Original Article

Androgen receptor expression distribution characteristics in young female breast cancer patients in China: a study of clinicopathological features

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Background: The expression of androgen receptor (AR) in breast cancer has potential implications for predicting clinical outcomes, especially amongst young female patients. Numerous studies have reported that the co-expression of AR with hormone receptors (HRs) is correlated with a favorable prognosis in breast cancer. However, research on the frequency and distribution of AR expression in Chinese breast cancer patients is limited. This study aims to investigate the relationship between AR expression and the expression of progesterone receptor (PR), estrogen receptor (ER), P53, human epidermal growth factor receptor 2 (HER2), and epidermal growth factor receptor (EGFR) in breast cancer patients, and the distribution of molecular subtypes of breast cancer. Further, we aim to explore the pattern of AR expression and its correlation with clinicopathological features and prognosis among young female patients in China.

Methods: Formalin-fixed paraffin-embedded tissue samples from 321 young female breast cancer patients were collected from the Third Hospital of Nanchang. Immunohistochemistry was used to assess the expression of AR, ER, PR, HER2, and Ki67. A statistical analysis was conducted to explore the correlation between the expression of AR and these molecular markers, as well as their distribution across different molecular subtypes of breast cancer, and their prognostic significance.

Results: A total of 321 breast cancer patients were included in this study. Significant correlations were found between the positive expression of AR and the high expression of PR and ER (P<0.001). The rate of P53 positivity was significantly higher in the AR-positive patients than the AR-negative patients (P=0.01). Additionally, HER2 expression was significantly higher in the AR-positive patients than the AR-negative patients (P<0.001). Notably, the rate of EGFR positivity was significantly lower in the AR-positive patients compared to AR-negative patients (P<0.001). In relation to the molecular subtypes, AR positivity was significantly associated with the luminal A subtype (P<0.001), while the triple-negative breast cancer (TNBC)/basal-like subtype was more common in the AR-negative patients.

Conclusions: This study revealed that in young female breast cancer patients in China, AR-positive breast cancer was significantly associated with the high expression of HRs, increased P53 expression and reduced EGFR expression. The expression status of AR can serve as a biomarker to predict therapeutic responses but could also influence the classification of molecular subtypes and the selection of treatment strategies.

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Introduction

Breast cancer is the most common cancer and leading cause of cancer-related death in women worldwide (1-3). Its incidence and mortality rates have steadily increased among young Chinese women (2). Breast cancer is a heterogeneous disease with various subtypes, each characterized by distinct clinical, pathological, and molecular features (4-6). Widely accepted predictive and/or prognostic factors for breast cancer include steroid or growth hormone receptors (HRs)—estrogen receptor (ER) and progesterone receptor (PR); and human epidermal growth factor receptor 2 (HER2) (7-10). With improved understanding of the molecular biology of breast cancer, targeted therapies for HER2 positive tumors have continued to evolve (11,12).

The androgen receptor (AR) is a steroid receptor expressed in various tissues including the prostate and testes, skin, cardiac muscle, liver parenchyma and the mammary glands (13). In its inactive form, the AR is located in the cytosol, but after binding by androgens the receptor-ligand complex translocates to the nucleus where it acts as a transcription factor (14). The AR also plays a complex role in the pathogenesis of breast cancer, and research has identified AR as a useful marker for further refining breast cancer molecular subtyping, and as an emerging clinical target (14-19). Although the potential therapeutic significance of AR in HR-positive breast cancer has been widely reported (20,21), the clinicopathological characteristics and impact on patient prognosis remains unclear. A study on the expression patterns of AR, its prognostic value and subsequent treatment, are limited in Asia, especially among its young female breast cancer population (22).

Recent study has highlighted the critical role of AR in breast cancer, particularly its potential clinical significance in hormone receptor-positive (HR+) and triple-negative breast cancer (TNBC) subtypes. AR has demonstrated an important role in modulating treatment response, suggesting that it could serve as a therapeutic target for HR+ and TNBC subtypes (23). For example, a study has shown that AR antagonists combined with existing therapies offer new hope for patients with limited treatment options (24). Furthermore, the potential association of AR expression with the efficacy of chemotherapy and targeted therapy provides a basis for exploring its role as a predictive biomarker for treatment response (25). These advances not only enhance the understanding of the relationship between AR expression and other key molecular markers, such as ER, Ki67, and EGFR, but also underscore its potential role in guiding individualized treatment decisions.

Some authors have suggested that AR should serve as an additional predictive and/or prognostic marker, and

Highlight box

Key findings

- This study found that androgen receptor (AR) positivity in young Chinese female breast cancer patients was significantly associated with the high expression of hormone receptors (HRs), such as progesterone receptor (PR) and estrogen receptor (ER), increased P53 expression, higher human epidermal growth factor receptor 2 (HER2) positivity, and lower epidermal growth factor receptor (EGFR) expression. AR positivity was correlated with the luminal A subtype, while AR negativity was more frequent in the triple-negative breast cancer/basal-like subtype. These findings suggest that AR may serve as a valuable biomarker for breast cancer subtype classification and prognosis.

What is known, and what is new?

- Previous studies have shown that AR co-expression with HRs (ER and PR) in breast cancer is associated with a favorable prognosis and improved response to endocrine therapy. However, research on the prevalence and distribution of AR expression in young Chinese breast cancer patients is limited.
- This study provided new insights into the correlation between AR expression and molecular markers (P53, HER2, and EGFR) and specific breast cancer subtypes in young Chinese women, highlighting the association between AR and the luminal A subtype, and the absence of AR in the TNBC/basal-like subtype.

What is the implication, and what should change now?

- AR expression may complement PR, ER, and HER2 as a biomarker, aiding personalized treatment, especially in endocrine therapy. Routine AR testing could improve treatment precision and outcomes. Further research on AR's role across subtypes is needed to refine therapeutic strategies.

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be evaluated in routine diagnostic assessments of breast cancer as part of a quadruple assessment with ER, PR, and HER2 (26-28). AR is expressed in all stages of breast cancer (*in situ*, primary, and metastatic) (29,30). Studies have indicated that AR may play differing prognostic roles in ER-positive and ER-negative breast cancers (31,32). The frequency of AR expression varies by clinical subtype, but is about 70–95% in ER positive tumors, 50–63% in ER negative/HER2 positive tumors, and 10–53% in TNBC (14,33-37). Recent pre-clinical and clinical studies support the role of AR-targeted therapy in the treatment of breast cancer (38,39). Specifically, therapies such as Enobosarm and other AR modulators have shown promise in certain breast cancer subtypes. These findings highlight the potential for AR-targeted approaches as a therapeutic strategy.

This study aimed to explore the expression of AR among young female breast cancer patients in Nanchang, China. It also assessed its correlation with clinicopathological characteristics. This study also sought to examine the correlation between AR expression and clinical outcomes in breast cancer patients, particularly in terms of treatment response and disease prognosis. This approach not only extends the understanding of the biological role of AR in the progression of breast cancer but also provides empirical support for population-based personalized treatments, which is crucial for developing more effective prevention and treatment strategies for young Chinese women. We present this article in accordance with the REMARK reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-147/rc).

Methods

Sample collection and processing

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Research Ethics Review Committee of the Third Hospital of Nanchang (No. NCSDSYYK-lw20230076). Written informed consent was obtained from each patient and tissue samples were completely anonymized prior to acquisition. Formalin fixed paraffin embedded (FFPE) slides were stained with hematoxylin and eosin (H&E) and examined by pathologists at the Third Hospital of Nanchang to locate the tumor in the sections.

Researchers reviewed the medical records of patients who underwent surgery from May 2019 to June 2024 to collect their sociodemographic and pathological data. A cross-sectional retrospective design was employed. Some of the participants had undergone pathological examinations. Researchers accessed patient medical records to collect variables including age, tumor type, grade, and disease stage. A total of 321 FFPE tissue samples from young female breast cancer patients were collected in accordance with strict inclusion and exclusion criteria to ensure the study's consistency and accuracy. The study's inclusion criteria were as follows: (I) female aged 20 to 35 years; (II) newly diagnosed invasive breast cancer; (III) pathologically confirmed diagnosis of breast cancer based on surgically resected specimens; and (IV) treatment naive (no previous chemotherapy, radiotherapy, or hormonal treatment prior to surgical intervention). Exclusion criteria were as follows: (I) previous treatment for breast cancer; (II) a history of other types of cancer; (III) samples did not meet the requirements for immunohistochemical analysis (e.g., poor fixation or an inappropriate slice thickness); and/or (IV) incomplete clinical-pathological data or follow-up information.

Immunohistochemical staining

Immunohistochemical staining was performed using specific antibodies targeting human AR, ER, PR, HER2, and Ki67. The procedure was conducted in accordance with the standard protocols provided by the manufacturers, and the following antibodies were used: AR antibody (Clone AR441, mouse monoclonal, ABclonal, Wuhan, China); ER antibody (Clone SP1, rabbit monoclonal, ABclonal, Wuhan, China); PR antibody (Clone PgR636, mouse monoclonal, ABclonal, Wuhan, China); HER2 antibody (Clone 4B5, rabbit monoclonal, ABclonal, Wuhan, China); and Ki67 antibody (Clone MIB-1, mouse monoclonal, ABclonal, Wuhan, China). Before staining, the FFPE tissue sections were deparaffinized and rehydrated. Specifically, the sections were treated twice with xylene for 15 minutes each, and then underwent dehydration through a graded ethanol series with each step lasting 5 minutes. After rinsing in water, antigen retrieval was performed by microwaving in citrate buffer (pH 6.0) for 15 minutes to restore the antigenicity of the tissue. The sections were then incubated in 3% hydrogen peroxide for 10 minutes to block endogenous peroxidase activity. Before the addition of each antibody, the sections were pre-incubated for 30 minutes in phosphate-buffered saline containing 10% normal goat serum to reduce non-specific binding. The sections were then incubated at room temperature for 1 hour. Two pathologists (W.Q., D.G.) independently scored

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Table 1 The baseline clinicopathological and molecular characteristics of the study participants (n=321)

Variables	Values
Age (years)	31.56±2.70
Side	
Left	155 (48.3)
Right	166 (51.7)
Histological grade	
I	11 (3.4)
II	151 (47.1)
III	158 (49.2)
Missing	1 (0.3)
AR	
Positive	250 (77.9)
Negative	70 (21.8)
Missing	1 (0.3)
ER	
Positive	221 (68.8)
Negative	100 (31.2)
PR	
Positive	186 (57.9)
Negative	135 (42.1)
HER2	
Positive	224 (69.8)
Negative	97 (30.2)
Ki67	
Positive	217 (67.6)
Negative	104 (32.4)
P53	
Positive	221 (68.8)
Negative	98 (30.5)
Missing	2 (0.6)
Histological type	
Infiltrating ductal	288 (89.7)
Lobular	7 (2.2)
Others/not classified	23 (7.2)
Missing	3 (0.9)

Values are presented as mean ± standard deviation or n (%). AR, androgen receptor; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor.

the immunostaining results.

Evaluation of immunohistochemical results

Standard methods were used to assess and score the expression of ER, PR, and HER2 as per the American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) 2013 guidelines and previous descriptions by Asano *et al.* Positive expression of AR, ER, and PR was defined as ≥1% positively stained nuclei (40,41). HER2 scoring was based on membrane staining intensity, categorized according to the ASCO/CAP guidelines, with a scoring scale ranging from 0 to 3 on which 0–1+ was considered negative, 2+ was considered equivocal, and 3+ was considered positive. The Ki67 scoring was conducted according to the recommendations of the St. Gallen International Expert Consensus (39), and scored based on the percentage of positively stained nuclei, with a score >20% indicating high expression.

The scoring process was independently conducted by two experienced pathologists. If a discrepancy arose, a third pathologist was consulted. Following the St. Gallen International Expert Consensus 2013 (42), tumors were classified into the following four molecular subtypes: luminal A (ER and/or PR positive & HER2 negative & Ki67 ≤20%), luminal B ER and/or PR positive & HER2 positive or negative & Ki67 >20%), HER2-enriched (ER negative & PR negative & HER2 positive), and triple-negative (ER negative & PR negative & HER2 negative).

Statistical analysis

The statistical analyses were performed using SPSS software (version 22.0, IBM). Continuous data is reported as mean ± standard deviation or as the median and range in case that they have a skewed distribution. Categorical data are reported as numbers (percentages). All P values are two-tailed, and a P value <0.05 was considered statistically significant. The Mann-Whitney *U* test was used to compare the median ages. The Chi-squared test and the analysis of variance were employed to determine correlations between categorical variables.

Results

In this study, the baseline clinicopathological and molecular characteristics of 321 participants were analyzed (*Table 1*). The patients had an average age of 31.56±2.70 years. In

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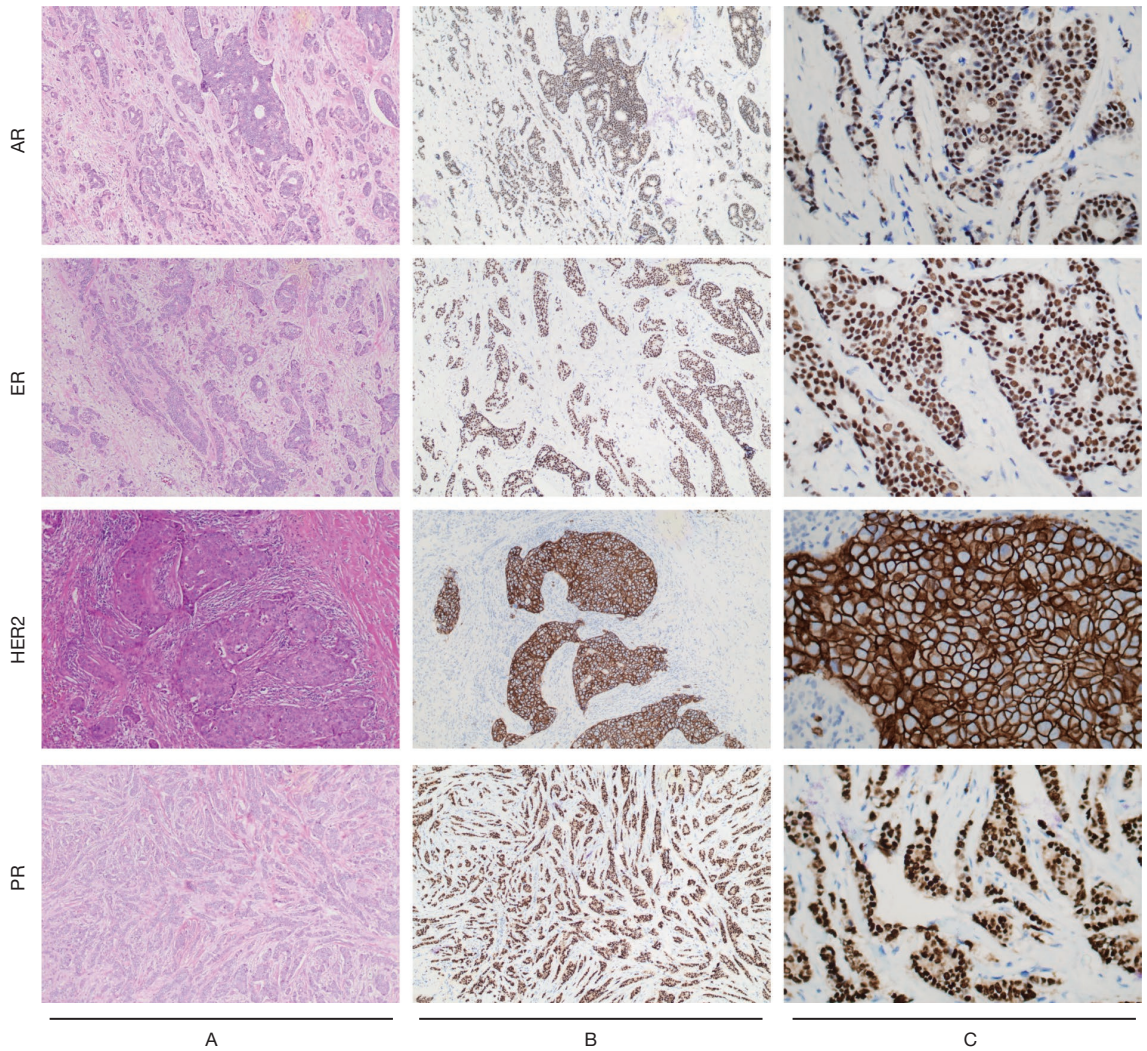

Figure 1 Representative immunohistochemical images of breast tumor tissues negative for AR, ER, HER2, and PR. (A) An H&E stain, magnified 100×, displaying the overall morphological characteristics of the tissue. (B) A negative immunohistochemical stain, magnified 100×, in which most tumor cells exhibit negative staining. (C) A negative immunohistochemical stain, magnified 400×, with detailed nuclear negative expression. AR, androgen receptor; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; H&E, hematoxylin & eosin; PR, progesterone receptor.

terms of tumor laterality, 155 patients (48.3%) had left-sided breast cancer and 166 (51.7%) had right-sided breast cancer. Histological tumor grading could be performed on 320 out of 321 samples and revealed that 11 patients (3.4%) had grade I, 151 (47.1%) had grade II, and 158 (49.2%) had grade III breast cancer. Representative immunostaining images are shown in *Figures 1*,*2*. Among the 321 patients, 221 (68.8%) were ER positive and 100 (31.2%) were ER negative. Additionally, 186 (57.9%) patients were PR positive and 135 (42.1%) were PR negative, while 224 (69.8%) patients were HER2 positive and 97 (30.2%) were HER2 negative. Two hundred-seventeen (67.6%) patients had Ki67-positive expression, while 104 (32.4%) had Ki67-negative expression. In relation to P53 protein expression, 221 (68.8%) patients were positive, and 98 (30.5%) were negative; data were missing for 2 (0.6%) patients. In relation to the tissue type, invasive ductal carcinoma (IDC) was the most common, accounting for 288 cases (89.7%), followed by invasive lobular carcinoma (ILC) in 7 cases (2.2%), and 23 patients (7.2%) coming under other types or unclassified.

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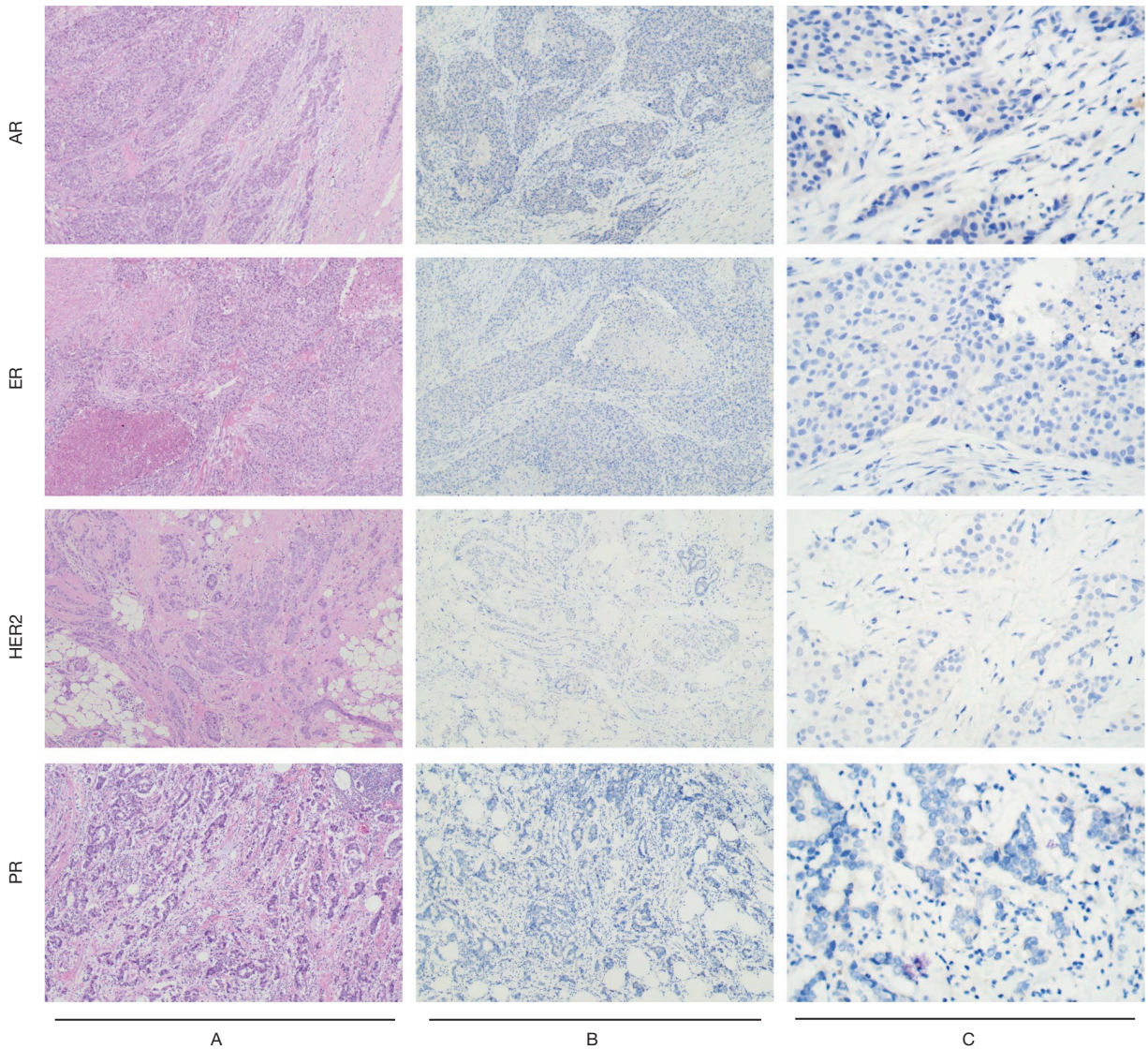

Figure 2 Representative immunohistochemical images of breast tumor tissues positive for AR, ER, HER2, and PR. (A) An H&E stain, magnified 100×, displaying the overall morphological characteristics of the tissue. (B) A positive immunohistochemical stain, magnified 100×, in which most tumor cells display intense staining. (C) A positive immunohistochemical stain, magnified 400×, with detailed nuclear positive expression. AR, androgen receptor; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; H&E, hematoxylin & eosin; PR, progesterone receptor.

Three patients (0.9%) had missing data.

The high proportion of HER2 positivity (69.8%) indicated a higher prevalence of HER2-positive breast cancer in this sample, and has important implications for targeted therapies. The high percentages of ER and PR positivity suggested that most patients would be suitable for endocrine therapy, which could potentially improve their prognosis. The expressions of Ki67 and P53 indicated possibly high proliferative activity and abnormalities in tumor suppressor genes, which might be correlated with more aggressive tumor behavior and a poorer prognosis. The results showed that most patients expressed ER positivity and AR positivity, while HER2 expression was predominantly negative, reflecting the high incidence of HR-positive breast cancer. Missing data on histological grading and cancer staging underscore the need for more

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Table 2 Relationship between patient AR expression and clinicopathological parameters

Parameter	AR negative	AR positive	Total	P value
Histological grade				<0.001
I	1 (1.4)	10 (4.0)	11 (3.4)	
II	11 (15.7)	140 (55.8)	151 (47.0)	
III	57 (81.4)	101 (40.2)	158 (49.2)	
Missing	1 (1.4)	0 (0.0)	1 (0.3)	
Stage				0.19
I	24 (34.3)	104 (41.4)	128 (39.9)	
II	45 (64.3)	134 (53.4)	179 (55.8)	
III	1 (1.4)	13 (5.2)	14 (4.4)	
Histological type				0.84
Infiltrating ductal	64 (91.4)	224 (89.2)	288 (89.7)	
Lobular	2 (2.9)	5 (2.0)	7 (2.2)	
Others/unknown	4 (5.7)	19 (7.6)	23 (7.2)	
Missing	0 (0.0)	3 (1.2)	3 (0.9)	

Values are presented as n (%). AR, androgen receptor.

precise diagnostic and recording standards to guide clinical treatment. These study results are crucial for understanding the roles of different biomarkers in breast cancer prognosis and treatment decision making.

These findings suggest that AR expression could serve as an important prognostic factor for personalized treatment strategies in HR-positive breast cancer. Further analysis of AR expression in tumor tissues may help physicians predict responses to specific hormonal therapies and provide more tailored treatment options. The results for AR expression in breast cancer and its association with histological grading, cancer staging, and histological types were analysed (*Table 2*). The results revealed that AR positivity was significantly associated with lower grades (grades I and II) of breast cancer (P<0.001). Grade III cancers were more prevalent in the AR-negative group (81.4%) than the AR-positive group (40.2%) (P<0.001).

With respect to cancer staging, while the AR-positive patients had a higher distribution in stage I and II than the AR-negative patients, this difference was not statistically significant (P=0.19). The diagnosis of IDC did not have statistical relevance to AR-positivity or AR-negativity (89.2% *vs.* 91.4%, respectively; P=0.84). Additionally, no significant differences between the two groups were found in terms of distribution of ILC and other unknown types of cancer.

Although the association between AR expression and cancer staging did not reach statistical significance (P=0.19), the trend of higher AR expression in stage I and II cancers suggests that AR-positive tumors may be diagnosed and treated earlier. This early-stage presentation could influence treatment strategies and outcomes, highlighting the potential role of AR in guiding personalized treatment approaches.

Table 3 summarizes the results of a comparative analysis of multiple molecular markers in breast cancer patients with positive and negative AR expression. The results revealed that AR positivity was significantly associated with the high expression of PR and ER. In the AR-positive group, the proportion of PR-positive expression was 68.9%, which was significantly higher than the 18.6% observed in the AR-negative group (P<0.001). Similarly, ER-positive expression in the AR-positive group was 78.9%, which was significantly higher than the 32.9% in the AR-negative group (P<0.001). For the tumor suppressor protein P53, the AR-positive group showed a statistically significant higher positive expression rate of 72.9%, compared to 57.1% in the AR-negative group (P=0.01). Additionally, the expression of HER2 was significantly higher in the AR-positive group (76.9%) than the AR-negative group (44.3%) (P<0.001). At only 17.6%, the expression of the EGFR was statistically

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Table 3 The relationship between patient AR expression and clinicopathological molecular parameters

Molecular parameters	AR negative	AR positive	Total	P value
PR				<0.001
Negative	57 (81.4)	78 (31.1)	135 (42.1)	
Positive	13 (18.6)	173 (68.9)	186 (57.9)	
ER				<0.001
Negative	47 (67.1)	53 (21.1)	100 (31.2)	
Positive	23 (32.9)	198 (78.9)	221 (68.8)	
P53				0.01
Negative	30 (42.9)	68 (27.1)	98 (30.5)	
Positive	40 (57.1)	183 (72.9)	223 (69.5)	
HER2				<0.001
Negative	39 (55.7)	58 (23.1)	97 (30.2)	
Positive	31 (44.3)	193 (76.9)	224 (69.8)	
EGFR				<0.001
Negative	35 (50.0)	202 (80.8)	237 (74.0)	
Positive	34 (48.6)	44 (17.6)	78 (24.4)	
Missing	1 (1.4)	4 (1.6)	5 (1.6)	
Molecular subtype				<0.001
Luminal A	18 (15.0)	102 (85.0)	120 (37.4)	
Luminal B	5 (7.0)	66 (93.0)	71 (22.1)	
HER2-enriched	5 (15.2)	28 (84.8)	33 (10.3)	
TNBC/basal-like	62 (63.9)	35 (36.1)	97 (30.2)	

Values are presented as n (%). AR, androgen receptor; EGFR, epidermal growth factor receptor; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor; TNBC, triple-negative breast cancer.

lower in the AR-positive patients than the AR-negative patients, for whom the expression was 48.6% (P<0.001). AR positivity was significantly inclined towards the luminal A subtype (85% *vs.* 15%, P<0.001), while the TNBC/basal-like subtype was more common in the AR-negative group (36.1% *vs.* 63.9%, P<0.001).

Discussion

This study highlights the potential role of AR by examining its correlations with key molecular markers, including ER, PR, HER2, P53, and EGFR in tumors from young Chinese women. These analyses provide valuable insights into AR's possible influence on the biological behavior and treatment responses of breast cancer We were able to confirm previous results which indicate that AR-positive breast cancer is significantly associated with higher expressions of PR and ER (36,43). Further, AR-positive breast cancer has a lower correlation with the expression of the EGFR. The distribution of AR among breast cancer molecular subtypes displays specific patterns that may be closely related to disease prognosis and treatment responsiveness (44). These findings are of critical clinical importance for the molecular classification and personalized treatment of breast cancer.

Notably, the high expression rates of PR and ER in AR-positive breast cancer patients suggest a potential association with better responsiveness to hormone therapy. This observation is consistent with the traditional understanding that HR-positive breast cancer patients generally have a better prognosis and respond well to endocrine

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therapy. However, as this study only demonstrates an association, further research is needed to establish a causal relationship between AR expression and hormone therapy responsiveness (45). However, the biological behavior of these tumors may change when they also express AR. The treatment responsiveness and disease progression patterns of breast cancers co-expressing AR with ER and PR are still poorly understood (46).

Our findings revealed a significant association between the positive expression of AR, and the positive expression of ER and PR, which suggests that the presence of AR might influence the activity of hormone signaling pathways, potentially affecting treatment. Specifically, in the AR-negative group, higher proportions of patients were ER-negative and PR-negative (ER: 67.1% and PR: 81.1%), while in the AR-positive group, higher proportions were ER-positive and PR-positive (ER: 78.9% and PR: 68.9%), with corresponding P values <0.001, indicating that these differences were statistically significant. These findings suggest that the expression status of AR maybe linked to the responsiveness to hormone therapy in HR-positive tumors (47).

In this study, the expression of P53 was significantly increased in the AR-positive group. The higher proportion of P53 positivity in the AR-positive group may indicate different regulatory mechanisms in cell cycle control and apoptosis pathways. The correlation between AR positivity and P53 positivity might suggest that these tumors possess more complex biological characteristics. However, further research is required to validate this finding, particularly in terms of predicting treatment outcomes and devising treatment plans.

In terms of the relationship with HER2 expression, we found a statistically significant correlation between AR expression status and HER2 positivity (P<0.001). The expression of HER2 might be more influenced by other regulatory mechanisms. This finding could have clinical implications, especially when considering HER2-targeted treatment strategies. The significant overexpression of HER2 in the AR-positive patients suggests that this group may be particularly suited for HER2-targeted treatments. Since there may be synergistic or antagonistic interactions between HER2 and AR in signaling and tumor growth, further exploration of their interactions could be crucial in optimizing treatment strategies. Our findings also provide new insights into the negative correlation between AR and EGFR expression, especially when considering potential indications for EGFR-targeted therapy. AR-positive breast cancer patients with low EGFR expression may be less likely to respond to EGFR inhibitors; thus, other treatment approaches may be necessary.

Conversely, this study also found significant differences in the distribution of AR expression across molecular subtypes. In the luminal A subtype, the proportion of AR-positive patients was significantly higher than the proportion of AR-negative patients (85.0% *vs.* 15.0%, P<0.001). However, in the TNBC/basal-like subtype, a higher proportion of AR-negative cases was observed (63.9% *vs.* 36.1%, P<0.001). These results suggest that the disease characteristics and prognosis of breast cancer patients with AR expression may be closely linked to the level of AR expression. The study also found a higher proportion of TNBC/basal-like subtype in the AR-negative breast cancer patients. This subtype generally has a poorer prognosis, but may be more sensitive to chemotherapy and emerging targeted therapies (48,49). The low expression of AR in this subtype may reveal a tumor growth mechanism that is independent of hormone signaling, potentially opening new avenues for TNBC treatment (50). This study did not directly explore the therapeutic potential of AR inhibitors; however, our results lay the groundwork for further exploration of AR as a therapeutic target.

From a prognostic and therapeutic perspective, AR expression can serve as a supplementary indicator for molecular typing and may become an important biomarker for assessing the prognosis of breast cancer patients (51). Given the correlation between AR positivity and hormone therapy response, the expression status of AR may help guide treatment choices (52). Moreover, AR may serve as a potential therapeutic target, particularly in HR-positive, HER2-negative breast cancers. For TNBC/basal-like breast cancer, which is by definition negative for HR and HER2, further study on AR receptor status are warranted. Understanding the role of AR in TNBC may help identify new therapeutic strategies and guide the management of this aggressive breast cancer subtype (53).

This study provides valuable insights into the role of AR expression in breast cancer and its relationship with other molecular markers such as ER, Ki67, and EGFR. Its potential lies in utilizing AR expression as a novel therapeutic target, particularly in HR+ breast cancer and possibly in TNBC. This could lead to more personalized treatment strategies and improve clinical outcomes. Despite the growing body of research on AR, there are still significant knowledge gaps regarding its precise molecular mechanisms, especially its role in different breast

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cancer subtypes. Researchers are addressing these gaps by employing multi-omics approaches and clinical trials to better understand AR's involvement in tumor progression and resistance. In the next five years, we anticipate that AR expression will become an important predictive biomarker in clinical practice to guide the evaluation of treatment response. With the development of AR-targeted therapies, including combination treatments, AR is expected to become a key factor in personalized treatment strategies for breast cancer. The integration of AR testing with genomic analysis may enhance treatment decision-making, improve patient outcomes, and avoid unnecessary treatments.

Importantly, although our findings provide interesting insights into the associations between different molecular markers, they need to be validated in a larger patient cohort and assessed through prospective studies to evaluate the impact of AR expression on breast cancer treatment outcomes. In clinical practice, AR assessment might become an additional factor in molecular typing, helping to identify patients who may benefit from specific therapeutic approaches (44,54). Further, as personalized medicine advances, understanding the specific role of AR across different HR statuses and molecular subtypes is crucial for devising personalized treatment plans.

Conclusions

This study conducted a comprehensive analysis of the expression of AR in breast cancer of young Chinese women and its association with other key molecular markers. The results showed that AR positivity was significantly associated with the high expression of the PR and ER, and negatively correlated with the expression of the EGFR. Additionally, a higher expression of P53 protein and HER2 was observed in patients with AR-positive breast cancer. The analysis of the molecular subtypes highlights the association of AR with the luminal A subtype. While AR positivity does not directly impact the favorable prognostic status of luminal A, its correlation may contribute to understanding the molecular characteristics of this subtype. In contrast, the TNBC/basal-like subtype was more common among the AR-negative patients, a subtype typically associated with a poorer prognosis and more complex treatment options. These findings provide crucial clinical information for molecular classification, prognostic assessment, and the selection of treatment strategies in breast cancer.

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None.

Footnote

Reporting Checklist: The authors have completed the REMARK reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-147/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-147/dss

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Research Ethics Review Committee of the Third Hospital of Nanchang (No. NCSDSYYK-lw20230076) and informed consent was taken from all the patients.

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