ORIGINAL ARTICLE
DOI: 10.29289/2594539420180000382

# A PREDICTIVE MODEL FOR AXILLARY LYMPH NODE PATHOLOGIC COMPLETE RESPONSE IN PREMENOPAUSAL BREAST CANCER PATIENTS AFTER NEOADJUVANT CHEMOTHERAPY: A CROSS-SECTIONAL STUDY IN A LATIN-AMERICAN POPULATION

## Um modelo preditivo para a resposta patológica completa axilar em pacientes com câncer de mama premenopausal após quimioterapia adjuvante: estudo transversal em uma população latino-americana

Carolina Benavides Duque[1], Luis Fernando Zapata Pérez[1], Ana María Fidalgo Zapata[1], Laura López[2], Elsa Vásquez[3], Javier Cuello López[2]

## ABSTRACT

**Introduction:** A large group of lymph node-positive breast cancer patients receive neoadjuvant chemotherapy and subsequently undergo axillary lymph node dissection. It has been previously proposed that axillary lymph node dissection may be avoided — and it's associated reduced morbidity — in patients showing pathologic complete response. Therefore, the purpose of this study was to develop a nomogram to predict axillary node pathologic response to neoadjuvant chemotherapy in breast cancer patients in order to guide the surgical treatment decision-making process for this group of patients. **Methods:** A cross-sectional, secondary data study was carried out between 2013-2016 on 222 lymph node-positive breast cancer patients who received neoadjuvant chemotherapy followed by locoregional management, including axillary lymph node dissection. Logistic regression analysis was performed to determine the association of the axillary pathologic complete response with the different clinical and pathological variables. Variables found to be statistically significantly associated with axillary pCR (pathologic complete response) were used to create the logistic regression model and the nomogram in pre-menopausal patients. Axillary pCR was defined as absence of residual disease in the breast and of micro-metastasis in axillary lymph nodes. Samples with isolated tumor cells were considered as positive for residual disease. **Results:** a total of 222 patients were included, of which 131 were premenopausal at the time of diagnosis. Axillary pathologic complete response was observed in 55.7% (73 of 131) of patients, and was significantly associated with estrogen receptor (ER) negative tumors (OR 2.59, 95%CI 1.21-5.53), progesterone receptor (PR) negative tumors (OR 2.63, 95%CI 1.28-5.38), and Her2 positive tumors (OR 0.40, 95%CI 0.19-0.84), for which a significant correlation with increased probability of achieving axillary pathologic complete response was evidenced. **Conclusion:** The performance of this model to predict axillary pCR in pre-menopausal patients was weak, and therefore the decision to avoid surgical axillary dissection should not be based solely on the developed nomogram. However, further studies may lead to validation of this model.

KEYWORDS: Breast neoplasm; sentinel lymph node; neoadjuvant therapy; nomograms.

[1]Breast Surgical Oncology Fellowship, CES University – Medellín, Antioquia, Colombia.
[2]Clinical Oncology Group, *Fundación Colombiana de Cancerología-Clínica Vida* – Medellín, Antioquia, Colombia
[3]Department of Clinical Epidemiology, CES University – Medellín, Antioquia, Colombia
***Corresponding author:** carobduque@gmail.com
**Conflict of interests:** nothing to declare.
**Received on:** 04/11/2018. **Accepted on:** 04/11/2018

## RESUMEN

**Introdução:** Um grande grupo de pacientes com câncer de mama linfonodo-positivo recebe quimioterapia neoadjuvante, que subsequentemente são submetidos a dissecção de linfonodos axilares. Foi proposto anteriormente que a dissecção de linfonodos axilares pode ser evitada – assim como a redução de sua morbidade - em pacientes que apresentam resposta patológica completa. Portanto, o objetivo deste estudo foi desenvolver um nomograma para prever a resposta patológica do linfonodo axilar à quimioterapia neoadjuvante em pacientes com câncer de mama, a fim de orientar o processo de decisão do tratamento cirúrgico para este grupo de pacientes. **Metodologia:** Foi realizado um estudo transversal, de dados secundários, entre os anos de 2013-2016 em 222 pacientes com câncer de mama linfonodo-positivo, que receberam quimioterapia neoadjuvante seguida de tratamento locorregional, incluindo dissecção de linfonodos axilares. A análise de regressão logística foi realizada para determinar a associação da resposta completa patológica axilar com as diferentes variáveis clínicas e patológicas. Variáveis estatisticamente associadas à pCR axilar (resposta completa patológica) foram usadas para criar o modelo de regressão logística e nomograma em pacientes na pré-menopausa. A pCR axilar foi definida como ausência de doença residual na mama e de micro-metástase nos linfonodos axilares. Amostras com células tumorais isoladas foram consideradas positivas para doença residual. **Resultados:** foram incluídos 222 pacientes, dos quais 131 estavam na pré-menopausa no momento do diagnóstico. A resposta patológica axilar completa foi observada em 55,7% (73 de 131) dos pacientes, e foi significativamente associada a tumores negativos para receptores de estrogênio(RE) (OR 2,59; IC 95% 1,21-5,53) e negativos para receptores de progesterona (RP) (OR 2.63, IC 95% 1.28-5.38), e Her2 positivos (OR 0.40, IC 95% 0.19-0.84), para o qual foi evidenciada uma correlação significativa com o aumento da probabilidade de atingir resposta completa patológica axilar. **Conclusão:** O desempenho deste modelo para prever a pCR axilar em pacientes na pré-menopausa era fraco e, portanto, a decisão de evitar a dissecção axilar cirúrgica não deve ser baseada apenas no nomograma desenvolvido. No entanto, estudos posteriores podem levar à validação desse modelo.


PALAVRAS-CHAVE: Neoplasias da mama; linfonodo sentinela; terapia neoadjuvante; nomogramas.

## INTRODUCTION

Determining lymph node involvement in breast cancer patients provides prognostic information and helps the treatment decision-making process for these patients[1]. Axillary lymph node-positive breast cancer patients are frequently subjected to neoadjuvant chemotherapy (NAC), of which 20% to 60% achieve axillary pathologic complete response (pCR)[1-7]. However, despite of the extent of pathologic response achieved with chemotherapy, axillary lymph node dissection continues to be considered the gold standard treatment for patients with axillary lymph node involvement[8]. Patients achieving axillary pCR have been shown to have better prognosis, and it has thus been proposed that in those patients achieving pCR, axillary lymph node dissection and its associated short and long term morbidities — such as lymphedema and reduced shoulder range of motion — could have been avoided [9,10]. Currently, there are no available methods to identify patients in whom this procedure could be avoided without negatively impacting survival[11]. Therefore, there is a need to identify factors that could be used to predict axillary node pathologic response after systemic neoadjuvant chemotherapy. Hence, the goal of this study was to identify variables and develop a model that could predict axillary pCR in Latin-American breast cancer patients.

## MATERIALS AND METHODS

### Ethics

The ethics committee of the Colombian Foundation for Cancer, *Clinica Vida,* approved this study.

### Study population

This was a cross-sectional, secondary data study carried out between 2013-2016. A total of 222 pre- and postmenopausal patients with stage T1-4 breast cancer, with axillary involvement confirmed by biopsy, and treated with neoadjuvant chemotherapy followed by locoregional management, including axillary lymph node dissection, were included in this study. Patients with bilateral breast cancer, inflammatory breast cancer, inadequate disease staging, pregnancy, or history of previous axillary surgery were excluded from this study.

### Data collection and analysis

Clinical and pathological reports were reviewed to determine diagnosis before neoadjuvant treatment. Biopsies of primary tumors were analyzed using standard hematoxylin and eosin (H&E) staining, and Bloom-Richardson staging system was used to classify histological grade. Estrogen receptor (ER) and progesterone receptor (PR) status was determined by immunohistochemistry (IHC), and reported as percentage of positive cells. Human epidermal growth factor receptor-2 (HER-2) overexpression was defined as positive either by a score of +3 by immunohistochemistry, or a score ≥2 by fluorescent *in situ* hybridization (FISH). Breast imaging reports were reviewed to determine tumor size, multicentricity, or multifocality. Clinical tumor-node-metastasis (TNM) cancer staging was performed according to the 7$^{th}$ edition of the American Joint Committee on Cancer . Data on lymph node status after neoadjuvant chemotherapy was extracted from the pathological report after axillary lymph node dissection.

## Statistical analysis

The quantitative variables were presented as means with their respective dispersion measures according to the distribution of the variables. Qualitative variables are shown as percentages. Student's *t* test was performed to compare means for independent samples. Group comparisons were performed using Chi-squared test ($\chi^2$). A p value <0.05 was considered statistically significant. Logistic regression analysis was performed to determine the association of the axillary pathologic complete response with the different clinical and pathological variables. Variables found to be statistically significantly associated with axillary pCR were used to create the logistic regression model and the nomogram in pre-menopausal patients. Estrogen receptor status was analyzed as a binary variable. Axillary cPR was defined as absence of residual disease in the breast and of micro-metastasis in axillary lymph nodes. Samples with isolated tumor cells were considered as positive for residual disease.

## RESULTS

The study included 222 patients with breast cancer, who had axillary lymph node involvement and were treated with neoadjuvant chemotherapy. The clinical pathological features are listed in Table 1. Of all patients, 59% were pre-menopausal, 78% had lymphovascular invasion, 41.4% were T4 tumors, and 36.4% were Her2 positive tumors. In the univariate analysis of the entire study population — which was stratified in pre- and post-menopausal —, only in the premenopausal subgroup, a significant impact in predicting the axillary response was demonstrated through a logistic regression model (data not shown).

Tables 2 and 3 show factors associated with the achievement of axillary pCR in pre-menopausal patients who underwent axillary lymph node dissection after neoadjuvant chemotherapy, and of which axillary pCR was observed in 55.7% of the cases (73 of 131).

Patients with T4 disease showed a higher probability of residual axillary lymph node disease. Axillary pCR was a significant correlation with increased probability of achieving axillary pathologic complete response in patients with ER-negative tumors (OR 2.59, 95%CI 1.21–5.53), PR-negative tumors (OR 2.63, 95%CI 1.28–5.38), and Her2-positive status (OR 0.40, 95%CI 0.19–0.84), for which a significant correlation with increased probability of achieving axillary pathologic complete response was evidenced.

These variables (ER-, PR-, Her2 status) were used in the multivariate logistic regression analysis model that correlated with an increase in the probability of achieving axillary complete pathologic response (Table 3). The resulting nomogram for predicting axillary complete pathologic response in premenopausal patients after neoadjuvant chemotherapy was generated based on variables with statistical significance, and three variables of clinical significance were also included (Figures 1 and 2).

**Table 1.** Characteristics of patients

| Category | N: 222 (%) |
|---|---|
| Mean age (range) | 52 (28–85) |
| <35 years | 20 (9.9) |
| 36–39 years | 24 (10.8) |
| 40–49 years | 53 (23.8) |
| 50–59 years | 69 (31.0) |
| 60–69 years | 38 (17.1) |
| >70 years | 18 (8.1) |
| Menopausal status | |
| Menopausal | 91 (40.9) |
| Pre-menopausal | 131 (59.0) |
| Histological type | |
| Ductal | 211 (95.0) |
| Lobular | 5 (2.2) |
| Others | 6 (2.7) |
| Histological grade | |
| Unknown | 15 (6.7) |
| I (Low) | 14 (6.3) |
| II (Moderate) | 106 (47.7) |
| III (High) | 87 (39.1) |
| Lymphovascular invasion | |
| Yes | 78 (35.1) |
| No | 71 (31.9) |
| Unknown | 73 (32.8) |
| Her2 | |
| Positive | 81 (36.4) |
| Negative | 140 (63.0) |
| Unknown | 1 (0.45) |
| Size (mm) (range) | 37.7 (6.3–120) |
| Tumor stage (T) | |
| Unknown | 3 (1.35) |
| T1 | 7 (3.1) |
| T2 | 64 (28.8) |
| T3 | 56 (25.2) |
| T4(a–c) | 92 (41.4) |
| Progesterone receptors | |
| Positive | 112 (50.4) |
| Negative | 110 (49.5) |
| Estrogen receptors | |
| Positive | 141 (63.5) |
| Negative | 81 (36.4) |
| Systemic therapy | |
| Taxane-based | 22 (9.9) |
| Anthracycline based | 7 (3.1) |
| Taxane/Anthracycline | 193 (86.9) |

**Table 2.** Univariate analysis of the Cox ratio of the factors that predict axillary pathologic complete response in premenopausal patients treated with neoadjuvant chemotherapy.

| Characteristics | ypN0 n=73 (55.7%) | ypN1 n=58 (44.2%) | OR (95%CI) | P |
|---|---|---|---|---|
| Mean age in years (range) | | | 1.0 (096–1.04) | 0.89 |
| Age range in years | | | | |
| <35 | 10 (13.7%) | 5 (8.6%) | | 0.65 |
| 35–39 | 14 (19.2% | 15 (25.9%) | 0.57 (0.16–1.99) | |
| 40–49 | 27 (37%) | 19 (32.8%) | 1.2 (0.47–3.21) | |
| 50–59 | 22 (30.1%) | 19 (32%) | 0.81 (0.34–1.90) | |
| Histological type | | | | |
| Ductal | 67 (91.8%) | 57 (98.3%) | | 0.24 |
| Lobular | 1 (1.4%) | 0 | 4.25 (0.48–37.4) | |
| Other | 5 (6.8%) | 1 (1.7%) | 0.0 | |
| Histological grade | | | | |
| Unknown | 6 (8.2%) | 1 (1.7%) | | 0.44 |
| 1 | 3 (4.1%) | 3 (5.2%) | 6.0 (0.42–85.2) | |
| 2 | 34 (46.6%) | 29 (50%) | 5.11 (0.58–45.0) | |
| Unknown | 30 (41.1%) | 25 (43.1%) | 5.0 (0.56–4.34) | |
| Lymphovascular invasion | | | | |
| Absent | 29 (39.7%) | 21 (36.2%) | | 0.002 |
| Present | 14 (19.2%) | 26 (44.8%) | 2.56 (1.08–6.05) | |
| Unknown | 30 (41.1%) | 11 (19%) | 0.50 (0.20–1.23) | |
| T status (clinical) | | | | |
| Tx | 2 (2.7%) | 0 | 0 | 0.01 |
| T1 | 2 (2.7%) | 1 (1.7%) | | |
| T2 | 22 (30.1%) | 13 (22.4%) | 0.30 (0.02–3.5) | |
| T3 | 27 (37%) | 11 (19%) | 0.35 (0.14–0.86) | |
| T4 | 20 (27.4%) | 33 (56.9%) | 0.24 (0.10–0.60) | |
| Initial size (mm) average DS | 33.8 (19.7) | 40.7 (22.8) | 1.01 (0.99–1.03) | 0.07 |
| Multifocal/centric | 14 (19.2) | 17 (29.3) | 1.43 (0.66–3.07) | 0.35 |
| Global status | | | | |
| IIA | 2 (2.7%) | 1 (1.7%) | | 0.01 |
| IIB | 19 (26%) | 10 (17.2%) | 1.05 (0.08–0.07) | |
| IIIA | 31 (42.5%) | 14 (24.1%) | 0.90 (0.07–10.8) | |
| IIIB | 18 (24.7%) | 32 (55.2%) | 3.5 (0.30–41.9) | |
| IIIC | 3 (4.1%) | 1 (1.7%) | 0.66 (0.02–18.8) | |
| ER status | | | | |
| Positive | 33 (45.2%) | 14 (24.1%) | 2.59 (1.21–5.53) | 0.01 |
| Negative | 40 (54.8%) | 44 (75.9%) | | |
| PR status | | | | |
| Negative | 41 (56.2%) | 19 (32.8%) | 2.63 (1.28–5.38) | 0.08 |
| Positive | 32 (43.8%) | 39 (67.2%) | | |
| Her2 status | | | | |
| Negative | | | | 0.01 |
| Positive | 39 (53.4%) | 43 (74.1%) | 0.40 (0.19–0.84) | |
| Unknown | 34 (46.6%) | 15 (25.9%) | 0.40 (0.19–0.84) | |

Continue...

**Table 2.** Continuation.

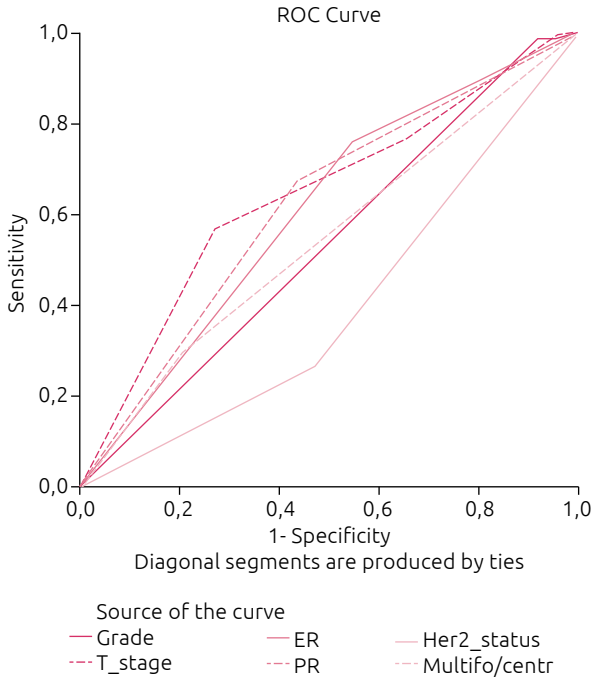
| Characteristics | ypN0 n=73 (55.7%) | ypN1 n=58 (44.2%) | OR (95%CI) | P |
|---|---|---|---|---|
| %KI67 (Median) (range-inter) | 0.4 (0.5) | 0.3 (0.48) | 0.56 (0.14–2.27) | 0.42 |
| Molecular sub-type | | | | |
| Luminal A | 6 (8.2%) | 8 (13.8%) | | 0.02 |
| Luminal B/Her2 (-) | 17 (23.3%) | 25 (43.1%) | 0.10 (0.32–3.75) | |
| Luminal B/Her2 (+) | 18 (24%) | 11 (19%) | 0.45 (0.12–1.67) | |
| Her2 enriched | 16 (21.9%) | 4 (6.9%) | 0.18 (0.04–0.86) | |
| Triple negative | 16 (21.9%) | 10 (17.2%) | 0.46 (0.12–1.75) | |
| Chemotherapeutic regimen | | | | |
| Anthracycline (single agent) | 0 | 4 (6.9%) | 0.49 (0.18–1.32) | 0.16 |
| Taxanes (single agent) | 4 (5.5%) | 1 (1.17%) | | |
| Anthracycline + Taxanes | 69 (94.5%) | 53 (91.4%) | | |

OR: ***odds ratio***; 95%: 95% confidence Interval; ypN0: axillary node pathologic complete response; ypN1: did not present axillary node pathologic complete response; ER: estrogen receptor; PR: progesterone receptor; %KI67; Her2: human epidermal growth factor receptor 2.

**Table 3.** Multivariate logistic regression analysis for prediction of axillary node pathologic complete response in pre-menopausal breast cancer patients

| Characteristics | OR | 95%CI | p value |
|---|---|---|---|
| Clinical stage T | | | 0.004 |
| 2 | 1.89 | 0.16-21.48 | 0.60 |
| 3 | 1.40 | 0.12-16.12 | 0.78 |
| 4 | 7.04 | 0.63-78.05 | 0.11 |
| ER | 2.66 | 1.15-6.12 | 0.02 |
| Her2 | 0.33 | 0.14-0.77 | 0.01 |

OR: ***odds ratio***; 95%CI: 95% confidence interval; ER: estrogen receptor; Her2: human epidermal growth factor receptor 2.




ER: estrogen receptor; PR: progesterone receptor; Her2: human epidermal growth factor receptor 2; multifo/centr: multifocal/multicentric tumor.

**Figure 1.** ROC curve.

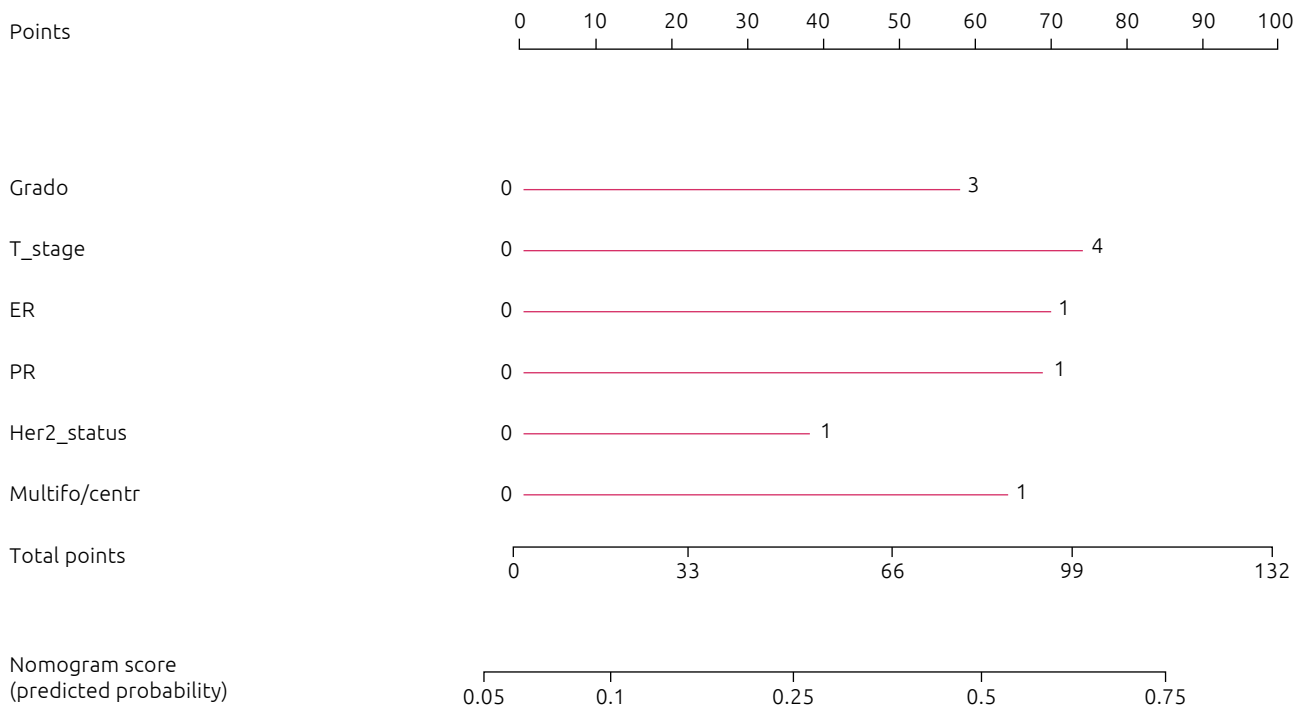
## DISCUSSION

In the context of breast cancer, axillary lymph node status has been shown to be an important prognostic factor that also guides treatment of these patients. Therefore, accurate nodal staging is essential for planning of appropriate breast cancer therapy[1]. Previously, several studies have reported different preoperative tools to determine axillary treatment options for axillary lymph node-positive breast cancer patients receiving neoadjuvant chemotherapy[12,13].

One of such tools are nomograms, which have been evaluated in breast cancer patients with axillary lymph node involvement in order to identify those patients presenting pathologic complete response of axillary lymph nodes to neoadjuvant chemotherapy, as well as to identify patients in which axillary lymph node dissection could be avoided[14-17].

In this study, we identified variables associated with axillary node pathologic complete response (pCR) to the use of neoadjuvant chemotherapy in pre-menopausal lymph node-positive breast cancer patients. In our study, the majority (90%) of chemotherapeutic regimens were anthracycline and taxane based, and axillary cPR was evidence in 55.7% of cases. This is comparable to the 20% to 60% pCR range previously reported by others[1-6].

Our data suggest that clinical stage, hormone receptor status, and Her2 status are relevant variables to predict pathologic response to systemic treatment in premenopausal breast cancer patients. This observations are in agreement with previous studies in which a greater response to therapy was observed in tumors of the triple negative (ER-/PR-/Her2-) and HER2 positive subtypes, followed by luminal A and B subtypes, albeit to a lesser extent [2,8,9]. In addition, using the




ER: estrogen receptor; PR: progesterone receptor; Her2: receptor 2 of the human epidermal growth factor; multifo/centr: multifocal/multicentric tumor.
**Figure 2.** Nomogram.

Surveillance, Epidemiology, and End Results (SEER) registry, Mattes and colleagues showed that breast cancer subtype is an independent risk factor for lymph node positivity, and for the response to neoadjuvant chemotherapy[18-20].

In this analysis, the vast majority of the available clinical-pathological variables in the preoperative context were considered. Our model predicts a complete pathologic response of 34% in premenopausal patients. To our knowledge, this is the first predictive model developed for axillary node pCR after neoadjuvant chemotherapy in a significant number of premenopausal patients. However, this result does not support the modification of the current recommendations in widely accepted clinical guidelines for the management of patients with lymph node involvement prior to neoadjuvant chemotherapy.

Our study presents some limitations including its retrospective nature, as well as the fact that the study population comprised a cohort from a single center. Thus, external validation of this model using independent cohorts is necessary before the nomograms can be applied in the clinical setting. On the other hand, while many of the analyzed factors are routinely obtained in the clinic, this may be challenging in some settings and render the nomograms without any practical value.

While the performance of this predictive model of axillary node pCR in premenopausal patients was weak in our study population, and the decision to avoid surgical axillary dissection cannot be currently based solely on this nomogram, future studies may validate our model and provide a tool that may ultimately contribute to improve care of breast cancer patients.

## REFERENCES

1. Hennessy BT, Hortobagyi GN, Rouzier R, Kuerer H, Sneige N, Buzdar AU, et al. Outcome after pathologic complete eradication of cytologically proven breast cancer axillary node metastases following primary chemotherapy. J Clin Oncol Off J Am Soc Clin Oncol. 2005;23(36):9304-11. https://doi.org/10.1200/JCO.2005.02.5023

2. von Minckwitz G, Untch M, Blohmer J-U, Costa SD, Eidtmann H, Fasching PA, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes. J Clin Oncol Off J Am Soc Clin Oncol. 2012;30(15):1796-804. https://doi.org/10.1200/JCO.2011.38.8595

3. Koolen BB, Valdés Olmos RA, Wesseling J, Vogel WV, Vincent AD, Gilhuijs KGA, et al. Early assessment of axillary response with 18F-FDG PET/CT during neoadjuvant chemotherapy in stage II-III breast cancer: implications for surgical management of the axilla. Ann Surg Oncol. 2013;20(7):2227-35. https://doi.org/10.1245/s10434-013-2902-0
4. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. JAMA. 2013;310(14):1455-61. https://doi.org/10.1001/jama.2013.278932
5. Yagata H, Yamauchi H, Tsugawa K, Hayashi N, Yoshida A, Kajiura Y, et al. Sentinel node biopsy after neoadjuvant chemotherapy in cytologically proven node-positive breast cancer. Clin Breast Cancer. 2013;13(6):471-7. https://doi.org/10.1016/j.clbc.2013.08.014
6. Buzdar AU, Ibrahim NK, Francis D, Booser DJ, Thomas ES, Theriault RL, et al. Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: results of a randomized trial in human epidermal growth factor receptor 2-positive operable breast cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2005;23(16):3676-85. https://doi.org/10.1200/JCO.2005.07.032
7. Alvarado R, Yi M, Le-Petross H, Gilcrease M, Mittendorf EA, Bedrosian I, et al. The role for sentinel lymph node dissection after neoadjuvant chemotherapy in patients who present with node-positive breast cancer. Ann Surg Oncol. 2012;19(10):3177-84. https://doi.org/10.1245/s10434-012-2484-2
8. Donegan WL. Prognostic factors. Stage and receptor status in breast cancer. Cancer. 1992;70(6 Suppl.):1755-64.
9. Ververs JM, Roumen RM, Vingerhoets AJ, Vreugdenhil G, Coebergh JW, Crommelin MA, et al. Risk, severity and predictors of physical and psychological morbidity after axillary lymph node dissection for breast cancer. Eur J Cancer. 2001;37(8):991-9.
10. Del Bianco P, Zavagno G, Burelli P, Scalco G, Barutta L, Carraro P, et al. Morbidity comparison of sentinel lymph node biopsy versus conventional axillary lymph node dissection for breast cancer patients: results of the sentinella-GIVOM Italian randomised clinical trial. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol. 2008;34(5):508-13. https://doi.org/10.1016/j.ejso.2007.05.017
11. Assi H, Sbaity E, Abdelsalam M, Shamseddine A. Controversial indications for sentinel lymph node biopsy in breast cancer patients. BioMed Res Int. 2015;2015:405949. https://doi.org/10.1155/2015/405949
12. Straver ME, Rutgers EJT, Russell NS, Oldenburg HSA, Rodenhuis S, Wesseling J, et al. Towards rational axillary treatment in relation to neoadjuvant therapy in breast cancer. Eur J Cancer. 2009;45(13):2284-92. https://doi.org/10.1016/j.ejca.2009.04.029
13. Pecha V, Kolarik D, Kozevnikova R, Hovorkova K, Hrabetova P, Halaska M, et al. Sentinel lymph node biopsy in breast cancer patients treated with neoadjuvant chemotherapy. Cancer. 2011;117(20):4606-16. https://doi.org/10.1002/cncr.26102
14. Schipper R-J, Moossdorff M, Nelemans PJ, Nieuwenhuijzen GAP, de Vries B, Strobbe LJA, et al. A model to predict pathologic complete response of axillary lymph nodes to neoadjuvant chemo(immuno)therapy in patients with clinically node-positive breast cancer. Clin Breast Cancer. 2014;14(5):315-22. https://doi.org/10.1016/j.clbc.2013.12.015
15. Jin X, Jiang Y-Z, Chen S, Shao Z-M, Di G-H. A Nomogram for Predicting the Pathological Response of Axillary Lymph Node Metastasis in Breast Cancer Patients. Sci Rep. 2016;6:32585. https://dx.doi.org/10.1038%2Fsrep32585
16. Kim JY, Park HS, Kim S, Ryu J, Park S, Kim SI. Prognostic Nomogram for Prediction of Axillary Pathologic Complete Response After Neoadjuvant Chemotherapy in Cytologically Proven Node-Positive Breast Cancer. Medicine (Baltimore). 2015;94(43):e1720. https://doi.org/10.1097/MD.0000000000001720
17. Vila J, Mittendorf EA, Farante G, Bassett RL, Veronesi P, Galimberti V, et al. Nomograms for Predicting Axillary Response to Neoadjuvant Chemotherapy in Clinically Node-Positive Patients with Breast Cancer. Ann Surg Oncol. 2016;23(11):3501-9. https://doi.org/10.1245/s10434-016-5277-1
18. Sørlie T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A. 2001;98(19):10869-74. https://doi.org/10.1073/pnas.191367098
19. Mattes MD, Bhatia JK, Metzger D, Ashamalla H, Katsoulakis E. Breast Cancer Subtype as a Predictor of Lymph Node Metastasis according to the SEER Registry. J Breast Cancer. 2015;18(2):143-8. https://dx.doi.org/10.4048%2Fjbc.2015.18.2.143
20. Weigelt B, Baehner FL, Reis-Filho JS. The contribution of gene expression profiling to breast cancer classification, prognostication and prediction: a retrospective of the last decade. J Pathol. 2010;220(2):263-80. https://doi.org/10.1002/path.2648