P2-10-03: Real world outcomes of adjuvant chemotherapy in invasive lobular carcinoma of the breast: a retrospective cohort from a reference center in Brazil

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Abstract

Key findings include:

- Survival Outcomes: Adjuvant chemotherapy led to better disease-free survival (DFS) and overall survival (OS) compared to neoadjuvant or omitted chemotherapy in early-stage ILC.
- Independent Risk Factors: Age, staging, and HER2+ status significantly impacted OS, with age increasing risk by 7% annually, higher stage by 4.2x, and HER2+ by 9x.
- Our findings suggest a limited benefit of neoadjuvant chemotherapy in ILC, supporting adjuvant treatment, particularly for early stages.

Introduction

Invasive Lobular Carcinoma (ILC) constitutes the second most prevalent type of breast cancer worldwide, accounting for approximately 15% of cases. It is classified into classical and non-classical types. The non-classical types include solid, pleomorphic, signet-ring, mucinous, alveolar, and mixed subtypes[1]. ILC is generally hormone receptor-positive and is characterized by a low pathological complete response (pCR) rate to neoadjuvant chemotherapy, typically between 1-3%[2]. Recent studies suggest that neoadjuvant chemotherapy may result in suboptimal surgical outcomes, with higher rates of positive margins due to the low pCR, as well as increased locoregional recurrence, metastatic disease, and mortality rates[3,4]. However, in a study evaluating over 1,000 ILC patients, response rates varied by hormone receptor status and grade: 4% for HR+/G1- and 17.8% for HR-/G3 tumors[5]. Moreover, pCR to chemotherapy did not correlate with improved overall survival or progression-free survival in invasive lobular tumors. Nonetheless, international guidelines, such as the NCCN Guidelines, recommend adjuvant chemotherapy, particularly for tumors larger than 2 cm and with positive lymph nodes[6]. Given this context, we hypothesize that chemotherapy may not provide the same benefit as adjuvant or neoadjuvant therapy in ILC. Here, we present overall survival outcomes from a retrospective cohort study.

Methods and Materials

This study has included patients seen at Instituto do Cancer do Estado de São Paulo, Brazil, between 2015 and 2020. Only patients with invasive lobular carcinoma in stages I-III have been enrolled.

Table 1. Characteristics of patients included in this cohort

	Neoadjuvant Chemo 16 (10%)	Adjuvant Chemo 76 (50%)	No chemo 61 (40%)	p
Age	59 (50 – 63)	57 (50 – 64)	72 (62 – 78)	0.0001[a]
Staging				0.002[b]
I	1 (8%)	11 (16%)	15 (33%)	
II	3 (23%)	35 (50%)	24 (52%)	
III	9 (69%)	24 (34%)	7 (15%)	
ER+	7 (100%)	65 (96%)	38 (97%)	
PR+	6 (86%)	62 (91%)	35 (90%)	
HER2				0.047[b]
Her2 0,1+,2+	6 (86%)	61 (91%)	37 (100%)	
Her2 3+	1 (14%)	6 (9%)	0 (0%)	
Ki67	7.5 (5 – 10)	15 (10 – 20)	10 (9 – 15)	0.278[a]
Surgery				0.002[b]
Mastectomy	14 (88%)	52 (68%)	28 (48%)	
Lumpectomy	1 (6%)	24 (32%)	28 (48%)	
No surgery	1 (6%)	0 (0%)	2 (4%)	
Histologic Type				0.340[b]
Classic	9 (90%)	58 (84%)	41 (91%)	
Pleomorphic	1 (10%)	10 (15%)	2 (4%)	
Signet-ring	0 (0%)	1 (1%)	2 (4%)	

a: Kruskall-Wallis; b: Likelihood-ratio; c: Grading of Nottingham

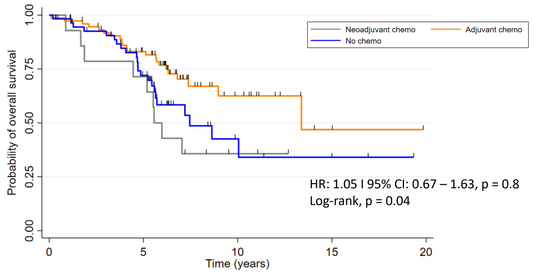

Figure 1 – Overall survival of chemotherapy at adjuvant setting

Results

After screening 213 records from the patients, 153 were included for review, divided into stages I (22%), II (47%), and III (31%). The mean age at diagnosis was 62y (range: 28 – 91 years). Received chemotherapy as adjuvant, neoadjuvant, and omitted in 76 (50%), 16 (10%), and 61 (40%) respectively (Table 1). The median of disease-free survival in adjuvant, neoadjuvant, and omitted were respectively 11y, 1.4y, and 9.4y (p=0.0001); and the median of overall survival (mOS) were 13.3y, 5.5y, and 7.5y (Figure 1). Analyzed by staging (Figure 2), for stage I mOS was not raged among groups (p=0.01), stage II 13y, 5.5y, and 7.2y (p=0.006), and stage III: 6.2y, 5.9y, and 4.6y (p=0.56). In a multivariable Cox proportional regression, the hazard ratio (HR) for age, staging, and HER2 3+ were 1.07 (p=0.001), 4.2 (p= 0.0001), and 8.9 (p=0.001) respectively (Figure 3).

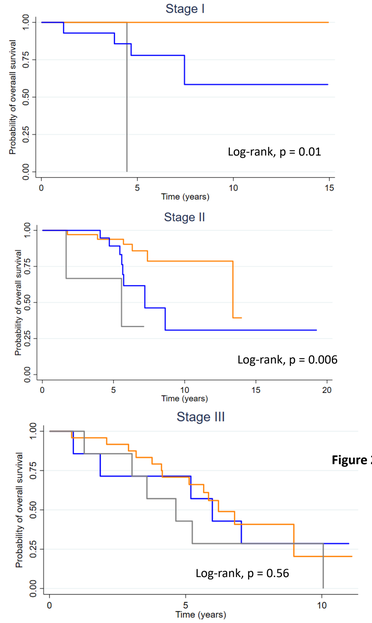

Figure 2- Overal survival by stage

Discussion

In our study, we found that patients with invasive lobular carcinoma in the early stage had better overall survival in the adjuvant chemotherapy than neoadjuvant or patients who did not take chemo: 13.3y, 5.5y, and 7.5y respectively. When we adjusted for staging, no difference in survival was seen in stage III. We performed a multivariable Cox proportional regression and found that chemotherapy was a confounder variable in our modeling. Age, staging, and HER2 3+ were independent risk factors for a lower overall survival. In other words, analyzing age as a continuous variable, each year raises a 7% risk of death; staging as an ordinal variable: each increase in staging increases the risk of death by 4.2x; HER2 as a categorical variable: HER2 positive increases the risk of death in 9x comparing HER2 negative. We believe that patients who have taken neoadjuvant chemo have progressed until surgery, decreasing their survival. However, this hypothesis will be investigated later.

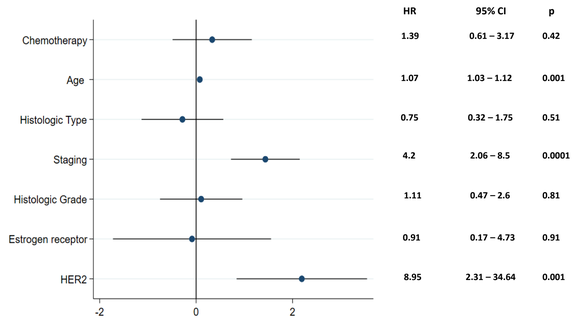

Figure 3 – Multivariable Cox proportional hazards model.

Conclusions

In our study, disease-free survival and overall survival were longer for adjuvant chemotherapy than neoadjuvant, especially for stage I and II. Although age, staging, and HER2 3+ were independent risk factors for shorter overall survival.

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