A Prospective Study Assessing the Impact of Different Chemotherapy Regimens and Type of Surgery on Quality of Life in Breast Cancer Patients Using the EORTC QLQ-BR45

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Abstract:

Background: Breast cancer (BC) treatment modalities significantly impact patient's quality of life (QoL). This study aimed to assess the effects of different chemotherapy (CHT) regimen and surgical approaches on QoL in BC patients using the EORTC QLQ-BR45 questionnaire.

Methods: A prospective single arm study was conducted on 100 BC patients. Patients received AC/TAXOL, TCHP, or AC/TC CHT and underwent BCS/SLNB, BCS/ALND, or MRM surgery. QoL was assessed using the EORTC QLQ-BR45 questionnaire. Statistical analysis included ANOVA, chi-square tests, and linear regression.

Results: BCS/SLNB showed superior outcomes in most QoL domains, including body image ($p=0.025$) and systemic therapy side effects ($p=0.004$). Linear regression analysis identified regaining menstruation ($\beta=6.90$, $p<0.001$), BCS/SLNB surgery ($\beta=4.40$, $p=0.003$), and TCHP CHT ($\beta=4.01$, $p=0.007$) as significant positive predictors of overall QoL, while age showed a slight negative association ($\beta=-0.31$, $p=0.025$).

Conclusions: TCHP CHT and BCS/SLNB surgery were associated with better QoL outcomes in BC patients. Regaining menstruation emerged as the strongest predictor of improved QoL. These findings highlight the importance of considering QoL impacts when selecting treatment strategies for BC patients.

Keywords: Breast cancer, chemotherapy, surgery, quality of life, EORTC QLQ-BR45

Background:

Breast cancer (BC) remains the most prevalent cancer among women globally, with an estimated 2.3 million new diagnoses and approximately 685,000 deaths annually [1, 2]. The management of locally advanced BC often involves a multifaceted approach, combining neoadjuvant chemotherapy (NACT) and surgical interventions [3].

The European Organization for Research and Treatment of Cancer (EORTC) has developed specialized quality of life (QoL) assessment tools, with the EORTC QLQ-BR45 representing an updated version of the earlier QLQ-BR23 module [4, 5]. This 45-item questionnaire assesses a range of symptoms and satisfaction levels, enabling healthcare providers to tailor support and enhance QoL outcomes based on individual patient needs [4, 6].

Research shows that chemotherapy (CHT) and surgery significantly impact BC patient's QoL, with initial declines in functioning and increased fatigue, but many patients adjust by 18 months, emphasizing the need for careful treatment timing considerations [7].

The timing of surgery after NACT significantly affects survival outcomes, highlighting the importance of precise treatment scheduling to optimize patient results [8, 9].

Age, educational status, comorbidities, and socioeconomic factors influence QoL, with younger BC patients experiencing impaired body image and future perspective due to treatment side effects. In contrast, advanced cancer stages and financial difficulties further reduce overall QoL [10].

Recent reviews show that complementary and alternative medicine, particularly yoga, positively impacts QoL by improving psychological well-being and reducing fatigue and sleep disturbances. However, better review methodologies are needed, especially in the transparency of quality appraisal and bias assessments [3].

The ongoing evolution of QoL instruments, exemplified by the transition from the EORTC QLQ-BR23 to the QLQ-BR45, is essential for adapting to the dynamic landscape of BC therapies [11].

The study aimed to elucidate the effects of various treatment modalities on the QoL of BC patients, with a particular focus on the impact of CHT regimens and surgical approaches.

Methods:

This prospective single arm study was conducted on 100 BC patients in the oncology department of Our University Hospital, Egypt, to assess the impact of different CHT regimens and types of surgery using the EORTC QLQ-BR45 QoL questionnaire.

Eligible patients were premenopausal women aged ≤45 years, the observed median age of 36 years is consistent, newly diagnosed with stage I–III breast cancer, who were candidates for neoadjuvant chemotherapy and surgery. Menstrual recovery was included as an independent clinical variable because of its well-established impact on fertility and quality of life in young breast cancer patients. Our regression analysis demonstrated that menstruation recovery was the strongest predictor of overall QoL. Exclusion criteria included: metastatic disease, prior malignancy, or previous chemotherapy/radiotherapy.

Demographic data was collected from all participants. The underlying pathology of each patient was documented, including histopathology invasive ductal carcinoma (IDC) or invasive lobular carcinoma (ILC) and cancer stage (I, II, or III). Patients were treated with one of three CHT regimens: adriamycin and taxol (AC/TAXOL), taxol, carboplatin, herceptin, and pertuzumab (TCHP), or adriamycin cyclophosphamide/taxol carboplatin (AC/TC). Surgical interventions were categorized as breast-conserving surgery/ sentinel lymph node biopsy (BCS/SLNB), breast-conserving surgery/ axillary lymph node dissection (BCS/ALND) or modified radical mastectomy (MRM). The regaining of menstruation was recorded as an outcome measure.

The QoL was assessed using the EORTC QLQ-BR45 questionnaire, which includes functional and symptom scales. The functional scales comprised body image (BI), future perspective (FU), sexual functioning (SX), sexual enjoyment (SE), and breast satisfaction (BS). Symptom scales included systemic therapy side effects (SYS), arm symptoms (ARM), breast symptoms (BR), endocrine therapy symptoms (ET), skin mucositis symptoms (SM), endocrine sexual symptoms (ES), and hair loss (HU).

The EORTC QLQ-BR45 [3]:

EORTC QLQ-BR45 was administered to patients through a single structured interview. All eligible patients visiting the BC oncology clinic were invited to participate. After agreeing and signing informed consent, they underwent a face-to-face interview. This interview took place in a private setting, ensuring patient confidentiality and comfort.

During the interview, patients completed the EORTC QLQ-BR45 questionnaire, which consists of 45 items addressing various aspects of BC and its treatment, including functional and symptom scales. Responses were recorded on a four-point Likert scale, ranging from "not at all" to "very much."

Following the interview, the responses were scored using the EORTC scoring manual. A linear transformation was applied to convert the Likert scale responses to a 0–100 scale. Higher scores on the functional scales indicated a better QoL, while higher scores on the symptom scales reflected greater symptom severity and a worse QoL. The single interview approach captured the patients' baseline QoL and any initial impacts of the treatment.

The study primarily aimed to evaluate the impact of different chemotherapy regimens and types of surgery on QoL outcomes.

Statistical analysis

Statistical analysis was done by SPSS v27 (IBM©, Armonk, NY, USA). Quantitative data was described as mean ± SD (standard deviation) and then compared using the ANOVA test with the post hoc Bonferroni test. Qualitative data is described as numbers and percentages and then compared using the Chi-square test as well as Fisher's Exact test according to expected numbers. Linear regression was used to find out independent factors affecting total QoL. The level of significance that was taken at p-value ≤ 0.050 was significant.

Results:

The mean ± SD of age was 35.9±5.3 years. Chemotherapies were AC/TAXOL (39.0%), TCHP (38.0%) and AC/TC (23.0%). Types of surgery were BCS/SLNB (48.0%), BCS/ALND (21.0%), and MRM (31.0%). Regaining menstruation was in 56.0% of cases. Table 1

QoL among the study cases was 83.4±9.1. Table 2

There is no significant difference according to CHT regimens regarding demographic characteristics, underlying pathology, and management. Regaining menstruation was most frequent in TCHP, followed by AC/TAXOL, and least frequent in AC/TC; the differences were significant in AC/TC, with no significant differences between TCHP and AC/TAXOL. Table 3

BI was highest in cases TCHP received, followed by AC/TAXOL, and lowest in AC/TC; the differences were statistically significant between all types of CHT. FU, SYS, SM, and total QoL were highest in cases received TCHP, followed by AC/TAXOL, and lowest in AC/TC, and the differences were statistically significant in AC/TC with no significant differences between TCHP and AC/TAXOL. SE and BS were significantly higher in TCHP than AC/TC, with no significant differences between AC/TAXOL and each of TCHP and AC/TC. ARM was significantly highest in TCHP, with no significant differences between AC/TAXOL and AC/TC. Table 4

No significant difference according to surgery regarding demographic characteristics, underlying pathology, and management. Regaining of menstruation was most frequent in BCS/SLNB, followed by BCS/ALND, and least frequent in MRM; the differences were significant in the MRM group, with no significant differences between BCS/SLNB and BCS/ALND. Table 5

BI, SYS, HU, ARM, BR, ET, and SM were significantly higher in cases that underwent BCS/SLNB than in cases that underwent MRM, with no significant differences between cases that underwent BCS/ALND or MRM. Total QoL was significantly high in BCS/SLNB, followed by BCS/ALND, and lowest in MRM; the differences were significant in MRM, with no significant differences between BCS/SLNB and BCS/ALND. Table 6

Regaining menstruation, BCS/SLNB surgery, and TCHP CHT were significant independent factors that increased total QoL, while age was a significant independent factor that decreased total QoL. Table 7

Table 1: Demographic characteristics, underlying pathology, management, and outcome among the studied cases

Variables		Mean ± SD	Range
Demographic characteristics			
Age (years)		35.9±5.3	23.0–45.0
Parity		1.7±1.1	0.0–4.0
		N	%
Marital status	Unmarried	25	25.0%
	Married	75	75.0%
Family history of BC		24	24.0%
Underlying pathology			
Histopathology	IDC	90	90.0%
	ILC	10	10.0%
Stage	I	15	15.0%
	II	58	58.0%
	III	27	27.0%
Management			
Chemotherapy	AC/TAXOL	39	39.0%
	TCHP	38	38.0%
	AC/TC	23	23.0%
Surgery	BCS/SLNB	48	48.0%
	BCS/ALND	21	21.0%
	MRM	31	31.0%
Outcome			
Regaining of menstruation		56	56.0%

Data are presented as mean ± SD, median (IQR), or frequency (%).

Table 2: Quality of life using the EORTC QLQ-BR45 questionnaire among the study cases

Items	Mean±SD	Range
Functional items		
BI	52.2±21.9	0.0–100.0
FU	46.3±31.4	0.0–100.0
SX	79.8±13.5	33.3–100.0
SE	86.7±19.5	33.3–100.0
BS	48.7±29.1	0.0–100.0
Symptoms items		
SYS	50.8±17.8	0.0–100.0
HU	49.3±31.6	0.0–100.0
ARM	50.7±17.7	16.7–100.0
BR	46.7±19.0	0.0–83.3
ET	42.3±16.4	8.3–83.3
SM	43.7±18.2	0.0–100.0
ES	65.0±23.7	16.7–100.0
Total		
QoL	83.4±9.1	53.3–100.0

Data are presented as mean ± SD, median (IQR). BI: body image, FU: future perspective, SX: sexual functioning, SE: sexual enjoyment, BS: breast satisfaction, SYS: symptom scales included systemic therapy side effects, ARM: arm symptoms, BR: breast symptoms, ET: endocrine therapy symptoms, SM: skin mucositis symptoms, ES: endocrine sexual symptoms, HU: hair loss, QoL: quality of life.

Table 3: Comparison according to CHT regarding demographic characteristics, underlying pathology, management, and outcome

Variables		Chemotherapy			P value
		AC/TAXOL (Total=39)	TCHP (Total=38)	AC/TC (Total=23)	
Demographic characteristics					
Age (years)		36.9±4.9	34.8±5.6	36.0±5.0	0.215
Parity		1.7±1.1	1.6±1.2	1.9±0.9	0.438
Marital status	Unmarried	8 (20.5%)	12 (31.6%)	5 (21.7%)	0.490
	Married	31 (79.5%)	26 (68.4%)	18 (78.3%)	
Family history of BC		8 (20.5%)	9 (23.7%)	7 (30.4%)	0.676
Underlying pathology					
Histopathology	IDC	33 (84.6%)	36 (94.7%)	21 (91.3%)	0.366
	ILC	6 (15.4%)	2 (5.3%)	2 (8.7%)	
Stage	I	8 (20.5%)	6 (15.8%)	1 (4.3%)	0.433
	II	22 (56.4%)	20 (52.6%)	16 (69.6%)	
	III	9 (23.1%)	12 (31.6%)	6 (26.1%)	
Management					
Surgery	BCS/SLNB	15 (38.5%)	22 (57.9%)	11 (47.8%)	0.264
	BCS/ALND	12 (30.8%)	6 (15.8%)	3 (13.0%)	
	MRM	12 (30.8%)	10 (26.3%)	9 (39.1%)	
Outcome					
Regaining of menstruation		23 (59.0%)	27 (71.1%)	6 (26.1%)	0.002*

Data are presented as mean ± SD, median (IQR), or frequency (%). IDC; Invasive Ductal Carcinoma, ILC; Invasive Lobular Carcinoma.

Table 4: Comparison to chemotherapy regarding QoL

Items	Chemotherapy			P value
	AC/TAXOL (Total=39)	TCHP (Total=38)	AC/TC (Total=23)	
Functional items				
BI	50.4±14.6	63.6±21.5	36.2±22.8	<0.001*
FU	46.2±31.2	58.8±28.4	26.1±26.5	<0.001*
SX	79.5±12.4	81.6±14.9	77.5±12.9	0.518
SE	86.3±22.6	92.1±14.4	78.3±19.1	0.025*
BS	44.0±30.5	59.2±26.5	39.1±26.4	0.013*
Symptoms items				
SYS	52.4±12.7	54.8±18.5	41.3±21.1	0.011*
HU	51.3±27.4	54.4±35.0	37.7±30.7	0.119
ARM	46.6±16.3	57.5±19.3	46.4±14.2	0.010*
BR	47.4±18.6	49.1±20.8	41.3±15.8	0.283
ET	42.7±15.1	44.7±16.6	37.7±17.9	0.263
SM	45.7±14.7	46.9±19.7	34.8±18.7	0.025*
ES	62.4±27.0	68.9±19.4	63.0±24.6	0.447
Total QoL	83.5±6.8	87.7±6.9	76.1±11.2	<0.001*

Data are presented as mean ± SD, median (IQR).

Table 5: Comparison to surgery regarding demographic characteristics, underlying pathology, management, and outcome

		Surgery			P value
		BCS/SLNB (Total=48)	BCS/ALND (Total=21)	MRM (Total=31)	
Demographic characteristics					
Age (years)		34.8±5.8	36.3±4.9	37.2±4.4	0.137
Parity		1.7±1.1	1.6±1.1	1.8±1.0	0.719
Marital status	Unmarried	11 (22.9%)	7 (33.3%)	7 (22.6%)	0.611
	Married	37 (77.1%)	14 (66.7%)	24 (77.4%)	
Family history of BC		11 (22.9%)	6 (28.6%)	7 (22.6%)	0.858
Underlying pathology					
Histopathology	IDC	46 (95.8%)	19 (90.5%)	25 (80.6%)	0.907
	ILC	2 (4.2%)	2 (9.5%)	6 (19.4%)	
Stage	I	8 (16.7%)	3 (14.3%)	4 (12.9%)	0.510
	II	31 (64.6%)	11 (52.4%)	16 (51.6%)	
	III	9 (18.8%)	7 (33.3%)	11 (35.5%)	
Management					
Chemotherapy	AC/TAXOL	15 (31.3%)	12 (57.1%)	12 (38.7%)	0.264
	TCHP	22 (45.8%)	6 (28.6%)	10 (32.3%)	
	ACTC	11 (22.9%)	3 (14.3%)	9 (29.0%)	
Outcome					
Regaining of menstruation		35 (72.9%)	14 (66.7%)	7 (22.6%)	<0.001*

Data are presented as mean ± SD, median (IQR), or frequency (%). IDC; Invasive Ductal Carcinoma, ILC; Invasive Lobular Carcinoma.

Table 6: Comparison according to surgery regarding QoL

Items	Surgery			P value
	BCS/SLNB (Total=48)	BCS/ALND (Total=21)	MRM (Total=31)	
Functional items				
BI	58.0±19.1	50.0±22.4	44.6±23.7	0.025*
FU	50.0±29.2	47.6±29.0	39.8±35.9	0.364
SX	81.3±14.4	81.0±13.2	76.9±11.9	0.342
SE	91.0±16.5	85.7±22.5	80.6±20.7	0.068
BS	47.9±30.5	42.1±27.2	54.3±27.9	0.323
Symptoms items				
SYS	55.9±14.9	51.2±16.3	42.5±20.2	0.004*
HU	55.6±29.4	55.6±28.5	35.5±33.3	0.012*
ARM	55.6±16.2	52.4±17.7	41.9±17.1	0.003*
BR	53.1±17.4	42.9±17.1	39.2±19.5	0.003*
ET	46.4±15.7	42.9±15.2	35.8±16.6	0.018*
SM	49.3±18.5	43.7±15.3	34.9±16.3	0.002*
ES	69.4±20.4	63.5±25.6	59.1±26.5	0.161
Total QoL	87.5±6.6	83.3±6.3	77.1±10.5	<0.001*

Data are presented as mean ± SD, median (IQR).

Table 7: Linear regression for factors affecting total QoL among the study cases

Variables	β	SE	P value	95% CI	R^2
Constant	87.11	5.38	<0.001*	76.42–97.79	
Regaining of menstruation	6.90	1.52	<0.001*	3.87–9.93	
BCS/SLNB surgery	4.40	1.45	0.003	1.52–7.28	0.466
TCHP chemotherapy	4.01	1.45	0.007	1.13–6.90	
Age (years)	-0.31	0.14	0.025	-0.59–-0.04	

β: Regression coefficient. SE: Standard error. *Significant. CI: Confidence interval. R^2: Coefficient of determination.

Discussion:

BC treatment modalities have evolved significantly over recent decades, with increasing emphasis on optimizing both survival outcomes and QoL for patients undergoing various therapeutic regimens [12].

Our study utilized the EORTC QLQ BR45 to assess the QoL in BC patients, revealing varying scores across functional and symptom domains. Notably, SX and SE scored highest among functional items (means of 79.8 ± 13.5 and 86.7 ± 19.5, respectively), while BI and FU showed lower scores (52.2 ± 21.9 and 46.3 ± 31.4, respectively). In the symptoms category, ES had the highest mean score (65.0 ± 23.7), while ET scored lowest (42.3 ± 16.4). The overall QoL score was relatively high at 83.4 ± 9.1.

These findings align with the growing recognition of the EORTC QLQ BR45 as a comprehensive tool for assessing QoL in BC patients. Bjelic-Radisic et al. [10] highlighted the need for this updated module to address QoL issues related to newer therapeutic options. Our results support the utility of this instrument in capturing a wide range of QoL aspects, particularly in areas such as sexual functioning and endocrine-related symptoms, which were not as thoroughly addressed in previous versions.

The relatively high scores in sexual functioning and enjoyment in our study are noteworthy, as they contrast with some earlier findings. For instance, Getu et al. [13] reported that future perspective and upset by hair loss were the most affected areas in terms of functioning and symptoms, respectively. This discrepancy might be attributed to differences in cultural contexts, treatment modalities, or the timing of assessment relative to diagnosis and treatment.

Our findings on body image and future perspectives align more closely with those of Getu et al. [13], who reported a mean score of 57.1 ± 37.3 for future perspectives. This consistency suggests that concerns about body image and future outlook are common across different populations of BC patients, highlighting areas where supportive interventions might be particularly beneficial.

The high overall QoL score in our study (83.4 ± 9.1) is encouraging and may reflect advancements in BC treatment and supportive care. However, it is essential to note that Barakat et al. [14] found some limitations in the psychometric properties of the EORTC QLQ-BR45, particularly in the body image scale (α = 0.51) and the systemic therapy side effects scale (α = 0.63). This underscores the need for ongoing validation and

refinement of QoL assessment tools in diverse populations.

Our study revealed significant differences in outcomes among various CHT regimens, particularly in the regaining of menstruation. The TCHP regimen showed the highest rate of menstruation recovery (71.1%), followed by AC/TAXOL (59.0%) and AC/TC (26.1%) (p=0.002). This finding is crucial, as it directly impacts patients' QoL and future fertility prospects.

While our study focused on menstruation recovery, it is essential to consider these findings in the context of broader treatment outcomes. The Early BC Trialists' Collaborative Group [11] meta-analysis, which compared NACT with adjuvant CHT, found no significant differences in distant recurrence, BC mortality, or overall mortality between the two approaches. However, they did note an increased risk of local recurrence with NACT.

Our observation of varying menstruation recovery rates across different CHT regimens adds an essential dimension to treatment considerations. This is particularly relevant in light of Ferreira et al. [15] findings from their trial, which showed that endocrine therapy had a persistent negative effect on QoL, while CHT 's impact was less pronounced at two years post-diagnosis.

The lack of significant differences in age, parity, marital status, family history, histopathology, and cancer stage between CHT groups in our study suggests that the observed differences in menstruation recovery are likely attributable to the specific CHT regimens rather than patient characteristics. This underscores the importance of considering the long-term effects of different CHT protocols on patients' endocrine function and QoL.

Our analysis demonstrated significant variations in QoL measures across different CHT regimens, with TCHP consistently showing superior outcomes in most domains. BI, FU, and BS were significantly better in the TCHP group (p<0.001, p<0.001, and p=0.013, respectively). SE was also highest in the TCHP group (p=0.025).

These findings contribute to the growing body of evidence on the differential impacts of various CHT regimens on patient-reported outcomes. The superior performance of TCHP in our study aligns with the evolving trend towards more targeted and potentially less toxic treatment approaches. However, it is crucial to consider these results in the context of other studies that have examined the long-term effects of CHT on QoL.

Battisti et al. [16], in their study of older BC patients, found that CHT had significant negative impacts on multiple QoL domains at 6 months, including global health score, physical functioning, and cognitive functioning. However, these negative impacts were no longer significant by 18-24 months. Our study's focus on specific regimens provides a more nuanced understanding of how different CHT protocols may affect QoL outcomes.

Interestingly, our study found that SYS, ARM, and SM were significantly lower in the AC/TC group. This contrasts with the overall superior performance of TCHP in other domains and highlights the complexity of assessing CHT impacts on QoL. It suggests that while TCHP may offer benefits in areas such as body image and future perspectives, it may also be associated with more pronounced side effects in certain areas.

The variation in QoL outcomes across different CHT regimens underscores the importance of personalized treatment approaches. As Hasanah et al. [12] emphasized in their systematic review, factors such as age, disease stage, and presence of comorbidities can influence QoL outcomes. Our findings suggest that the choice of CHT regimen should be considered alongside these factors when aiming to optimize both treatment efficacy and patient QoL.

Our study revealed significant differences in outcomes based on the surgical approach used. Notably, the regaining of menstruation was markedly higher in BCS/SLNB (72.9%) and BCS/ALND (66.7%) compared to MRM (22.6%) (p<0.001).

These findings align with the growing body of evidence supporting the benefits of BCS in terms of QoL outcomes. Kovačević et al. [17] similarly found that BCS or MRM with breast reconstruction was associated with a statistically significant increase in QoL compared to total mastectomy.

The substantial difference in menstruation recovery rates between breast-conserving surgeries and MRM in our study is particularly noteworthy. This outcome has significant implications for patients' fertility and long-term endocrine function, which are crucial aspects of QoL for many BC survivors. The higher rates of menstruation recovery in breast-conserving surgeries suggest that these approaches may offer advantages beyond cosmetic outcomes, potentially preserving ovarian function to a greater extent than more extensive surgeries.

It is important to note that our study did not find significant differences in age, parity, marital status, family history, histopathology, cancer stage, or CHT regimen among the surgical groups. This suggests that the observed differences in menstruation recovery are likely attributable to the surgical approach itself rather than patient or disease characteristics.

However, we did observe a trend in the distribution of CHT regimens across surgical approaches, though it did not reach statistical significance (p=0.264). This trend warrants further investigation, as it may indicate subtle interactions between surgical approach and CHT choice that could influence long-term outcomes.

Our analysis of QoL measures across different surgical approaches revealed consistently superior outcomes for BCS/SLNB in most domains. BI was significantly better in the BCS/SLNB group (p=0.025), a finding that aligns with previous research on the psychological impacts of different BC surgeries [18-20].

Notably, SYS, HU, ARM, BR, ET, and SM were all significantly lower in the BCS/SLNB group (p=0.004, p=0.012, p=0.003, p=0.003, p=0.018, and p=0.002, respectively). These results suggest that BCS/SLNB may offer advantages not only in terms of cosmetic

outcomes and body image but also in reducing the overall symptom burden associated with BC treatment.

The superior outcomes associated with BCS/SLNB in our study are consistent with the findings of Kovačević et al. [17], who reported that BCS was associated with improved QoL compared to total mastectomy. Our results provide a more detailed breakdown of specific QoL domains affected by surgical approach, offering valuable insights for clinical decision-making.

The lower rates of arm symptoms in the BCS/SLNB group are particularly noteworthy, as arm morbidity is a common concern following axillary surgery. This finding supports the growing trend towards less invasive axillary staging procedures and underscores the potential QoL benefits of sentinel lymph node biopsy over more extensive axillary dissection.

Our observation of lower endocrine therapy symptoms in the BCS/SLNB group is intriguing and warrants further investigation. While the direct mechanism linking surgical approach to endocrine symptoms is not immediately apparent, this finding may reflect complex interactions between surgery, adjuvant therapies, and overall treatment burden.

The consistently superior QoL outcomes associated with BCS/SLNB in our study provide strong support for the use of this approach when oncologically appropriate. However, it's important to note that factors such as tumor size, location, and patient preferences must also be considered in surgical decision-making.

Our linear regression analysis identified several factors significantly affecting the overall QoL in BC patients. Regaining menstruation emerged as the most potent positive predictor (β=6.90, $p<0.001$), followed by BCS/SLNB surgery (β=4.40, $p=0.003$) and TCHP CHT (β=4.01, $p=0.007$). Age showed a small but significant negative association with QoL (β=-0.31, $p=0.025$).

Our results regarding the impact of CHT regimens on QoL can be contextualized within the broader literature on NACT outcomes. While our study focused on QoL measures, it is essential to consider these findings alongside survival outcomes reported in other studies. For instance, Xia et al. [6] found that NACT was associated with poorer overall survival compared to adjuvant CHT in triple-negative BC patients. However, they also noted that patients achieving pathological complete response after NACT demonstrated significantly improved survival outcomes. This underscores the importance of considering both QoL and survival outcomes when evaluating treatment strategies.

The timing of surgery following NACT is another critical factor that may influence outcomes. While our study did not directly address this issue, the findings of Sanford et al. [9] suggest that the interval between NACT and surgery may impact overall survival, with surgery at 4-6 weeks post-NACT showing the most favorable outcomes. This highlights the need for future research to investigate potential associations between treatment timing, QoL outcomes, and survival rates.

The strong positive association between menstruation recovery and overall QoL underscores the importance of fertility and endocrine function in BC survivors' well-being. This finding aligns with the growing recognition of fertility preservation as a crucial aspect of comprehensive cancer care, particularly for younger patients.

The positive impact of BCS/SLNB on QoL is consistent with our earlier findings and supports the trend towards less invasive surgical approaches in BC treatment. This result corroborates the findings of Kovačević et al. [17], who reported improved QoL outcomes with BCS.

The positive association between TCHP CHT and QoL is noteworthy, especially given the mixed findings on CHT 's impact on QoL in the literature. For instance, Battisti et al. [16] found initial negative impacts of CHT on QoL in older patients, which diminished over time. Our finding suggests that specific CHT regimens may have differential effects on long-term QoL, highlighting the importance of considering these factors in treatment planning.

The negative association between age and QoL, while small, is consistent with some previous studies. However, it contrasts with findings from other research, such as Ferreira et al. [15], who found that younger, premenopausal patients were more susceptible to QoL deterioration following CHT. This discrepancy highlights the complex relationship between age and QoL in BC patients and suggests that age-specific interventions may be necessary to optimize outcomes across different age groups.

Our model explained 46.6% of the variance in QoL scores, indicating moderate predictive power. While this suggests that the identified factors play a significant role in determining QoL, it also implies that other unmeasured variables contribute to QoL outcomes in BC patients.

This study's limitations include its single-center design, which may limit generalizability. The small sample size could be considered modest for detecting subtle differences between treatment groups. The cross-sectional nature of the QoL assessment does not capture longitudinal changes in patient experiences. Additionally, the study did not control for potential confounding factors such as socioeconomic status or comorbidities. Future research should consider multi-center designs, larger sample sizes, and longitudinal assessments to provide more comprehensive insights into the long-term QoL outcomes of BC treatments.

Conclusion:

The comprehensive assessment of QoL in BC patients, facilitated by tools like the EORTC QLQ-BR45, plays a pivotal role in enhancing patient care. By considering the multifaceted impacts of CHT and surgical interventions on patients' physical, psychological, and social well-being, clinicians can make more informed decisions and provide tailored support throughout the treatment.

List of abbreviations:
Adriamycin and taxol (AC/TAXOL)
Adriamycin Cyclophosphamide/Taxol Carboplatin (AC/TC)
Arm symptoms (ARM)
Body image (BI)
Breast cancer (BC)
Breast satisfaction (BS)
Breast symptoms (BR)
Breast-conserving surgery/ axillary lymph node dissection (BCS/ALND)
Breast-conserving surgery/ sentinel lymph node biopsy (BCS/SLNB)
Chemotherapy (CHT)
Chemotherapy (CHT)
Endocrine sexual symptoms (ES)
Endocrine therapy symptoms (ET)
European Organization for Research and Treatment of Cancer (EORTC)
Future perspective (FU)
Invasive ductal carcinoma (IDC)
Invasive lobular carcinoma (ILC)
Modified radical mastectomy (MRM)
Neoadjuvant chemotherapy (NACT)
Quality of life (QoL)
Sexual enjoyment (SE)
Sexual functioning (SX)
Skin mucositis symptoms (SM)
Taxol, Carboplatin, Herceptin, and Pertuzumab (TCHP)

Competing interests:
Not applicable

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