Section: General Surgery

Original Research Article

IMMUNOHISTOCHEMICAL SUBTYPES OF BREAST CARCINOMA: CORRELATION WITH STAGE AT PRESENTATION AND PROGNOSTIC OUTCOME: A RETROSPECTIVE STUDY

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Received *: 20/05/2025*
Received in revised form *: 05/07/2025*
Accepted *: 29/07/2025*

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DOI: 10.70034/ijmedph.2025.3.513

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 2795-2800

ABSTRACT

Background: Breast cancer is one of the major public health problems particularly in low- and middle-income countries including India. It has a substantial mortality owing to late-stage presentation. Immunohistochemical (IHC) profiling is a cost-effective surrogate for molecular subtyping. It enables tailored management in cases of invasive breast carcinoma. This study aimed to analyse the correlation between IHC subtypes and stage at diagnosis, nodal involvement and clinical outcomes.

Materials and Methods: A retrospective observational study was conducted in which 30 confirmed cases of invasive breast carcinoma from January 2018 to December 2022 in a tertiary-care teaching hospital were included on the basis of a predefined inclusion and exclusion criteria. ER, PR, and HER2 status were recorded from IHC reports using ASCO/CAP guidelines. Molecular subtypes (Luminal A, Luminal B, HER2-enriched, and triple-negative) were determined accordingly. Clinicopathological data, including age, tumour stage, lymph node involvement and outcomes were analysed using SPSS v25. P value less than 0.05 was taken as statistically significant.

Results: The most affected age group was 40–49 years (33.3%). ER and PR positivity were observed in 60.0% and 53.3% of cases respectively. HER2 positivity was seen in 30.0% of the cases. Luminal A was the most common subtype (40.0%) which was followed by TNBC (23.3%), Luminal B (20.0%), and HER2-enriched (16.7%). Most of the patients presented at Stage II (50.0%) with Luminal A cases were found to be significantly more likely to present at early stages (p=0.037). Lower nodal metastasis (p=0.045) was seen in ER-positive patients. Better survival rates were seen in ER and PR positive cases whereas HER2 and triple-negative subtypes had higher recurrence and mortality rates. At median follow-up of 24 months, 77.8% of ER-positive patients were disease-free compared to 33.3% of ER-negative.

Conclusion: Immunohistochemical subtyping can effectively divide breast carcinoma into prognostically distinct categories. Luminal A subtype was found to be associated with early-stage presentation and favourable outcomes, while HER2-enriched and TNBC correlated with advanced disease and poorer prognosis. IHC profiling remains an effective alternative to molecular subtyping in resource-limited settings.

Keywords: Breast Neoplasms, Immunohistochemistry, Molecular Subtypes, Prognosis.

INTRODUCTION

Breast cancer remains an important public health problem worldwide and represents the most frequently diagnosed malignancy and the leading cause of cancer-related death among women. The Global Cancer Observatory estimated that over 2.26

million new cases and approximately 685 000 fatalities in 2020 alone. The age-standardized incidence rate globally stands at 47.8 per 100 000 women, with a mortality rate of 13.6 per 100 000.[1] In India, the scenario is particularly alarming: recent data indicate an age-adjusted incidence of 25.8 per 100 000 and a mortality rate of 12.7 per 100 000.[2] Despite advances in diagnostic modalities and therapeutic approaches, a large proportion of patients present at an advanced stage of cancer thereby compromising overall outcomes and imposing considerable burden on healthcare system of the country.

Breast carcinoma comprises of histopathological and molecular subtypes with distinct biological, clinical and prognostic implications. Histologically, invasive ductal carcinoma (IDC) accounts for approximately 70–80% of cases followed by invasive lobular carcinoma (ILC) at 5–10% and special variants such as mucinous, tubular and medullary carcinomas.[3] Regional studies from Asia and Africa have demonstrated variability in histological subtype prevalence and grade distribution with a higher proportion of high-grade tumours reported in low- and middle-income countries. ILC is seen to be affecting individuals at older ages. Moreover, ILC may also present with multifocal disease. Molecular classification based on gene expression profiling subdivides carcinoma breast in at least four principal subtypes—Luminal A (≈ 40%), Luminal B (≈ 20%), HER2-enriched (≈ 15–20%), and triple-negative breast cancer (TNBC, ≈ 10–15%). This classification is based on distinct patterns of hormone receptor, proliferative indices (e.g., Ki-67) as well as HER2/neu status.[4] The distribution of molecular subtypes also varies and higher proportions of TNBC and HER2-enriched phenotypes in younger patients are reported to disparities in outcomes.

Immunohistochemistry (IHC) plays an important role in the diagnostic and therapeutic management of breast cancer. It provides a cost-effective alternative to complex molecular assays which is expensive and not widely available. Standardized IHC assessment of oestrogen receptor (ER) and progesterone receptor (PR) employs the Allred scoring system or percentage.[5] HER2/neu overexpression is reported via membrane staining intensity (0 to 3+) with 3+ denoting positivity and 2+ requiring reflex fluorescence in situ hybridization (FISH) confirmation.[6] ER and PR positivity is an important determinant of outcome in cases of carcinoma breast as it can predict response to endocrine therapies such as tamoxifen and aromatase inhibitors. Such a management strategy is known to improve disease-free survival in receptor-positive cohorts.[7] HER2-positive tumours, prior to the advent of targeted therapy, conferred an adverse prognosis but with the integration of trastuzumab and other HER2-directed agents, outcomes have markedly improved.[8] In resource-constrained settings, IHC remains the primary method for molecular subtyping and can guide treatment in lieu of expensive genomic assays.

Stage at presentation remains an important factor which influences prognosis and therapeutic planning. Early-stage (American Joint Committee on Cancer Stages I–II) breast cancer is often managed with breast-conserving surgery along with adjuvant therapy. On the other hand, regionally advanced disease (Stage III) or metastatic presentation (Stage IV) is associated with poorer outcomes with survival rates dropping to 60% and below 30% respectively. Epidemiological studies in India report that up to 60–70% of patients present with Stage II or higher disease reflecting limited screening and healthcare facilities that may undertake such screening methods.[9]

we undertook a retrospective study of 30 patients with histopathology confirmed invasive breast carcinoma to analyse the relationship between ER, PR, and HER2 status and stage at presentation, alongside key prognostic parameters. Through improved characterization of IHC-based prognosis, this study aims to optimize therapeutic selection and follow-up strategies appropriate to our clinical environment.

MATERIALS AND METHODS

This retrospective observational study was conducted in the Department of General surgery of a tertiary-care teaching hospital. The duration of study was 5-year extending from January 2018 to December 2022. The study was approved by the Institutional Ethics Committee. Requirement of obtaining Informed consent from patients was waivered due to the retrospective nature of data collection exclusively from medical records.

A total of 30 consecutive patients who met the inclusion criteria were identified from departmental records. Demographic details, clinical presentation, radiological findings, pathological diagnosis, tumour grade, and immunohistochemical (IHC) profiles were retrieved from Hospital Medical Records Department. Cases with incomplete documentation or lacking follow-up data were excluded from analysis.

Data on oestrogen receptor (ER), progesterone receptor (PR), and HER2 status were extracted from existing IHC reports. ER and PR positivity were defined as nuclear staining in ≥1% of tumour cells, and HER2 scores were interpreted on a scale of 0 to 3+ according to the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines in force at the time of diagnosis. Cases with equivocal (2+) HER2 results were noted based on reported reflex fluorescence in situ hybridization (FISH) outcomes, if available in the record.

All statistical analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Categorical variables such as IHC subtypes, tumour stage, and nodal involvement were expressed as frequencies and percentages. Associations between

receptor status and clinicopathological features were analysed using chi-square or Fisher's exact tests, as appropriate. A p-value < 0.05 (two-tailed) was considered statistically significant.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Histologically confirmed invasive breast carcinoma
- Availability of histopathological examination reports with IHC status of excised specimen
- Complete clinicopathological and staging data

Exclusion Criteria

- Non-availability of IHC status reports
- Prior neoadjuvant therapy before tissue sampling
- Histological diagnoses other than invasive carcinoma
- Incomplete clinical or follow-up information.

RESULTS

The most commonly affected age group was 40–49 years (33.3%) followed by those under 40 years (26.7%). The age group 50–59 years comprised 7 cases (23.3%), while patients aged 60 years and above constituted the least affected group (16.7%). The mean age of the studied cases was found to be 47.72 +/- 10.29 [Table 1].

Table 1: Age distribution of patients (n = 30)

Age Group (years)	Number of cases	Percentage
< 40	8	26.7 %
40–49	10	33.3 %
50–59	7	23.3 %
≥ 60	5	16.7 %
Total	30	100.0 %
Mean age = 47.72 +/- 10.29		

The analysis of the immunohistochemical (IHC) marker status in carcinoma breast cases revealed that oestrogen receptor (ER) positivity was observed in 18 cases (60.0%), making it the most commonly expressed marker, followed by progesterone receptor (PR) positivity in 16 cases (53.3%). Human epidermal growth factor receptor 2 (HER2) positivity was seen in only 9 cases (30.0) [Table 2].

Table 2: Distribution of hormone receptor and HER2 status

Marker	Positive n (%)	Negative n (%)
ER	18 (60.0)	12 (40.0)
PR	16 (53.3)	14 (46.7)
HER2	9 (30.0)	21 (70.0)

Table 3: Molecular subtypes (n = 30)

Subtype	n	%
Luminal A	12	40.0
Luminal B	6	20.0
HER2-enriched	5	16.7
Triple-negative	7	23.3
Total	30	100.0 %

The analysis of molecular subtypes based on IHC status in carcinoma breast cases showed that the most common subtype was Luminal A, found in 12 patients (40.0%), followed by triple-negative breast cancer (TNBC) in 7 cases (23.3%). Luminal B subtype was identified in 6 patients (20.0%), while HER2-enriched tumours accounted for 5 cases (16.7%) [Table 3].

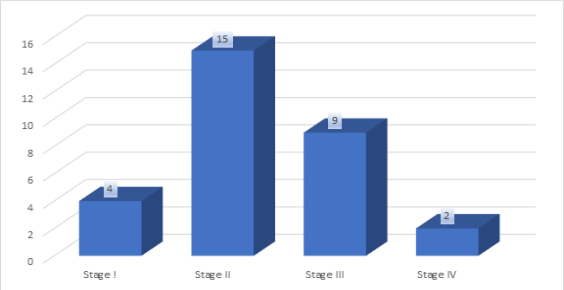

Figure 1. Stage at presentation (n = 30)

The analysis of the stage at presentation among the studied breast carcinoma cases demonstrated that the majority of patients were diagnosed at Stage II, comprising 15 cases. This was followed by 9 cases at Stage III, 4 cases at Stage I, and the least number of cases—only 2—presented at Stage IV [Figure 1].

The analysis of receptor status in relation to lymph node involvement among breast carcinoma cases showed that ER-positive patients had a lower rate of node positivity, with 5 cases (22.2 %) being node-positive and 13 cases (72.2 %) node-negative, whereas ER-negative patients had a higher rate of node involvement, with 9 cases (75.0%) being node-positive. This difference was statistically significant (p = 0.1414). For PR status node positivity was observed in 7 cases (43.8%) among PR-positive patients and in 10 cases (71.4%) among PR-negative patients (p = 0.068). HER2-positive patients showed node positivity in 6 cases (66.7%) compared to 11 cases (52.4%) among HER2-negative individuals (p = 0.400). Overall, only ER status demonstrated a statistically significant correlation with lymph node involvement (P=0.023) [Table 4].

Table 4: Association between receptor status and axillary lymph node metastasis

Receptor Status	Node-positive n (%)	Node-negative n (%)	p-value
ER-positive	5 (22.2)	13 (72.2)	0.023
ER-negative	9 (75.0)	3 (25.0)	
PR-positive	7 (43.8)	9 (56.2)	0.159
PR-negative	10 (71.4)	4 (28.6)	
HER2-positive	6 (66.7)	3 (33.3)	0.400
HER2-negative	11 (52.4)	10 (47.6)	

The analysis of the association between molecular subtypes of breast carcinoma and stage at presentation showed that the majority of Luminal A cases presented at earlier stages (Stage I–II) (83.3%) compared to only 2 cases (16.7%) at advanced stages (Stage III–IV). In contrast, Luminal B cases were evenly distributed, with 3 cases (50.0%) each in early and advanced stages. HER2-enriched and triple-negative subtypes showed a higher tendency for late-stage presentation, with 3 out of 5 HER2-enriched cases (60.0%) and 4 out of 7 triple-negative cases (57.1%) presenting at Stage III–IV ($p < 0.05$ [Table 5].

Table 5: Correlation between molecular subtype and stage at presentation

Subtype	Stage I–II n (%)	Stage III–IV n (%)	p-value
Luminal A	10 (83.3)	2 (16.7)	P < 0.05
Luminal B	3 (50.0)	3 (50.0)	
HER2-enriched	2 (40.0)	3 (60.0)	
Triple-negative	3 (42.9)	4 (57.1)	

The analysis of immunohistochemical (IHC) markers in relation to patient outcomes showed that ER-positive cases had the most favourable prognosis, with 14 patients (77.8%) alive without disease, only 3 (16.7%) experiencing recurrence, and 1 (5.6%) death. In contrast, ER-negative patients had poorer outcomes, with only 4 (33.3%) alive without disease, while an equal number—4 (33.3%)—experienced recurrence and death. A similar pattern was observed with PR status, where 12 PR-positive patients (75.0%) remained disease-free compared to 6 (42.9%) among PR-negative patients; death was seen in only 1 PR-positive case (6.3%) but in 4 PR-negative cases (28.6%). For HER2 status, better outcomes were seen in HER2-negative cases, with 14 (66.7%) alive without disease compared to 4 (44.4%) in HER2-positive cases; HER2-positive patients also had higher recurrence (33.3%) and death rates (22.2%) than HER2-negative ones [Table 6].

Table 6: Outcomes by IHC Status (n = 30; median follow-up: 24 months)

IHC Marker	Alive without disease n (%)	Disease recurrence n (%)	Death n (%)
ER positive	14 (77.8)	3 (16.7)	1 (5.6)
ER negative	4 (33.3)	4 (33.3)	4 (33.3)
PR positive	12 (75.0)	3 (18.8)	1 (6.3)
PR negative	6 (42.9)	4 (28.6)	4 (28.6)
HER2 positive	4 (44.4)	3 (33.3)	2 (22.2)
HER2 negative	14 (66.7)	4 (19.0)	3 (14.3)
Median follow-up: 24 months (range: 12–36 months).			

DISCUSSION

The findings of this study show distinct prognostic and clinical implications of immunohistochemically defined molecular subtypes of invasive breast carcinoma. Our cohort demonstrated a predominance of hormone receptor-positive subtypes particularly Luminal A (40%). This is consistent with global trends reported in other retrospective studies. For instance, Jonnada PK et al undertook a systematic review and meta-analysis of cases of breast carcinoma in India and reported Luminal A to be the most common subtype.[10] Similarly, Al-Thoubaity reported Luminal A in 58.5 % of cases in a Saudi Arabian population.[11] These findings show that Luminal A tumours are common across diverse geographic regions and support the prognostic value of hormonal receptor positivity. In our study, ER-positive tumours were associated with lower nodal involvement and improved survival rate. These findings show that oestrogen receptor expression has a protective role on clinical outcomes.

Our study also identified a relatively higher proportion of triple-negative breast cancer (TNBC; 23.3%) and HER2-enriched tumours (16.7%). Both TNBC and HER2-enriched tumours were more commonly associated with advanced-stage presentation and adverse outcomes. Similar patterns have been noted in a study done by Mudduwa LKB who observed a high burden of TNBC in younger South Asian patients, with increased lymph node involvement and poorer prognosis.[12] Our findings showed that HER2-positive patients had higher recurrence (33.3%) and mortality (22.2%) rates despite a smaller overall proportion of HER2-enriched tumours. This emphasizes the need for timely diagnosis and broader access to HER2-

directed therapies to mitigate poor outcomes in such high-risk groups.

The age distribution in our cohort showed the highest incidence in the 40–49 years group (33.3%), consistent with other Indian population-based studies where breast cancer peaks earlier compared to Western countries. Parmar V et al in a study also reported a majority of breast cancer patients being under 50 years of age.[13] Likewise, Kour A et al also reported that early onset disease is a hallmark of breast carcinoma in Indian women. The authors also reported that a significant percentage of women (38%) are diagnosed with carcinoma breast before menopause.[14] These findings have significant implications for screening and awareness programs which must be tailored to detect disease earlier in younger women.

In this study statistically significant association between ER negativity and increased nodal involvement was found ($p = 0.023$). This is similar to findings from studies by Prabhu et al,[15] and Yeo et al.[16] Both of these studies reported that higher rates of lymph node metastasis and advanced stage at presentation was more likely to be seen in ER-negative tumours. ER positivity was found to be associated with reduced nodal burden and favourable outcomes in such cases. Our analysis did not find a statistically significant association for PR or HER2 status with nodal involvement. The significant correlation between molecular subtype and stage at presentation ($p = 0.037$) further validates the clinical utility of IHC-based classification. In this study aggressive subtypes like HER2-enriched and TNBC more frequently presented at advanced stages consistent with findings by Adebamowo et al,[17] in Nigeria and Kumar et al. in India.[18]

Finally, the prognostic impact of IHC markers was evident in survival outcomes in our study. ER and PR positivity correlated strongly with better disease-free survival and lower mortality. This is supported by multivariate analyses in studies by Sorlie et al,[19] and Voduc et al,[20] where Luminal A subtype was associated with the most favourable prognosis, whereas HER2-enriched and basal-like (TNBC) subtypes were predictive of early recurrence and cancer-specific mortality. In our study, 77.8% of ER-positive patients were alive without disease at a median follow-up of 24 months as compared to only 33.3% of ER-negative patients. Similarly, mortality was significantly lower in PR-positive (6.3%) compared to PR-negative (28.6%) patients. Thus, our findings underscore the importance of incorporating receptor status in treatment decision-making in case of carcinoma breast.

CONCLUSION

This retrospective study underscores the importance of immunohistochemical subtyping in cases of invasive breast carcinoma. In this study luminal A subtype was found to have relatively favourable outcomes and earlier-stage presentation as compared to HER2-enriched and triple-negative subtypes. ER positivity was found to be significantly associated with lower nodal involvement and better survival. These findings emphasize the role of cost-effective IHC profiling in cases of carcinoma breast. IHC profiling can be as effective as molecular profiling in guiding treatment and follow-up strategies. This is more important particularly in resource-limited settings.

REFERENCES

1. Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, Vignat J, Gralow JR, Cardoso F, Siesling S, Soerjomataram I. Current and future burden of breast cancer: Global statistics for 2020 and 2040. Breast. 2022 Dec;66:15-23. doi: 10.1016/j.breast.2022.08.010. Epub 2022 Sep 2. PMID: 36084384; PMCID: PMC9465273.
2. Madhav MR, Nayagam SG, Biyani K, Pandey V, Kamal DG, Sabarimurugan S, Ramesh N, Gothandam KM, Jayaraj R. Epidemiologic analysis of breast cancer incidence, prevalence, and mortality in India: Protocol for a systematic review and meta-analyses. Medicine (Baltimore). 2018 Dec;97(52):e13680. doi: 10.1097/MD.0000000000013680. PMID: 30593138; PMCID: PMC6314759.
3. Arps DP, Healy P, Zhao L, Kleer CG, Pang JC. Invasive ductal carcinoma with lobular features: a comparison study to invasive ductal and invasive lobular carcinomas of the breast. Breast Cancer Res Treat. 2013 Apr;138(3):719-26. doi: 10.1007/s10549-013-2493-2. Epub 2013 Mar 28. PMID: 23535842; PMCID: PMC3906642.
4. Cho N. Molecular subtypes and imaging phenotypes of breast cancer. Ultrasonography. 2016 Oct;35(4):281-8. doi: 10.14366/usg.16030. Epub 2016 Jul 21. PMID: 27599892; PMCID: PMC5040136.
5. Ahmad Fauzi MF, Wan Ahmad WSHM, Jamaluddin MF, Lee JTH, Khor SY, Looi LM, Abas FS, Aldahoul N. Allred Scoring of ER-IHC Stained Whole-Slide Images for Hormone Receptor Status in Breast Carcinoma. Diagnostics (Basel). 2022 Dec 8;12(12):3093. doi: 10.3390/diagnostics12123093. PMID: 36553102; PMCID: PMC9776763.
6. Goud KI, Dayakar S, Vijayalaxmi K, Babu SJ, Reddy PV. Evaluation of HER-2/neu status in breast cancer specimens using immunohistochemistry (IHC) & fluorescence in-situ hybridization (FISH) assay. Indian J Med Res. 2012 Mar;135(3):312-7. PMID: 22561616; PMCID: PMC3361866.
7. Lu Z, Wang T, Wang L, Ming J. Research progress on estrogen receptor-positive/progesterone receptor-negative breast cancer. Transl Oncol. 2025 Jun;56:102387. doi: 10.1016/j.tranon.2025.102387. Epub 2025 Apr 14. PMID: 40222338; PMCID: PMC12018574.
8. Swain SM, Shastry M, Hamilton E. Targeting HER2-positive breast cancer: advances and future directions. Nat Rev Drug Discov. 2023 Feb;22(2):101-126. doi: 10.1038/s41573-022-00579-0. Epub 2022 Nov 7. PMID: 36344672; PMCID: PMC9640784.
9. Weerarathna IN, Luharia A, Uke A, Mishra G. Challenges and Innovations in Breast Cancer Screening in India: A Review of Epidemiological Trends and Diagnostic Strategies. Int J Breast Cancer. 2024 Nov 28;2024:6845966. doi: 10.1155/ijbc/6845966. PMID: 39639925; PMCID: PMC11620809.
10. Jonnada PK, Sushma C, Karyampudi M, Dharanikota A. Prevalence of Molecular Subtypes of Breast Cancer in India: a Systematic Review and Meta-analysis. Indian J Surg Oncol. 2021 Apr;12(Suppl 1):152-163. doi: 10.1007/s13193-020-01253-w. Epub 2020 Oct 28. PMID: 33994741; PMCID: PMC8119535.
11. Al-Thoubaity FK. Molecular classification of breast cancer: A retrospective cohort study. Ann Med Surg (Lond). 2020;49:44-48. doi:10.1016/j.amsu.2019.11.010
12. Mudduwa LKB. Quick score of hormone receptor status of breast carcinoma: Correlation with the other

clinicopathological prognostic parameters. Indian J Pathol Bacteriol. 2009;52(2):159-63.
13. Parmar V. Rising Incidence of Breast Cancer in the Young Fertile Indian Population-a Reality Check. Indian J Surg Oncol. 2018 Sep;9(3):296-299. doi: 10.1007/s13193-018-0800-4. Epub 2018 Jul 23. PMID: 30287986; PMCID: PMC6154358.
14. Kour A, Sharma S, Sambyal V, Guleria K, Singh NR, Uppal MS, Manjari M, Sudan M, Kukreja S. Risk Factor Analysis for Breast Cancer in Premenopausal and Postmenopausal Women of Punjab, India. Asian Pac J Cancer Prev. 2019 Nov 1;20(11):3299-3304. doi: 10.31557/APJCP.2019.20.11.3299. PMID: 31759352; PMCID: PMC7062992.
15. Prabhu JS, Korlimarla A, Desai K, et al. A majority of low (1–10%) ER positive breast cancers behave like hormone receptor negative tumors. J Cancer. 2014;5(2):156–165. doi:10.7150/jca.8282
16. Yeo MK, Kim SH, Kim HJ, et al. Tumor-infiltrating lymphocytes in breast cancer: Correlation with clinicopathological factors and prognosis. Korean J Pathol. 2013;47(1):22-31. doi:10.4132/KoreanJPathol.2013.47.1.22
17. Adebamowo CA, Famooto AO, Ogundiran TO, et al. Immunohistochemical and molecular subtypes of breast cancer in Nigeria. Breast Cancer Res Treat. 2008;110(1):183–188. doi:10.1007/s10549-007-9700-5
18. Kumar C, Yadav M, Shukla S, et al. Distribution pattern of molecular breast cancer subtypes and its association with clinicopathological features: A study in North India. J Lab Physicians. 2021;13(2):141-147. doi:10.1055/s-0041-1728765
19. Sorlie T, Perou CM, Tibshirani R, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A. 2001;98(19):10869–10874. doi:10.1073/pnas.191367098
20. Voduc KD, Cheang MC, Tyldesley S, et al. Breast cancer subtypes and the risk of local and regional relapse. J Clin Oncol. 2010;28(10):1684–1691. doi:10.1200/JCO.2009.24.9284