status and AR Expression with Residual Cancer Burden Following NACT (N=268)

HER2 status	AR status	RCB-0, n (%)	RCB-I, n (%)	RCB-II, n (%)	RCB-III, n (%)	Total	p-value
Her2 negative	AR positive	9 (15.8)	3 (5.3)	28 (49.1)	17 (29.8)	57	0.016
	AR negative	20 (34.5)	3 (5.2)	13 (22.4)	22 (37.9)	58	
HER2-low	AR positive	2 (4.2)	1 (2.1)	22 (45.8)	23 (47.9)	48	0.028
	AR negative	5 (27.8)	0 (0.0)	4 (22.2)	9 (50.0)	18	
HER2-positive	AR positive	17 (27.0)	9 (14.3)	19 (30.2)	18 (28.6)	63	0.066
	AR negative	6 (25.0)	0 (0.0)	5 (20.8)	13 (54.2)	24	

Irrespective of HER2 status, AR-negative tumors demonstrated a higher RCB-0 rate than AR-positive tumors

(31.0% vs 16.7%). AR-positive tumors were more frequently classified as RCB-II (41.1% vs 22.0%), while RCB-III occurred in 34.5% of AR-positive and 44.0% of AR-negative tumors. The overall association between AR expression and the four RCB categories was statistically significant (p=0.019) [Table 7].

Table 7: Association Between Androgen Receptor Expression and Residual Cancer Burden Following NACT (N=268)

RCB class	AR positive, n (%)	AR negative, n (%)	Total, n (%)	p-value
RCB-0	28 (16.7)	31 (31.0)	59 (22.0)	
RCB-I	13 (7.7)	3 (3.0)	16 (6.0)	
RCB-II	69 (41.1)	22 (22.0)	91 (34.0)	
RCB-III	58 (34.5)	44 (44.0)	102 (38.1)	0.019
Total	168 (100)	100 (100)	268 (100)	

Discussion

The present prospective observational study evaluated 268 patients with breast carcinoma, with particular emphasis on the relationship between HER2 status, androgen receptor (AR) expression, and pathological response following neoadjuvant chemotherapy (NACT). After incorporating FISH results for IHC 2+ tumors, patients were categorized as Her2 negative, HER2-low, or HER2-positive. The principal findings were that AR was expressed in 62.7% of tumors, AR expression differed significantly across the revised HER2 categories, and pathological response also varied according to HER2 phenotype. Of particular interest, the HER2-low/AR-positive subgroup demonstrated a markedly high residual cancer burden following NACT. The mean age of patients in the present study was 50.97 ± 10.27 years, with a median age of 51 years, and 55.2% were postmenopausal. Anand et al,[15] reported a somewhat younger Indian cohort, with a mean age of 47.6 ± 10.1 years, while Jaine et al,[16] also evaluated predominantly middle-aged women with breast carcinoma. Thus, the demographic profile of the present cohort was broadly comparable with previously reported Indian breast cancer populations. The study population predominantly comprised patients with locally advanced disease, with 85.4% presenting with T3–T4 tumors, 93.3% with clinically node-positive disease, and 88.1% with Stage III disease. Anand et al,[15] similarly reported a substantial burden of advanced disease, although the corresponding proportions were lower, with 58.7% having T4 tumors, 71.6% having node-positive disease, and 68.9% having Stage III disease. The greater proportion of advanced disease in the present cohort may reflect referral patterns at a tertiary oncology centre and the selection of patients undergoing NACT.AR positivity was observed in 168 of 268 patients (62.7%), demonstrating that AR is expressed in a substantial proportion of breast carcinomas. This prevalence was comparable with previous reports. Anand et al,[15] demonstrated AR positivity in 56% of Indian breast cancer patients, while Jaine et al,[16] reported AR expression in 64.3% of cases. Similarly, Loibl et al,[17] in a cohort of 673 patients treated with NACT, reported AR expression in 53.2% of primary breast cancers. The variation in reported AR prevalence may be attributable to differences in patient populations, molecular subtype distribution, immunohistochemical methodology, and thresholds used to define AR positivity. Nevertheless, the consistently substantial prevalence across studies supports the potential value of AR as an additional biomarker beyond conventional ER, PR, and HER2 assessment. An important modification in the present analysis was the incorporation of FISH results for IHC 2+ tumors, thereby eliminating HER2-equivocal disease as a final analytical category. Based on the revised classification, 115 (42.9%) tumors were Her2 negative, 66 (24.6%) were HER2-low, and 87 (32.5%) were HER2-positive. The HER2-low category comprised tumors with IHC 1+ expression or IHC 2+ with negative FISH, whereas HER2-positive disease comprised IHC 3+ tumors and IHC 2+/FISH-positive tumors. A significant relationship was identified between HER2 phenotype and AR expression. AR positivity was observed in only 49.6% of Her2 negative tumors, compared with 72.7% of HER2-low tumors and 72.4% of HER2-positive tumors (p<0.001). Thus, both HER2-low and HER2-positive tumors demonstrated substantially greater AR expression than Her2 negative tumors. This revised analysis provides a clearer association than the initial analysis, in which HER2 IHC 2+ tumors were retained as an equivocal category and the association between HER2 positivity and AR expression approached but did not reach statistical significance. Loibl et al,[17] similarly demonstrated considerable variation in AR expression across breast cancer molecular phenotypes, with greater AR expression among hormone receptor-positive tumors and substantially lower expression in triple-negative disease. Anand et al,[15] also reported a strong relationship between AR expression and hormone receptor-driven phenotypes. Taken together, these findings support biological heterogeneity of AR expression according to HER2 and hormone receptor phenotype. The relationship between AR and conventional molecular phenotype was also evident in the present cohort. AR positivity was highest in HR+/HER2+ tumors (73.3%), followed by HR−/HER2+ (70.4%) and HR+/HER2− tumors (69.7%), whereas only 35.5% of triple-negative breast cancers (TNBC) were AR-positive (p<0.001).These findings are consistent with Loibl et al,[17] who reported marked variation in AR expression according to molecular subtype, ranging from approximately 21.2% in TNBC to about 67% in luminal A-like tumors. Anand et al,[15] similarly observed greater AR expression among luminal breast cancers. Although AR expression is less frequent in TNBC, its presence in a distinct subset is clinically relevant because AR-positive TNBC has been recognized as representing a biologically distinct phenotype. The high AR expression observed in HER2-associated tumors in the present study further indicates that AR biology extends beyond conventional hormone receptor-positive breast cancer. A major finding of the revised analysis was the significant association between HER2 phenotype and pathological response following NACT (p=0.024). Overall, 59 patients (22.0%) achieved RCB-0, while

16 (6.0%) had RCB-I, 91 (34.0%) had RCB-II, and 102 (38.1%) had RCB-III disease. Thus, a substantial proportion of the cohort had residual disease following systemic therapy. The HER2-low group demonstrated the least favourable pathological response. Only 10.6% of HER2-low tumors achieved RCB-0, compared with 25.2% of Her2 negative and 26.4% of HER2-positive tumors. Conversely, RCB-III disease was observed in 48.5% of HER2-low tumors, compared with 33.9% of Her2 negative and 35.6% of HER2-positive tumors. These findings suggest that, within the present cohort, HER2-low disease represented a subgroup characterized by greater residual tumor burden following NACT. The higher RCB-0 proportion among HER2-positive tumors should be interpreted in the context of contemporary HER2-directed systemic treatment, whereas HER2-low tumors were historically managed according to their hormone receptor status without HER2-targeted treatment in the neoadjuvant setting. The present results therefore support evaluating HER2-low disease separately rather than combining it with all HER2-negative tumors when investigating pathological response.AR expression itself was significantly associated with RCB response (p=0.019). RCB-0 was achieved in 16.7% of AR-positive tumors compared with 31.0% of AR-negative tumors. Conversely, AR-positive tumors were more frequently represented within residual disease categories, particularly RCB-II.These observations are broadly consistent with Loibl et al,[17] who demonstrated significantly lower pathological complete response among AR-positive compared with AR-negative tumors (12.8% vs 25.4%, p<0.0001). Interestingly, despite their lower pCR rate, AR-positive tumors in that study demonstrated more favourable disease-free and overall survival, indicating that AR may reflect a distinct biological phenotype rather than merely chemotherapy resistance. In contrast, Anand et al,[15] reported greater AR expression among patients demonstrating favourable clinical response, although the association was not statistically significant (p=0.218). Therefore, the predictive significance of AR for NACT response remains heterogeneous across studies and may depend on underlying molecular subtype and treatment regimen. The most clinically relevant observation of the present study emerged when HER2 phenotype and AR expression were considered simultaneously. The distribution of RCB classes differed significantly across the combined HER2/AR phenotypes (overall p<0.001), indicating that the relationship between AR and treatment response may vary according to HER2 status Among Her2 negative tumors, RCB-0 was achieved in 15.8% of AR-positive compared with 34.5% of AR-negative tumors. Furthermore, RCB-II disease was substantially more frequent among Her2 negative/AR-positive tumors (49.1%) than Her2 negative/AR-negative tumors (22.4%). The most striking pattern, however, was observed among patients with HER2-low/AR-positive disease. Only 2 of 48 patients (4.2%) in this subgroup achieved RCB-0, while 45 of 48 (93.8%) had RCB-II or RCB-III disease. Specifically, 45.8% were classified as RCB-II and 47.9% as RCB-III. In comparison, 27.8% of HER2-low/AR-negative tumors achieved RCB-0. These findings suggest that AR expression may identify a subgroup within HER2-low breast cancer characterized by particularly poor pathological response to NACT. In HER2-positive disease, the RCB-0 rate was relatively similar between AR-positive and AR-negative tumors (27.0% vs 25.0%). However, RCB-III disease was more frequent among AR-negative HER2-positive tumors (54.2%) than among AR-positive HER2-positive tumors (28.6%). This observation suggests that the relationship between AR and chemotherapy response may not be uniform across HER2 phenotypes. The findings of Loibl et al,[17] showing lower pCR among AR-positive breast cancers.

Conclusion

The present study demonstrated that HER2 status was significantly associated with AR expression and pathological response following NACT. AR expression was more frequent in HER2-low and HER2-positive tumors than in Her2 negative tumors. HER2-low tumors showed a higher residual cancer burden, with the HER2-low/AR-positive subgroup demonstrating particularly low RCB-0 and high RCB-II/III rates. These findings suggest that combined assessment of HER2 phenotype and AR expression may help identify biologically distinct breast cancer subgroups with differential response to neoadjuvant therapy.

Limitations: This was a single-centre study, which may limit the generalizability of the findings. The relatively small numbers within some HER2/AR subgroups and absence of long-term disease-free and overall survival data limited assessment of their prognostic significance. Variations in NACT regimens may also have influenced pathological response.

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Conflicts of interest

There are no conflicts of interest.

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