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Disease-free Survival in Locally Advanced Breast Cancer According to Pathological Response to Neoadjuvant Treatment

Supervivencia libre de enfermedad en cáncer de mama localmente avanzado según respuesta patológica al tratamiento neoadyuvante

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ABSTRACT

Introduction: Neoadjuvant chemotherapy is the standard treatment for locally advanced breast cancer, as it increases rates of breast-conserving surgery and improves disease-free survival (DFS) in patients who achieve a complete pathological response. **Methodology:** A retrospective observational cohort study was conducted that included 31 patients with locally advanced breast cancer treated with neoadjuvant chemotherapy at the Solón Espinosa Ayala Oncology Hospital (SOLCA-Quito) between 2010 and 2014. Data were obtained from the Hospital Tumor Registry. The 5-year SLE was estimated using the Kaplan-Meier method, and prognostic factors were analyzed using logistic regression. **Results:** The mean age was 52.5 years. 93.5% presented invasive ductal carcinoma, with 48.5% showing moderate differentiation. The TAC regimen (docetaxel, doxorubicin, and cyclophosphamide) was administered to 96.8% of patients. Complete pathological response (Miller and Payne grade 5) was observed in 12.9%, while the most frequent partial response was grade 3 (48.4%). The 5-year SLE was 64.4%. A Ki-67 proliferation index greater than 14% was found to be associated with a lower SLE (OR: 0.067; 95% CI: 0.05-0.93; p<0.05). **Conclusions:** The 5-year SLE rate in this cohort was comparable to that reported in the literature. However, the limited sample size restricts the generalizability of- the results, so studies with a larger number of patients are needed to confirm these findings.

Keywords: Breast cancer; neoadjuvant chemotherapy; pathologic complete response; disease-free survival; immunohistochemistry.

RESUMEN

Introducción: La quimioterapia neoadyuvante es el tratamiento estándar para el cáncer de mama localmente avanzado, pues aumenta las tasas de cirugía conservadora y mejora la supervivencia libre de enfermedad en pacientes que alcanzan respuesta patológica completa. **Metodología:** Se realizó un estudio observacional retrospectivo de cohorte que incluyó 31 pacientes con cáncer de mama localmente avanzado tratadas con quimioterapia neoadyuvante en el Hospital Oncológico Solón Espinosa Ayala (SOLCA-Quito) entre el 2010 y el 2014. Los datos se obtuvieron del Registro Hospitalario de Tumores. La supervivencia libre de enfermedad a cinco años se estimó con el método de Kaplan-Meier y los factores pronósticos se analizaron mediante regresión logística. **Resultados:** La edad media fue de 52,5 años. El 93,5 % presentó carcinoma ductal infiltrante, con un 48,5 % de grado de diferenciación moderado. El esquema TAC (docetaxel, doxorrubicina y ciclofosfamida) se administró en el. 96,8 % de las pacientes. La respuesta patológica completa (grado 5 de Miller y Payne) se observó en el 12,9 %, mientras que la respuesta parcial más frecuente fue grado 3 (48,4 %). La supervivencia libre de enfermedad a cinco años fue

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del 64,4 %. Se encontró que un índice de proliferación Ki-67 superior al 14 % se asoció con una menor supervivencia libre de enfermedad (OR: 0,067; IC 95 %: 0,05-0,93; p < 0,05). **Conclusiones:** La supervivencia libre de enfermedad a cinco años en esta cohorte fue comparable con la reportada en la literatura. Sin embargo, el tamaño muestral limitado restringe la generalización de los resultados, por lo que se requieren estudios con mayor número de pacientes para confirmar estos hallazgos.

Palabras clave: cáncer de mama, quimioterapia neoadyuvante, respuesta patológica completa, supervivencia libre de enfermedad, inmunohistoquímica.

1. Introduction

Breast cancer has become the most commonly diagnosed neoplasm worldwide; it surpassed lung cancer with 2.3 million new cases in 2020 and represents 11.7% of cancer diagnoses. In the same year, 684,996 deaths from breast cancer were recorded, accounting for 6.9% of all cancer deaths globally. In Latin America and the Caribbean, 210,100 cases were reported (14.3% of regional cancer diagnoses), it remains the most frequent neoplasm among women [1]. In Ecuador, the National Tumor Registry reported 2,787 new cases and 821 deaths from breast cancer in 2018. In Quito, the incidence from 2011–2015 was 39.4 per 100,000 women, with a five-year overall survival (OS) of 84.2% [2].

In high-income countries, therapeutic advances and the expansion of mammographic screening programs have substantially reduced mortality, although incidence continues to rise. It is estimated that 1 in 8 women will develop breast cancer before age 85. In this context, primary prevention strategies and early detection remain the most cost-effective interventions to reduce the societal burden of the disease [3].

Locally advanced breast cancer (LABC) is defined by tumors larger than 5 cm (T3), skin or chest wall involvement (T4), or matted axillary lymph nodes (N2), with no evidence of distant metastasis [4]. It accounts for approximately 20% of diagnoses and, when treated with surgery alone, five-year survival ranges from 13% to 24%, with local recurrence rates approaching 48%. Adding chemotherapy and radiotherapy to the perioperative setting has improved survival up to 30–55%, although it is still much lower than the ~99% reported in patients diagnosed with early-stage disease (clinical stage I) [5, 6].

In this context, neoadjuvant chemotherapy (NAC) constitutes the initial therapeutic cornerstone for initially inoperable LABC. Administered before surgery, it reduces tumor size, increases rates of breast-conserving surgery, and allows early assessment of tumor sensitivity to systemic agents [7, 8]. Its benefit is particularly notable in high-risk subtypes—such as triple-negative and human epidermal growth factor receptor 2 (HER2)–positive disease—which achieve higher rates of pathologic complete response (pCR). In turn, luminal tumors (hormone receptor–positive/HER2-negative) show more modest responses [8, 9]. This heterogeneity underscores the importance of individualizing both the indication for and the regimen of NAC according to each patient's biological profile.

Achieving a pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC) is associated with improved disease-free survival (DFS) and overall survival (OS). Therefore, its assessment is considered a fundamental treatment objective. Response can be evaluated clinically, by imaging methods, or through histopathologic analysis, using systems such as the Miller–Payne grading system or Residual Cancer Burden [10–12].

However, evidence on the relationship between pCR and DFS in Latin America—and particularly in Ecuador—is scarce. Collecting local data would enable validating the benefits of NAC and optimizing therapeutic algorithms in this population. Therefore, the present study aimed at determining five-year DFS according to pathologic response to neoadjuvant treatment in patients with LABC treated between 2010 and 2014 at the Solón Espinosa Ayala Oncology Hospital (SOLCA–Quito).

2. Methods

Ethics approval was obtained from the Human Research Ethics Committee (CEISH by its Spanish acronym) of the Solón Espinosa Ayala Oncology Hospital (SOLCA–Quito) for access to and use of information from the Hospital Tumor Registry (HTR).

2.1 Study design and setting

A retrospective cohort study was conducted using data from the Hospital Tumor Registry (HTR). We included all patients diagnosed with locally advanced breast cancer (LABC; clinical stages IIB–IIIC according to the 2010 AJCC classification), who received neoadjuvant chemotherapy (NAC) followed by surgery and were treated at SOLCA–Quito between 2010 and 2014, with complete five-year follow-up through December 31, 2019. Data were analyzed anonymously.

2.2 Materials

Data were obtained from the Hospital Tumor Registry (HTR), entered into a Microsoft Excel® spreadsheet, and subsequently exported to IBM SPSS Statistics® version 23.0 for analysis.

2.3 Participants

Inclusion criteria:

- Patients ≥25 years of age.
- Histopathological diagnosis of locally advanced breast cancer (LABC; clinical stages IIB–IIIC, AJCC 2010).
- Patients treated with neoadjuvant chemotherapy (NAC) followed by surgery.

Exclusion criteria:

- Locoregional or distant recurrence at the time of diagnosis.
- Discontinuation of neoadjuvant chemotherapy (NAC).
- Synchronous or metachronous second primary tumor.
- Metastatic progression during neoadjuvant therapy.
- Medical records with incomplete data for the primary variables.

2.4 Variables

Demographic variables (age, sex); clinical variables (tumor size, nodal involvement, initial clinical stage); histopathologic variables (histologic subtype, grade of differentiation, biomarker profile, molecular subtype); therapeutic variables (NAC regimen, type of surgery); and outcome variables (pathologic response assessed using the Miller–Payne system, and five-year disease-free survival [DFS]) were included.

2.5 Bias control

The database was anonymized in accordance with the Regulation for the Management of Confidential Information in the National Health System. Medical records with incomplete data were excluded, with no imputation of missing values. Information was verified by two independent reviewers, cross-checking hospitalization records against institutional statistics.

2.6 Statistical methods

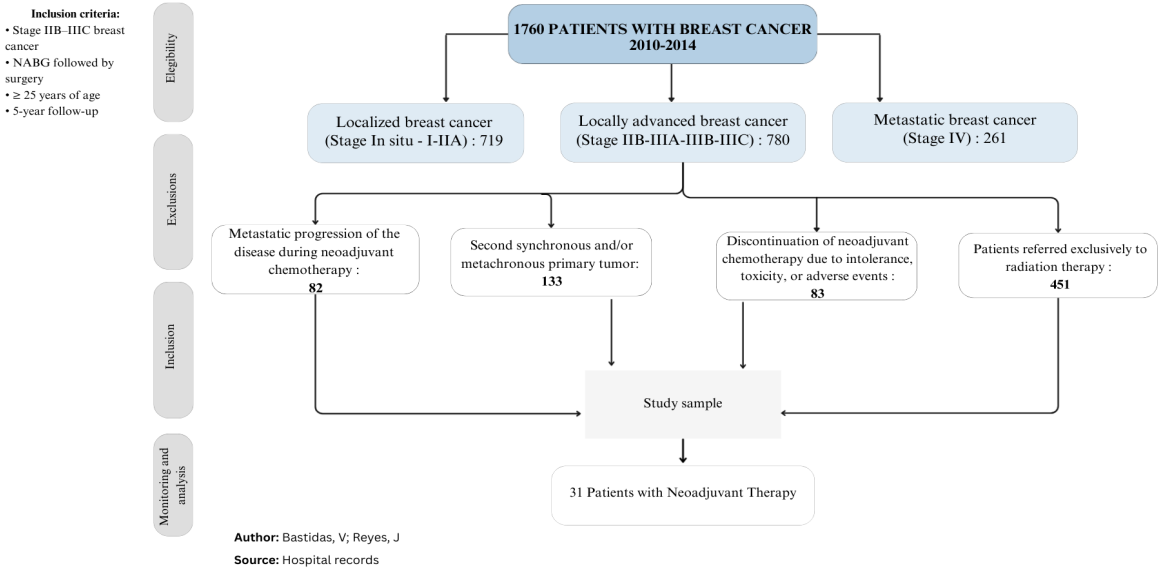
A descriptive analysis was performed using measures of central tendency and dispersion for quantitative variables, and absolute and relative frequencies for qualitative variables. For bivariate analyses, the Chi-square test or Fisher's exact test was used as appropriate, and odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated. Disease-free survival (DFS) was estimated using the Kaplan–Meier method, and differences between groups were evaluated with the log-rank test. A p value <0.05 was considered statistically significant.

3. Results

3.1 Characteristics of the patients

Thirty-one patients with LABC treated with NAC, who met the inclusion criteria, were included (Figure 1). The mean age was 52.5 ± 13.5 years. Large tumors predominated: T3 = 38.7%, T4 = 29.0%, and T2 = 32.3%. Therefore, the most frequent clinical stages were IIIA (38.7%), IIB (32.3%), and IIIB (29.0%). Nodal involvement was high: N1 in 61.3% and N2 in 19.3% of cases. Histologically, nearly half of tumors were grade II (moderately differentiated) in 15 cases (48.4%), followed by grade I (well differentiated) in 11 cases (35.5%), and grade III (poorly differentiated) in 5 cases (16.1%); 93.5% were invasive ductal carcinomas (Table 1).

Figure 1. Patient selection



In the immunohistochemical evaluation, Ki-67 ≥ 14% was observed in 80.6% of patients; estrogen and progesterone receptors were positive in 58.1% and 51.6%, respectively; and HER2 overexpression was present in 9.7%. According to the molecular classification, the luminal B/HER2-negative subtype predominated (35.5%), followed by triple-negative (32.3%), luminal B/HER2-positive (19.4%), and luminal A (12.9%).

Taken together, these findings describe a cohort with locally advanced disease and high biological risk, characterized by substantial tumor and nodal burden, high tumor proliferative activity (Ki-67), and a predominance of aggressive subtypes. This supports the choice of neoadjuvant chemotherapy (NAC) as the initial therapeutic approach.

Table 1. Distribution by tumor characteristics. Patients with LABC who received neoadjuvant therapy. SOLCA- Quito Hospital. 2010- 2014 (n = 31).

Characteristics of the injury	n	%
Tumor size		
T2	10	32.3
T3	12	38.7
T4	9	29.0
Clinical stage		
II B	10	32.3
III A	9	29.0
III B	12	38.7
Lymph node involvement		
No	6	19.4
N1	19	61.3
N2a	5	16.1
N2b	1	3.2
Initial histological grade		
Grade I (well differentiated)	11	35.5
Grade II (moderately differentiated)	15	48.4
Grade III (poorly differentiated)	5	16.1
Biomarkers		
Estrogen receptors	18/31	58.1
Progesterone receptors	16/31	51.6
Ki-67 receptors	25/31	80.6
HER2/Neu receptors	3/31	9.7
Molecular subtypes		
Luminal A (KI-67 < 14%)	4	12.9
Luminal B HER2+ (KI-67 ≥ 14%)	6	19.4
Luminal B HER2− (KI-67 ≥ 14%)	11	35.5
Triple negative	10	32.3
Histological classification		
Ductal carcinoma	29	93.5
Papillary carcinoma	1	3.2
Other (medullary)	1	3.2
Total	31	100.0

Author: Reyes, J; Bastidas, V
Fuente: Hospital records

3.2 Sample characteristics

The entire sample of breast cancer patients was female (n = 31; 100%), with an average age of 52.5 years (SD: 13.5 years).

3.3 Tumor characteristics

Clinical stage IIIA represented 38.7% of cases. With respect to nodal involvement, the N1 category predominated (61.3%) according to the TNM (Tumor–Node–Metastasis) classification. Grade II lesions (moderately differentiated) accounted for 48.4%, and ductal carcinomas accounted for 93.5%. Ki-67 markers were identified in 80.6% of cases; the most frequent molecular subtype was luminal B HER2, present in 35.5% of cases (Table 1).

3.4 Distribution according to neoadjuvant therapy

In relation to QNA, the most commonly used regimen was TAC x 6c (Docetaxel, Doxorubicin, and Cyclophosphamide) for six cycles (96.8%), followed by the TCH chemotherapy regimen (Docetaxel + Carboplatin + Trastuzumab) with limitations on the administration of Trastuzumab because it was not included in the basic drug regimen during the study period (Table 2).

Table 2. Distribution according to neoadjuvant therapy. Patients with locally advanced breast cancer, who received neoadjuvant treatment. SOLCA Hospital, Quito. 2010–2014 (n = 31)

Neoadjuvant chemotherapy regimen	n	%
TAC x 6 cycles every 21 days	30	96,8
TCH	1	3,2
Total	31	100,0

TAC: Docetaxel – Doxorubicin- Cyclophosphamide; TCH: Docetaxel- Carboplatin- Trastuzumab

Author: Reyes, J; Bastidas, V.

Source: Hospital records.

3.5 Preoperative evaluation and complete pathological response

When assessing the relationship between tumor characteristics and pCR to NAC, no statistically significant associations were found ($p>0.05$).

None of the patients with T3 tumors, N2a or N2b nodal involvement, clinical stage IIIA, histologic grade II, HER2 expression, or the luminal A or luminal B/HER2+ molecular subtypes achieved pCR (G5 according to the Miller–Payne classification).

In cases treated with the TAC regimen (Docetaxel, Doxorubicin, and Cyclophosphamide) for six cycles and subsequently undergoing modified radical mastectomy, the pCR rate was 13.3%. Likewise, no patient with positive biomarkers on postoperative evaluation achieved pCR. Among cases with locoregional recurrence, only one case showed pCR (9.1%).

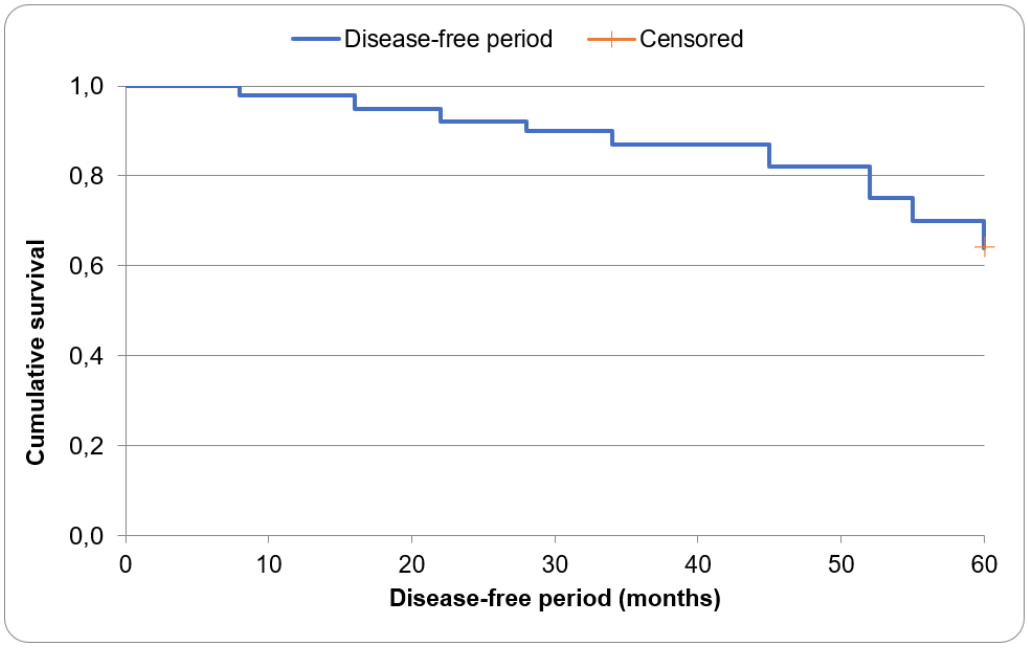
These findings indicate that, in this cohort, there was no significant association between the variables analyzed and the likelihood of achieving pCR.

3.6 Disease-free survival

The overall median DFS was 51.7 months (95% CI, 46.4–56.9). Among patients who achieved pCR, the median DFS was 58.3 months (95% CI, 55.3–61.2); whereas among those without pCR, it was 50.6 months (95% CI, 44.7–56.6) with no statistically significant difference between groups ($p = 0.566$).

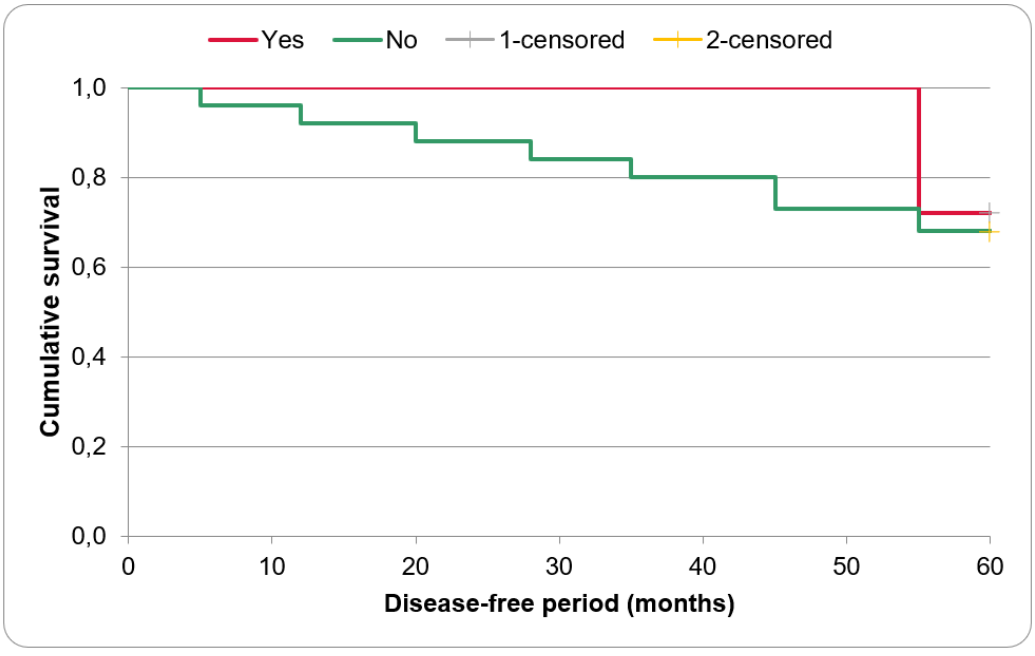
After a five-year follow-up, overall DFS was 64.4% (Figure 1). Although the difference between groups did not reach statistical significance, a favorable trend is observed in patients with pCR. This is consistent with prior reports found in the literature (Figures 2 and 3).

Figure 2. Disease-free survival. Patients with locally advanced breast cancer, who received neoadjuvant therapy. SOLCA–Quito Hospital. 2010–2014 (n = 31).



Author: Reyes, J; Bastidas, V.
Source: Hospital records.

Figure 3. Disease-free survival according to pathologic complete response. Patients with locally advanced breast cancer, who received neoadjuvant therapy. SOLCA–Quito Hospital. 2010–2014.



Author: Reyes, J; Bastidas, V.
Source: Hospital records.

3.7 Survival analysis

No statistically significant differences in OS were found between patients who achieved pCR and those who did not (p = 0.770). The median overall survival was 120.2 months (95% CI, 102.9–137.5) in patients with complete response, versus 117.2 months (95% CI, 96.3–138.1) in those who did not achieve it.

As shown in Table 3, median disease-free survival (DFS) was similar between patients who achieved a pathologic complete response (120.230 months; 95% CI, 102.974–137.486) and those who did not (117.173 months; 95% CI, 96.255138.091). Comparison of the curves using the log-rank test revealed no statistically significant differences (p = 0.770).

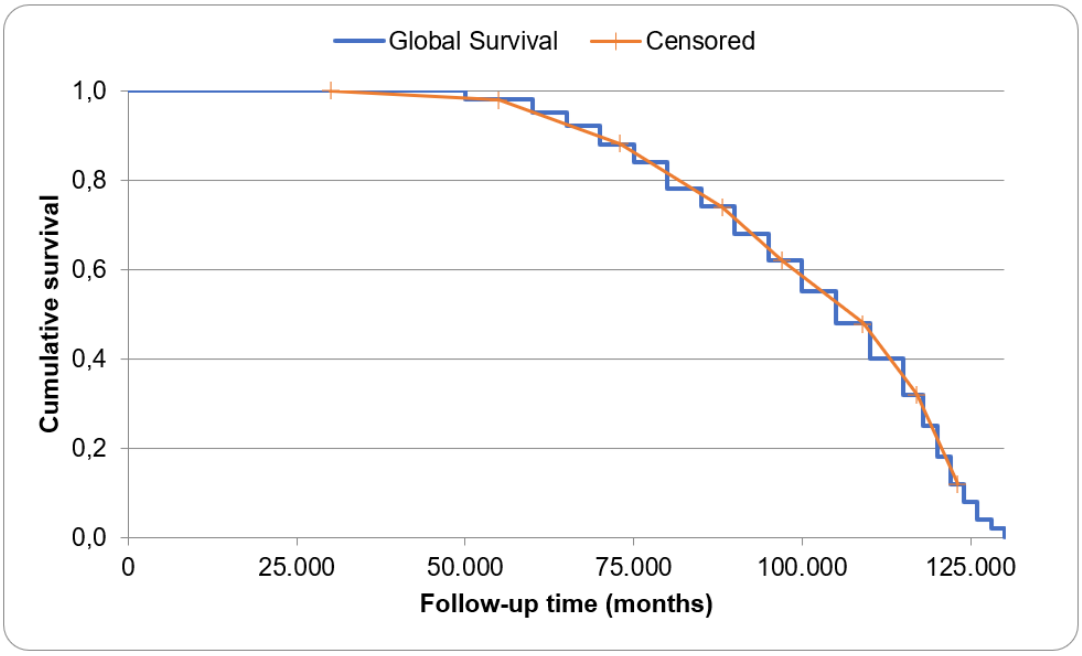
Figure 4 shows the overall survival (OS) function estimated using the Kaplan–Meier method for the entire cohort (n = 31). The curve remains high during the first years of follow-up and declines gradually toward the end of the observation period, a pattern consistent with a median OS close to 10 years. This behavior is consistent with the analysis stratified by pathologic complete response (pCR), in which the medians were 120.2 months (95% CI, 102.9–137.5) among those who achieved pCR and 117.2 months (95% CI, 96.3–138.1) among those who did not, with no significant differences between curves (log-rank p = 0.770). Taken together, the figure summarizes prolonged survival in the series with no detectable effect of pCR on OS.

Table 3. Median survival. Patients with locally advanced breast cancer, who received neoadjuvant therapy. SOLCA–Quito Hospital. 2010–2014 (n = 31).

Complete pathological response	Survival according to complete pathological response (months)			Log Rank
	Median	95 % CI		
		Lower	Higher	
Yes	120.230	102.974	137.486	
No	117.173	96.255	138.091	*p = 770*

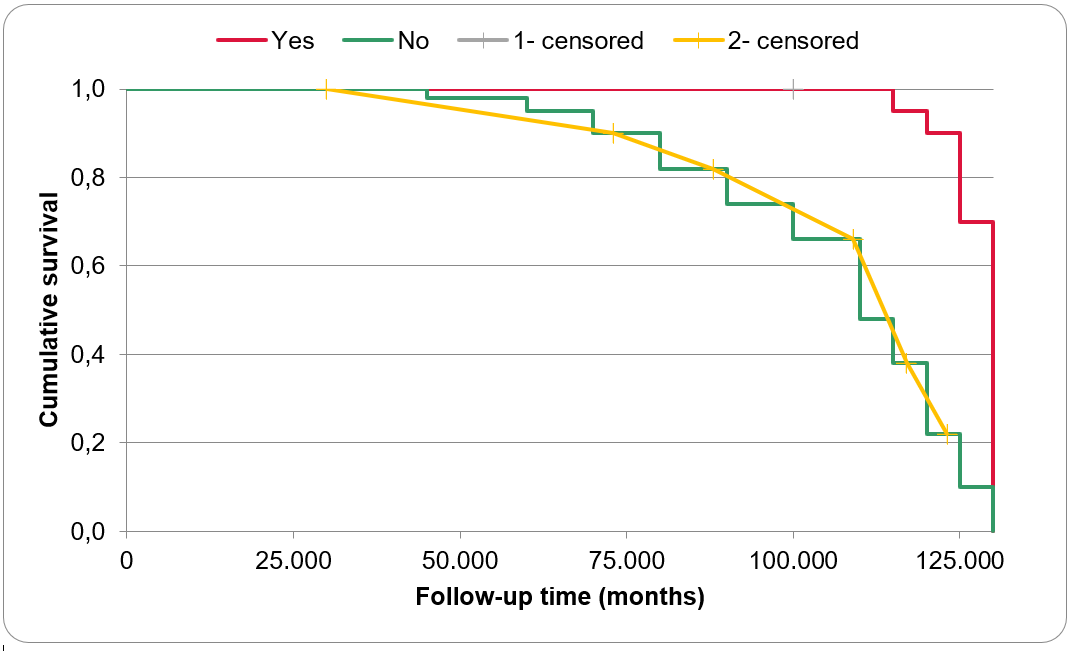
Figure 5 presents the Kaplan–Meier overall survival curves stratified by pathologic complete response (pCR). The trajectory of the pCR group remains slightly higher throughout follow-up, but the separation between curves is limited, and the comparison does not show statistically significant differences (log-rank p = 0.770). In line with the figure, the estimated medians were 120.2 months (95% CI, 102.9–137.5) for those who achieved pCR and 117.2 months (95% CI, 96.3–138.1) for those who did not, suggesting no detectable effect of pCR on OS in this cohort. This result should be interpreted in light of the sample size and the low frequency of pCR (12.9%), factors that may reduce the power to detect modest differences between groups.

Figure 4. Overall survival of patients with locally advanced breast cancer.



Author: Reyes, J; Bastidas, V.
Source: Hospital records.

Figure 5. Survival according to complete pathological response.



Author: Reyes, J; Bastidas, V.
Source: Hospital records.

4. Discussion

In this study, we analyzed a series of 31 cases of LABC treated with NAC, focusing on five-year disease-free survival (DFS) and overall survival (OS). The cohort had a mean age of 52.5 years; tumors were mainly T2 (32.3%) and T3 (38.3%), with stage IIB in 32.3% and N1 nodal involvement in 61.3%. Histologically, moderately differentiated invasive ductal carcinomas predominated. Regarding molecular subtypes, luminal B/HER2-negative with Ki-67 >14% (35.5%) and triple-negative (32.3%) were most frequent. Nevertheless, these features were not associated with chemotherapy response in our cohort, in contrast to Tan et al. [13], who reported these subtypes to be associated with better response and longer DFS.

Tumor size is an important prognostic factor and, by definition, all tumors in LABC are 5 cm or larger. In this case series, tumor size was not associated with response to neoadjuvant therapy, which is likely attributable to the small sample size. In this regard, the study by Dhanushkodi et al. [14] provides evidence that patients with larger tumors have a poorer response to neoadjuvant therapy.

In an international pooled analysis conducted by Cortazar et al. [15], patients who achieved pCR showed better long-term outcomes compared with those who had residual disease at the time of surgery. However, given the small number of cases and the fact that only 12.9% achieved a complete response to neoadjuvant therapy, this association could not be established in our series. Nevertheless, when outcomes in this cohort were analyzed, non-statistically significant differences were observed in both DFS and OS according to response to neoadjuvant therapy.

In this population, a locoregional recurrence rate of 35.5% and a five-year DFS of 64.4% were documented, with an overall median of 51.6 months. Among patients who achieved pCR, the median DFS was 58.3 months, with no statistically significant differences compared with those who did not ($p > 0.05$). These results are comparable to those of Ospino et al. [16], who reported a five-year DFS of 63.3% in a series of 171 cases in Colombia, with age and clinical-stage characteristics similar to those of this cohort. Regarding locoregional recurrence, the rate observed in this study is similar to that reported by Trabulsi et al. [17], who described a 34% recurrence rate in patients treated at a referral center in Saudi Arabia. Likewise, the absence of significant differences in DFS by pathologic response is consistent with Spring et al. [18], who despite demonstrating a favorable trend among patients with complete response note that the magnitude of the benefit remains a matter of debate.

PCR following NAC is recognized as a key prognostic indicator in LABC, as it is associated with better long-term outcomes. In this study, only 12.9% of patients achieved pCR, which limits the ability to demonstrate statistically significant differences in survival. Similar results were described by Dhanushkodi et al. [19], who also observed low pCR rates in cohorts with advanced disease. In turn, Cortazar et al. [15], in a large-scale meta-analysis (CTNeoBC), confirmed that achieving pCR predicts longer DFS and OS. Additionally, Spring et al. [18] reported that although pCR correlates with a lower risk of recurrence and death, the magnitude of this benefit varies by molecular subtype. Moreover, debate persists regarding its absolute prognostic value. Huang et al. [20] demonstrated, in a meta-analysis focused on triple-negative breast cancer (TNBC), that pCR is associated with up to a 76% reduction in the risk of progression or death, thus reinforcing its value as a marker of therapeutic efficacy. Therefore, although no statistically significant differences were found in this cohort, international evidence supports pCR as a robust predictor of better prognosis, underscoring the need for studies with larger sample sizes in our population to confirm this relationship.

With respect to OS, this study found a mean of 120.2 months, which is higher than that reported by Trabulsi et al. [17], who, in a series of 153 LABC cases, described survival of 108 months. This difference is likely explained by their cohort being made up of predominantly young women (<50 years), which was associated with poorer response to neoadjuvant therapy and worse OS.

These results are also consistent with the findings of Spring et al. [19], who determined that pCR to neoadjuvant therapy is associated with better DFS and OS in patients with LABC. According to these authors, the prognostic significance of pCR after NAC remains somewhat controversial. While pCR demonstrates sensitivity to the agents administered in the neoadjuvant setting, the true test of treatment efficacy depends on its ability to predict long-term outcomes of recurrence and death, which varies according to immunohistochemical classification.

Accordingly, Huang et al. [20] found that achieving pCR was associated with a 76% lower risk of progression, recurrence, or death. Moreover, the association between pCR and survival was consistent across clinical trial and real-world settings and was not significantly affected by variation in molecular subtype or the use of adjuvant chemotherapy. According to those investigators, patients with early-stage TNBC, who achieved pCR, had substantially better long-term outcomes than those who did not.

In the multivariable analysis, Ki-67 expression was associated with poorer disease-free survival (DFS). This is consistent with reports by Tan et al. [21], indicating that Ki-67 expression—whether assessed before or after treatment—is associated with poorer DFS, though not with overall survival (OS).

Regarding Ki-67 expression, multiple studies have demonstrated its utility as a prognostic and predictive marker in breast cancer, as it directly reflects the rate of cellular proliferation and correlates with the risk of recurrence and tumor progression. This index is particularly relevant for differentiating between luminal A and luminal B subtypes, with a 14% cutoff commonly used for this biological classification, thereby informing more individualized therapeutic decisions. Likewise, the literature indicates that Ki-67 can predict the magnitude of benefit from chemotherapy, particularly in luminal tumors treated with anthracycline- and taxane-based regimens. Thus, it represents a prognostic factor for survival in hormone receptor–positive patients [22, 23]. Nevertheless, despite its clinical value, controversies persist regarding the standardization of its assessment and the optimal interpretative threshold, underscoring the need for prospective studies and international consensus to strengthen its applicability as a prognostic and predictive tool in routine clinical practice.

The role of Ki-67 as a dynamic marker has attracted interest, as variations in its expression could anticipate changes in tumor growth rate and provide prognostic value in patients who do not achieve pCR. Nevertheless, its clinical utility is controversial because most evidence comes from retrospective studies and lacks robust methodological standardization. In particular, disagreement persists regarding the most appropriate cutoff to define high proliferation, as the values used have been largely arbitrary and heterogeneous across studies. Moreover, literature has focused mainly on Ki-67 assessment in pre- and post-treatment contexts within neoadjuvant settings; to date, there is no consensus on its incorporation into post-surgical therapeutic decision-making [24]. These gaps highlight the need for prospective studies and international consensus to validate its use as a prognostic and predictive tool in LABC.

The results of this study suggest that pCR after NAC in LABC may be associated with better outcomes in terms of DFS and OS; however, given the small sample size and the fact that pCR was achieved in only four cases, this interpretation should be made with caution, as no statistical significance was observed in the analyses performed. This is the primary limitation of this work.

5. Conclusions

The findings of this study reaffirm the importance of NAC in the management of LABC, while highlighting the need to strengthen understanding of its real-world impact on our population. Although statistically significant differences in survival by pathologic response were not demonstrated, there is a trend supporting the prognostic value of complete (pathologic) response (pCR) and of the tumor proliferative index. In this regard, we consider that Ki-67 though not yet established as a standard marker in clinical practice should be prioritized as a complementary tool for prognostic stratification and therapeutic decision-making. Likewise, the low frequency of complete responses observed in this cohort underscores the need to optimize treatment regimens and to explore more effective therapeutic alternatives in high-risk subtypes, such as luminal B and triple-negative tumors. From the authors' perspective, it is essential to promote multicenter studies with larger sample sizes and prolonged follow-up, not only to confirm these observations but also to provide robust evidence to adapt and improve treatment protocols in the local and regional context.

Results should be interpreted with caution due to the small sample size, the retrospective nature of the design, and the absence of analyses stratified by molecular subtype, which limits the generalizability of the findings and reinforces the need for studies with greater statistical power.

6. Abbreviations

HREC: Human Research Ethics Committee (by its Spanish acronym)

LABC: locally advanced breast cancer

TNBC: triple-negative breast cancer

HER2: human epidermal growth factor receptor 2

TNM: Tumor, Node, Metastasis

OR: odds ratios

NAC: neoadjuvant chemotherapy

HTR: Hospital Tumor Registry

pCR: pathologic complete response

OS: overall survival

DFS: disease-free survival

7. Administrative information

7.1 Acknowledgements

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7.2 Contributions from authors

Reyes, J: conceptualization, validation, visualization, methodology, project management, methodology, writing: review and editing

Bastidas, V: conceptualization, visualization, supervision of original draft writing, revision, and editing.

All authors read and approved the final version of the manuscript.

7.3 Financing

The authors did not receive any financial compensation for this research work.

The authors financed the expenses incurred in this research.

7.4 Statements

7.4.1 Ethics Committee Approval

The study protocol was approved by the Human Research Ethics Committee (CEISH) of SOLCA Quito, code 059-2021-MSP-VGVS.

7.4.2 Conflict of interest

None declared by the authors.

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