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Research Article/Özgün Araştırma

The role of surgery type in breast cancer patients with recurrent breast cancer receiving neoadjuvant chemotherapy

Neoadjuvan kemoterapi alan nüks meme kanserli hastalarda cerrahi tipinin rolü

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Abstract

Aim: To assess the impact of surgical approach on recurrence and survival in breast cancer patients with recurrence post-neoadjuvant chemotherapy (NACT).

Materials and Methods: A retrospective analysis included 108 female patients (≥18 years) who completed NACT (2010–2024) and developed recurrence. Patients underwent breast-conserving surgery (BCS) or mastectomy (MX), with sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND). Recurrence-free survival (RFS), overall survival (OS), and associated factors were evaluated.

Results: Among 108 patients (68 BCS, 40 MX, 18 SLNB, 90 ALND), the median RFS was 23.67 months (BCS: 24.53 vs. MX: 18.97; p=0.65; SLNB: 25.87 vs. ALND: 22.30; p=0.65). Five-year RFS rates were 1% and 10% in the two groups, respectively. The median OS was 55.57 months (BCS: 56.07 vs. MX: 50.43; p=0.607; SLNB: 75.90 vs. ALND: 48.70; p=0.019). Molecular subtype (HR=2.12, p<0.001) and axillary surgery type (HR=4.41, p=0.005) were independent predictors of OS. The mean follow-up duration was 59.96 ± 3.62 months.

Conclusion: BCS and MX provide comparable RFS and OS in patients with recurrence after NACT. SLNB is associated with significantly improved OS compared with ALND, underscoring the importance of tailoring axillary management to tumor biology and patient-specific factors.

Keywords: Breast cancer; Neoadjuvant chemotherapy; Surgical approach; Recurrence; Survival.

Öz

Amaç: Neoadjuvan kemoterapi (NACT) sonrası nüks eden meme kanseri hastalarında cerrahi yaklaşımın nüks ve sağkalım üzerindeki etkisini değerlendirmek.

Gereç ve Yöntem: Retrospektif analiz, NACT'yi tamamlayan (2010-2024) ve nüks gelişen 108 kadın hastayı (≥18 yaş) içermektedir. Hastalar, sentinel lenf nodu biyopsisi (SLNB) veya aksiller lenf nodu diseksiyonu (ALND) ile meme koruyucu cerrahi (BCS) veya mastektomi (MX) geçirdi. Nükssüz sağkalım (RFS), genel sağkalım (OS) ve ilişkili faktörler değerlendirildi.

Bulgular: Toplam 108 hastanın (68 MKC, 40 MX, 18 SLNB, 90 ALND) medyan RFS süresi 23,67 aydı (MKC: 24,53 vs. MX: 18,97; p=0,65; SLNB: 25,87 vs. ALND: 22,30; p=0,65). Beş yıllık RFS oranları iki grupta sırasıyla %1 ve %10 idi. Medyan OS 55,57 ay olarak bulundu (MKC: 56,07 vs. MX: 50,43; p=0,607; SLNB: 75,90 vs. ALND: 48,70; p=0,019). Moleküler alt tip (HR=2.12, p<0.001) ve aksiller cerrahi tipi (HR=4,41, p=0,005) OS için bağımsız belirleyicilerdi. Ortalama takip süresi 59,96 ± 3,62 aydı.

Sonuç: MKC ve MX, NAKT sonrası nüks gelişen hastalarda benzer RFS ve OS sonuçları sağlamaktadır. SLNB'nin ALND'ye kıyasla anlamlı derecede daha iyi OS ile ilişkili olması, aksiller cerrahi yaklaşımının tümör biyolojisi ve hasta özelliklerine göre kişiselleştirilmesinin önemini vurgulamaktadır.

Anahtar Kelimeler: Meme kanseri; Neoadjuvan kemoterapi; Cerrahi yaklaşım; Nüks; Hayatta kalma.

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intihal incelemesinden geçirilmiştir.

Introduction

Breast cancer remains the most common cancer diagnosis among women worldwide. In 2022, approximately 2.3 million new cases were reported, accounting for 11.6% of all female cancer diagnoses.[1] Neoadjuvant chemotherapy (NACT) plays a pivotal role in decreasing the risk of both local and distant recurrence. It also facilitates axillary lymph node downstaging and improves the viability of BCS by reducing tumor burden.[2,3] BCS offers numerous clinical and quality-of-life advantages, including favorable aesthetic outcomes, a less invasive procedure, a lower risk of postoperative complications, and improved patient satisfaction.[4] In early-stage disease, robust clinical evidence demonstrates that BCS followed by radiotherapy yields overall survival outcomes comparable to those achieved with mastectomy in appropriately selected patients.[5] Given the morbidity associated with ALND, alternative approaches such as SLNB and targeted axillary dissection have become increasingly common, supported by randomized trials showing no significant differences in long-term survival. Nevertheless, the comparative effects of surgical modality (BCS versus mastectomy) and lymph node management strategy (SLNB versus ALND) on recurrence and survival after NACT remain under debate.[6] This study was conducted to investigate the effect of surgical type on survival and recurrence in patients with non-metastatic breast cancer who underwent surgery after NACT and developed recurrence, as well as to identify potential prognostic factors.

Materials and Methods

Type of research

In this retrospective observational study, the medical records of female patients diagnosed with breast cancer who underwent NACT between 2010 and 2024 and subsequently received surgical intervention were thoroughly reviewed.

Research population and sample

Prior to initiating NACT, all patients underwent detailed staging procedures, including breast MRI, ultrasound, and PET-CT scans, to assess potential distant metastases and evaluate lesions in the contralateral breast. Eligibility criteria included female patients aged ≥18 years with a primary tumor ≥2 cm, lymph node metastasis, or inflammatory breast cancer. Clinically positive axillary lymph node status was not mandatory for inclusion; patients with tumor size ≥2 cm were eligible even if the axilla was clinically negative, and individuals who were clinically node-negative but found to be pathologically node-positive after surgery were also included. Additionally, patients who developed recurrence following completion of the prescribed NACT regimen were included. Exclusion criteria comprised a concurrent diagnosis of another malignancy, incomplete pathological or clinical data in the hospital system, failure to complete NACT, absence of recurrence post-NACT, or evidence of distant metastasis at initial diagnosis. Treatment decisions were informed by the institution's multidisciplinary tumor board. Of 466 identified patients, recurrence was absent in 260 of 328 patients who underwent BCS and in 98 of 138 patients who underwent mastectomy. The final cohort included 108 patients with recurrence, of whom 68 had received BCS and 40 had undergone mastectomy.

Data collection tools

Histologic type and molecular subtyping were accepted before NACT. In our study, patients with an ER (estrogen receptor) and PgR (progesterone receptor) ratio above 10% were considered positive.[7] Patients with an IHC HER2 score of 3+ or an IHC score of 2+ with positive FISH results were considered HER2-positive. The pathology laboratory of our hospital reported the Ki-67 cut-off value for luminal distinctions as "18" and this cut-off value was used in statistical analyses. Tumor pathological staging was performed according to the AJCC TNM classification. Based on previous studies, subtype groups were defined as a) hormone receptor positive (ER and/or PgR positive) and Her2 negative, b) Her2 positive regardless of hormonal status, and c) triple negative (ER, PgR and Her2 negative).[8] Patients who underwent SLNB were defined as those with 1-10 lymph nodes examined in the pathology reports, and patients who underwent

ALND were defined as those with 10 or more lymph nodes examined.The classification of SLNB and ALND in this study was based on pathology reports, and all SLNB procedures during the study period were performed using the standard blue-dye mapping technique.

Patients' age, gender, treatment initiation dates, type of breast and axilla surgery (BCS: /mastectomy and SLNB/ALND), recurrence dates, and dates of last follow-up or death, if alive, were recorded from the hospital's medical data record system.

All patients received standard neoadjuvant chemotherapy consisting of four cycles of cyclophosphamide plus an anthracycline (epirubicin or doxorubicin), followed by either docetaxel every three weeks for four cycles or weekly paclitaxel for twelve cycles. In Her2-positive tumors, trastuzumab was incorporated into the neoadjuvant regimen, and a subset of patients also received pertuzumab. Surgical interventions following chemotherapy included breast-conserving procedures or modified radical mastectomy, as well as axillary evaluation performed through either SLNB or ALND, based on nodal status and surgeon decision. Postoperatively, Her2-positive patients continued trastuzumab to complete one year of therapy, while hormone receptor–positive patients received adjuvant endocrine treatment. Patients who underwent breast-conserving surgery also received adjuvant radiotherapy (50 Gy).Because the study cohort consisted exclusively of patients who developed recurrence after completing neoadjuvant chemotherapy, the number of individuals achieving pathological complete response (pCR) was extremely limited; therefore, pCR could not be included as a meaningful variable in the statistical analyses. Combined surgical subgroup analysis (BCS+SLNB, BCS+ALND, mastectomy+SLNB, mastectomy+ALND) was not performed because several subgroups contained very small patient numbers, which would have resulted in statistically unreliable estimates.

Statistical analysis

The statistical evaluation of the study data was conducted using SPSS software version 24 (SPSS Inc., Chicago, IL, USA). For categorical variables, descriptive statistics were summarized as frequencies and their respective percentages. The chi-square test was used to investigate possible relationships between categorical variables (e.g., type of surgery performed (mastectomy status)) and the presence of cancer-related characteristics.

Recurrence-free survival (RFS) was determined as the interval from the date of breast cancer diagnosis to the occurrence of either local or distant tumor recurrence. Patients without recurrence were censored at their last documented follow-up. OS was defined as the period from initial diagnosis to death from any cause, with patients still alive censored at their final follow-up date.

Survival probabilities were estimated using Kaplan-Meier survival curves, while differences between patient groups were analyzed using the log-rank test. Factors influencing survival outcomes were further assessed through both univariate and multivariate analyses, applying Cox proportional hazards regression modeling. The results were presented as hazard ratios (HR) with corresponding 95% confidence intervals (CI), and statistical significance was established at a p-value of less than 0.05

Ethics committee approval

This retrospective cohort study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Tekirdağ Namık Kemal University (Approval No: 2024-292-10.20, date: 30.10.2024). Written informed consent was obtained from all participants prior to their inclusion in the study.

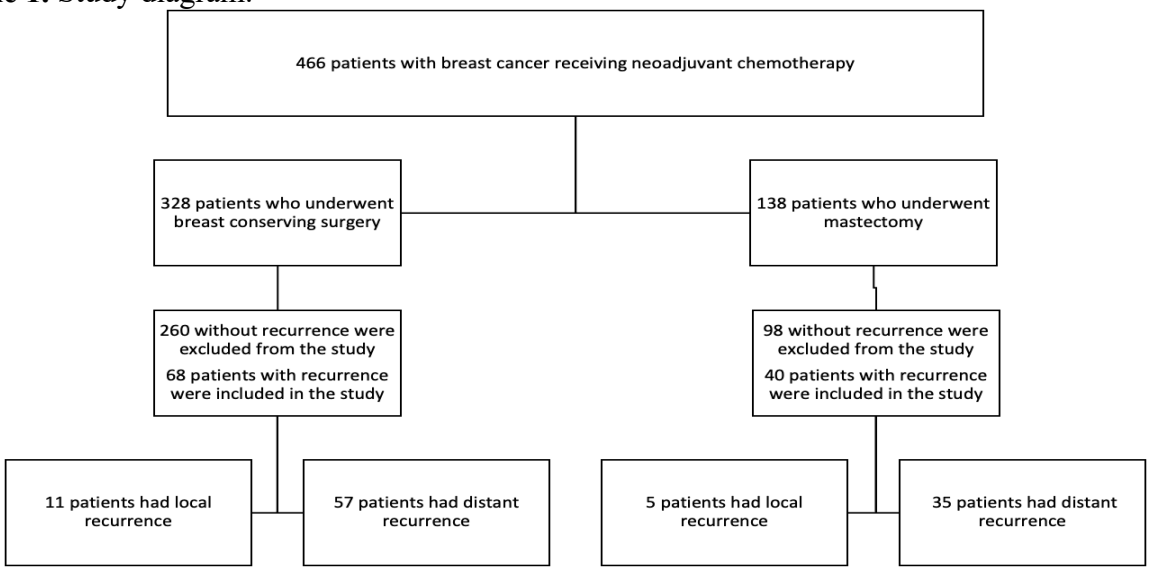
Results

Patient and tumor baseline characteristics

In total, 466 female patients meeting the inclusion criteria were evaluated. Of these, 328 underwent breast-conserving surgery (BCS) while 138 had mastectomy procedures performed (Table 1). The median age of the entire cohort was 49 (range: 41-59) years. During the follow-up period, 108 patients (23.1%) experienced disease recurrence, either locally or at distant sites. Among all

participants, cancer-related mortality was recorded in 59 individuals (54.6%). The median follow-up duration was 53.60 ± 4.78 months. Mean follow-up was 59.96 ± 3.62 months.

Table 1. Study diagram.



Among those with documented recurrence, 40 patients (37%) had been treated with mastectomy and 68 patients (63%) underwent breast-conserving surgery. Regarding axillary surgery, 18 patients (17%) had SLNB while 90 patients (84%) underwent ALND. The variability in the number of nodes removed during SLNB reflects post-NACT alterations in lymphatic drainage patterns as well as the retrospective pathology-based classification used in this study. In our cohort, SLNB was more frequently performed in patients undergoing breast-conserving surgery, consistent with routine clinical practice; however, the number of SLNB cases remained too limited to support a reliable combined subgroup analysis. According to receptor-based classification, 56 patients (51.9%) were categorized as hormone receptor positive but Her2-negative (HR+/Her2-), 30 patients (27.8%) as Her2-positive, and 22 patients (20.4%) had triple-negative breast cancer (Table 2).

Recurrence-free survival (RFS) analysis

There was no statistically significant difference in RFS between mastectomy and breast-conserving surgery groups, with 3-year and 5-year recurrence-free survival rates of 25% vs. 20% and 1% vs. 10%, respectively. Similarly, no significant difference in RFS was observed when comparing SLNB and ALND groups, with 3-year and 5-year rates of 24 % vs. 22 % and 1% vs. 4 %, respectively. Despite the apparent absolute differences between the groups, statistical significance was not reached due to the small sample size and limited number of events.

The overall median RFS (mRFS) for the cohort was 23.67 ± 2.19 months (95 % CI: 19.36–27.97). Stratified analyses showed mRFS values of 24.53 ± 1.82 months (95 % CI: 20.95–28.11) in patients who underwent BCS, and 18.97 ± 2.79 months (95 % CI: 13.48–24.45) in the mastectomy group. For axillary procedures, mRFS was 25.87 ± 5.7 months (95 % CI: 14.69–37.04) in the SLNB group and 22.30 ± 2.44 months (95 % CI: 17.50–27.10) in the ALND group (log-rank p=0.65) (Figures 1-A, 2-A).

In univariate Cox regression analysis, factors significantly associated with RFS included Ki-67 level (HR=2.41; 95 % CI: 1.15–5.02; p=0.019), tumor grade (HR=2.03; 95 % CI: 1.22–3.37; p=0.006), preoperative tumor size (HR=1.01; 95 % CI: 1.01–1.02; p=0.003), and presence of lymphovascular invasion (LVI) (HR=0.66; 95 % CI: 0.44–0.99; p=0.047) (Table 3). However, multivariate Cox regression analysis did not identify any independent prognostic factor for RFS (p>0.05) (Table 4).

Table 2. Patient and tumor characteristics of breast cancer patients receiving neoadjuvant chemotherapy according to type of surgery.

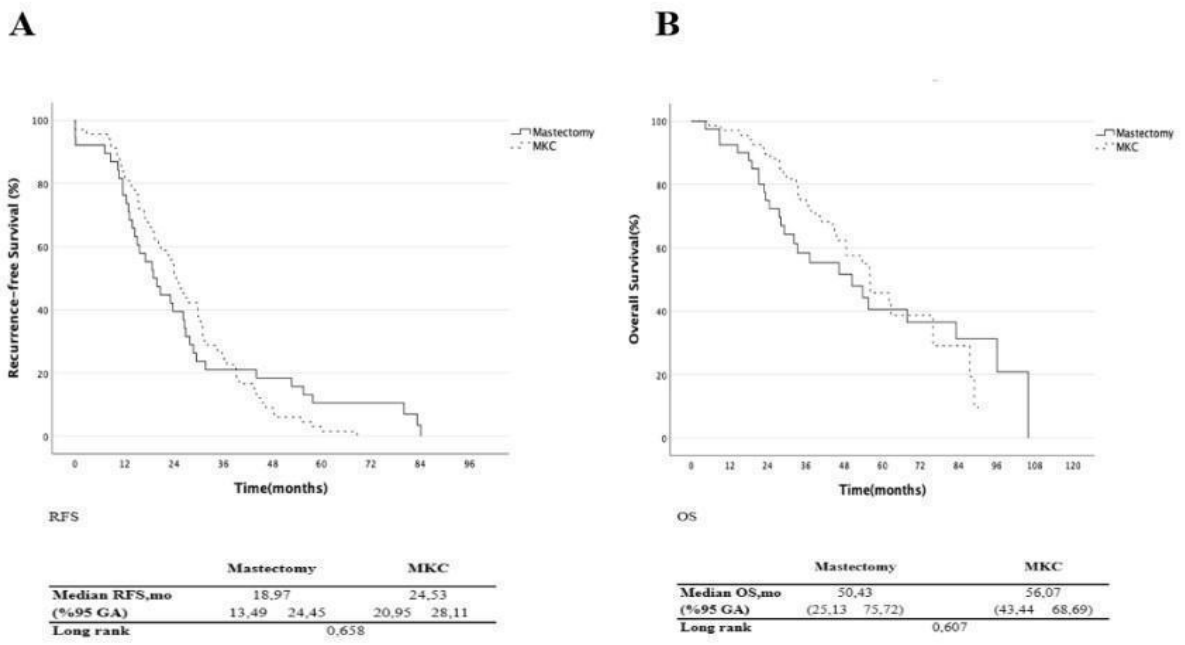
		Primary surgical management				Total (n:108)		*p*	
		Mastectomy(n:40)		BCS (n:68)					
		n	%	n	%	n	%		
Age of diagnosis(y)	<40	6	15%	16	24%	22	20%	0.29	x²
	≥40	34	85%	52	76%	86	80%		
Axillary surgery Type	SLNB	3	8%	15	22%	18	17%	***0.05***	x²
	ALND	37	93%	53	78%	90	84%		
Molecular Subtype	Hormone positive her2 negative	21	53%	35	51%	56	52%	0.83	x²
	Her2 positive	12	30%	18	26%	30	28%		
	Triple negative	7	18%	15	22%	22	20%		
Histologic Type	Ductal	35	88%	60	88%	95	88%	0.91	x²
	Other	5	13%	8	12%	13	12%		
PgR Status. n (%)	Negative	21	53%	25	37%	46	43%	0.11	x²
	Positive	19	48%	43	63%	62	57%		
ER Status	<10	14	35%	22	32%	36	33%	0.78	x²
	≥10	26	65%	46	68%	72	67%		
Ki67	<18	7	18%	4	6%	11	10%	0.05	x²
	≥18	33	83%	64	94%	97	90%		
HER2 Status	Negative	27	68%	49	72%	76	70%	0.76	x²
	Positive	12	30%	19	28%	31	29%		
Grade	<3	25	63%	42	62%	67	62%	0.94	x²
	3	15	38%	26	38%	41	38%		
Preop-Tumor Size	<2cm	8	20%	10	15%	18	17%	0.39	x²
	≥ 2cm	29	73%	57	84%	86	80%		
	missing	3	8%	1	1%	4	4%		
Clinical Axiller Status	Negative	4	10%	10	15%	14	13%	0.51	x²
	Positive	35	88%	58	85%	93	86%		
	missing	1	3%	0	0%	1	1%		
LVI	Negative	14	35%	34	50%	48	44%	0.13	x²
	Positive	26	65%	34	50%	60	56%		
PNI	Negative	21	53%	32	47%	53	49%	0.42	x²
	Positive	16	40%	34	50%	50	46%		
	missing	3	8%	2	3%	5	5%		
pCR	Yes	2	5%	5	7%	7	6%	0.63	x²
	No	38	95%	63	93%	101	94%		

x² = Ki-kare test

Overall survival (OS) analysis

No significant association was found between surgery type (mastectomy vs. BCS) and OS (log-rank p=0.607), with 3-year and 5-year survival rates of 73% vs. 55% and 42% vs. 40% for mastectomy vs. BCS, respectively. However, OS differed significantly between axillary surgery groups, with patients undergoing axillary lymph node dissection (ALND) exhibiting worse OS compared to those who underwent sentinel lymph node biopsy (SLNB; log-rank p=0.019), as evidenced by 3-year and 5-year survival rates of 64% vs. 87% and 36% vs. 50% for ALND vs. SLNB, respectively.

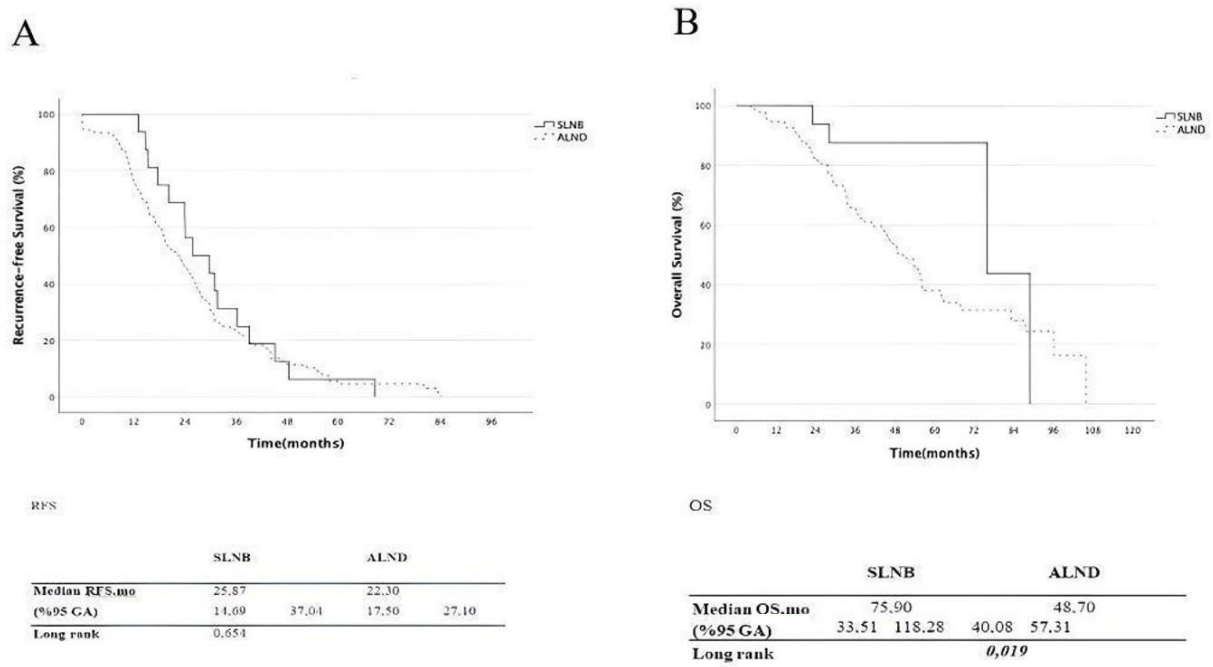
The median OS for all patients was 55.57 months (95% CI: 48.40–62.73). For BCS patients, mOS was 56.07 ± 6.44 months (95 % CI: 43.44–68.69), while it was 50.43 ± 12.90 months (95 % CI: 25.13–75.72) for mastectomy patients. For axillary surgery,, mOS was 75.90 ± 21.62 months (95 % CI: 33.51–118.28) in the SLNB group and 48.70 ± 4.39 months (95 % CI: 40.08–57.31) in the ALND group (log-rank *p*=0.019) (Figures 1-B, 2-B).



	Mastectomy		MKC	
Median RFS,mo	18,97		24,53	
(%95 GA)	13,49	24,45	20,95	28,11
Long rank	0,658			

	Mastectomy		MKC	
Median OS,mo	50,43		56,07	
(%95 GA)	(25,13	75,72)	(43,44	68,69)
Long rank	0,607			

Figure 1. Recurrence-free survival analysis and overall survival analysis by surgery type.



	SLNB		ALND	
Median RFS,mo	25,87		22,30	
(%95 GA)	14,69	37,04	17,50	27,10
Long rank	0,654			

	SLNB		ALND	
Median OS,mo	75,90		48,70	
(%95 GA)	33,51	118,28	40,08	57,31
Long rank	*0,019*			

Figure 2. Recurrence-free survival analysis and overall survival analysis by axillary surgery type.

In univariate analysis, significant factors associated with worse OS included molecular subtype (HR=1.84; 95% CI: 1.33–2.55; p<0.001), indicating increased risk across more aggressive subtypes (hormone receptor-positive/Her2-negative as reference, followed by Her2-positive, and triple-negative as highest risk), and tumor grade (HR=2.45; 95% CI: 1.19–5.02; p=0.015), reflecting higher hazard for advanced grades. Protective factors included positive estrogen receptor (ER) status (HR=0.46; 95% CI: 0.27–0.77; p=0.003) and positive progesterone receptor (PR) status (HR=0.45; 95% CI: 0.27–0.77; p=0.003), both indicating reduced hazard compared to negative status (Table 3).

Multivariate Cox regression identified molecular subtype (HR=2.12; 95% CI: 1.51–2.96; *p*<0.001), signifying a more than twofold increased hazard for progressively aggressive subtypes, and axillary surgery type (HR=4.41 for ALND vs. SLNB; 95% CI: 1.57–12.40; *p*=0.005), indicating a 4.41-fold higher hazard of death with ALND, as independent prognostic indicators for OS (Table 4).

Tablo 3. Univariate analyses of factors for survival times.

Variable	Category	Recurrence-Free Survival (RFS)		Overall Survival (OS)	
		HR (95% CI)	*p*	HR (95% CI)	*p*
Clinicopathologic Caracters					
Age	<40/≥40	0.90(0.73-1.12)	0.356	1.03(0.78-1.36)	0.821
Breast-Surgery Type	BCS/Mastectomy	1.08(0.71-1.64)	0.722	0.87(0.50-1.50)	0.611
Axillary surgery Type	SLNB/ALND	1.03(0.62-1.70)	0.924	3.40(1.23-9.41)	***0.018***
Molecular Subtype	A/B/C*	1.26(0.99-1.62)	0.062	1.84(1.33-2.55)	***<0.001***
Histologic Type	Ductal/Others	1.39(0.77-2.50)	0.278	1.16(0.53-2.56)	0.714
PgR Status	Negative/Positive	0.81(0.54-1.20)	0.292	0.45(0.27-0.77)	***0.003***
ER Status	<10/≥10	1.0(0.99-1.00)	0.306	0.46(0.27-0.77)	***0.003***
Ki67	<18/≥18	2.41(1.15-5.02)	***0.019***	2.18(0.86-5.55)	0.102
HER2 Status	Negative/Positive	1.02(0.88-1.18)	0.776	0.97(0.80-1.18)	0.753
Grade	<3/3	2.03(1.22-3.37)	***0.006***	2.45(1.19-5.02)	***0.015***
Preop-Tumor Size	<2cm/≥ 2cm	1.01(1.01-1.02)	***0.003***	1.25(0.62-2.51)	0.538
Clinical Axiller Status	Negative/Positive	1.0(0.56-1.79)	0.998	0.75(0.37-1.53)	0.429
LVI	Negative/Positive	0.66(0.44-0.99)	***0.047***	0.66(0.39-1.12)	0.124
PNI	Negative/Positive	1.29(0.87-1.93)	0.209	1.33(0.77-2.30)	0.302
pCR	No/Yes	1.43(0.66-3.01)	0.361	1.65(0.51-5.29)	0.400

*A: Hormone positive her2 negative. B: Her2 positive. C: Triple negative

Tablo 4. Multivariate analyses of factors for survival times.

Variable	Category	Overall Survival (OS)	
		HR (95% CI)	*p*
Molecular Subtype	A/B/C*	2.12(1.51-2.96)	***<0.001***
Axillary surgery Type	SLNB/ALND	4.41(1.57-12.40)	***0.005***

*A: Hormone positive her2 negative. B: Her2 positive. C: Triple negative

Discussion

This study sought to evaluate the impact of varying surgical approaches on survival outcomes in breast cancer patients treated with NACT. In our cohort, over 60% of patients underwent BCS, a proportion notably higher than those reported in prior studies from diverse regions. For example, an Indian study documented a BCS rate of 37.6%, a Turkish study reported 41.0%, and a US study indicated 44.4%.[9–11] These variations may be attributed to differences in healthcare infrastructure, cultural attitudes, patient preferences, and surgical decision-making practices.

Our findings revealed no statistically significant differences in RFS or OS between patients undergoing BCS and those receiving mastectomy, consistent with results from prior studies.[12–14] Although BCS is a technically demanding procedure with a potential benefit in reducing local recurrence, the lack of survival advantage over mastectomy may be explained by the routine use of postoperative radiotherapy (RT), which enhances local disease control following BCS.[15] It is well established that pathological response to neoadjuvant chemotherapy, particularly pathological complete response (pCR), strongly influences long-term outcomes. However, because our study included only patients who developed recurrence after NACT, individuals achieving pCR were inherently underrepresented, minimizing the potential confounding effect of treatment response. Moreover, molecular subtype distribution was similar across surgical groups, supporting that the observed survival outcomes primarily reflect surgical and biological factors within this recurrence-only cohort.

Among the variables evaluated in terms of their prognostic relationship with RFS, significant correlations were found between lymphovascular invasion (LVI), Ki-67 proliferation index, tumor grade, and preoperative tumor size. These histopathological features emphasize that the biology of the tumor has a more significant impact than the surgical method applied.[16] Nevertheless, a retrospective single-center investigation indicated that while LVI was associated with disease-free survival and overall survival (OS), it did not emerge as an independent predictor.[17] Moreover, elevated Ki-67 expression, indicative of heightened

tumor cell proliferation, has been consistently correlated with increased risks of early recurrence across several meta-analyses.[18] Consequently, our results advocate for the integration of biological markers such as LVI and Ki-67 into surgical decision-making and treatment planning.

In comparing sentinel lymph node biopsy (SLNB) with axillary lymph node dissection (ALND), no significant differences were observed in recurrence-free survival (RFS) between the groups; however, overall survival (OS) was markedly diminished in patients undergoing ALND. Prior investigations have yielded inconsistent findings on this matter. While certain studies reported no disparities in OS or RFS[19,20], others indicated inferior outcomes linked to ALND.[14] For example, Ling et al. determined that ALND conferred no further diminution in local recurrence relative to SLNB and failed to enhance survival metrics.[21] Analogously, contemporary data imply that ALND is predominantly employed in cases involving high-risk pathology or extensive tumor burden.[14] The association between ALND and poorer OS in our study may reflect the advanced disease stage or unfavorable tumor characteristics in patients selected for ALND. Of particular note, randomized controlled trials, including ACOSOG Z0011 and AMAROS, have substantiated that SLNB yields comparable survival outcomes to ALND in suitable candidates, while mitigating postoperative morbidities such as lymphedema.[19,20] Accordingly, axillary surgical decisions ought to incorporate both clinical parameters and tumor biological profiles to optimize patient prognoses.

Limitations

The limitations of our research include its retrospective design, single-center setting, and the limited number of patients who developed recurrence, potentially affecting generalizability. Consequently, larger-scale, multicenter, prospective studies are warranted to validate these findings. Another limitation is the inability to perform a detailed analysis of pre- and post-NACT axillary nodal response, which should be further evaluated in future studies.

The absence of detailed pathological response metrics, including pathological complete response (pCR) and Residual Cancer Burden (RCB) scores, represents a limitation of this study, and future prospective research with larger sample sizes should incorporate these variables to more comprehensively evaluate the interaction between NACT response and surgical outcomes. Another limitation is that combined breast–axillary surgical subgroup analysis could not be conducted due to insufficient sample sizes, and future studies with larger cohorts should evaluate the long-term outcomes of specific surgical combinations.

Finally, the heterogeneity of adjuvant hormone therapy regimens and the inability to analyze their differential impact in detail constitute another important limitation. Future prospective studies with larger cohorts should further investigate the long-term effects of various hormone therapy strategies.

Conclusion

In summary, breast-conserving surgery with radiotherapy and mastectomy provide equivalent recurrence-free and overall survival outcomes in breast cancer patients who recurred following neoadjuvant chemotherapy. Sentinel lymph node biopsy confers superior overall survival compared to axillary lymph node dissection, despite similar recurrence-free survival. Molecular subtype and axillary surgery type represent independent prognostic factors for overall survival, underscoring the primacy of tumor biology over surgical radicality. These findings advocate for individualized surgical planning and necessitate prospective validation to optimize therapeutic strategies.

Ethics Committee Approval

This study, conducted in accordance with the Declaration of Helsinki, was approved by the local Institutional Ethics Committee on 2024-10-30 with approval number 2024-292-10.20.

Author Contributions

Concept and design: O.Yalıcı. Administrative support: O.Yalıcı. Data collection and integration: all authors. Data

analysis and interpretation O.Yalıcı. Writing of the paper: all authors. Final approval of the paper: all authors. Responsible for all aspects of the work: all authors.

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Conflict of Interest

The authors declare that there is no conflict of interest for this article.

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References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229-263. doi:10.3322/caac.21834
2. Fisher B, Jeong JH, Anderson S, et al. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. *N Engl J Med*. 2002;347(8):567-575. doi:10.1056/NEJMoa020128
3. Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. *JAMA*. 2011;305(6):569-575. doi:10.1001/jama.2011.90
4. Zwakman M, Tan A, Boersma C, et al. Long-term quality of life and aesthetic outcomes after breast conserving surgery in patients with breast cancer. *Eur J Surg Oncol*. 2022;48(8):1692-1698. doi:10.1016/j.ejso.2022.03.001
5. Rajan KK, Fairhurst K, Birkbeck B, et al. Overall survival after mastectomy versus breast-conserving surgery with adjuvant radiotherapy for early-stage breast cancer: meta-analysis. *BJS Open*. 2024;8(3):zrae040. doi:10.1093/bjsopen/zrae040
6. Vila J, Mittendorf EA, Farante G, et al. Nomograms for predicting axillary response to neoadjuvant chemotherapy in clinically node-positive patients with breast cancer. *Ann Surg Oncol*. 2017;24(7):1941-1947. doi:10.1245/s10434-017-5791-6
7. Ahn JH, Choi SB, Park JM, et al. Level of combined estrogen and progesterone receptor expression determines the eligibility for adjuvant endocrine therapy in breast cancer patients. *Cancers (Basel)*. 2021;13(19):5007. doi:10.3390/cancers13195007
8. Liu YL, Saraf A, Lee SM, et al. Lymphovascular invasion is an independent predictor of survival in breast cancer after neoadjuvant chemotherapy. *Breast Cancer Res Treat*. 2016;157(3):555-564. doi:10.1007/s10549-016-3836-9
9. Al-Gaithy ZK, Yaghmoor BE, Koumu MI, et al. Trends of mastectomy and breast-conserving surgery and related factors in female breast cancer patients treated at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, 2009-2017: a retrospective cohort study. *Ann Med Surg (Lond)*. 2019;41:47-52. doi:10.1016/j.amsu.2019.03.012
10. Çiftci F. The role of breast-conserving surgery in the treatment of early-stage breast cancer. *Dicle Med J*. 2020;47(4):852-858. doi:10.5798/dicletip.850178
11. Liu J, Zheng X, Lin S, Han H, Xu C. Breast conserving therapy for central breast cancer in the United States. *BMC Surg*. 2022;22(1):31. doi:10.1186/s12893-022-01481-0
12. Fisher B, Bryant J, Wolmark N, et al. Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. *J Clin Oncol*. 1998;16(8):2672-2685. doi:10.1200/JCO.1998.16.8.2672
13. van der Hage JA, van de Velde CJ, Julien JP, et al. Preoperative chemotherapy in primary operable breast cancer: results from the European Organization for Research and Treatment of Cancer trial 10902. *J Clin Oncol*. 2001;19(22):4224-4237. doi:10.1200/JCO.2001.19.22.4224
14. Cavalcante FP, Zerwes FP, Alcantara R, et al. Oncological outcomes of breast-conserving surgery versus mastectomy following neoadjuvant chemotherapy in a contemporary multicenter cohort. *Sci Rep*. 2025;15(1):9032. doi:10.1038/s41598-025-59542-2
15. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Darby S, McGale P, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet*. 2011;378(9804):1707-1716. doi:10.1016/S0140-6736(11)61629-2
16. Schoppmann SF, Bayer G, Aumayr K, et al; Austrian Breast and Colorectal Cancer Study Group. Prognostic value of lymphangiogenesis and lymphovascular invasion in invasive breast cancer. *Ann Surg*. 2004;240(2):306-312. doi:10.1097/01.sla.0000133355.48672.22
17. Cavdar E, Iriagac Y, Karaboyun K, Avci O. Prognostic role of lymphovascular invasion and perineural invasion in breast cancer treated with neoadjuvant chemotherapy. *UHOD*. 2022;32(3):141-149. doi:10.4999/uhod.226300
18. Inwald EC, Klinkhammer-Schalke M, Hofstädter F, et al. Ki-67 is a prognostic parameter in breast cancer patients: results of a large population-based cohort of a cancer registry. *Breast Cancer Res Treat*. 2013;139(2):539-552. doi:10.1007/s10549-013-2560-8
19. Giuliano AE, Ballman KV, McCall L, et al. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the ACOSOG Z0011 (Alliance) randomized clinical trial. *JAMA*. 2017;317(16):1667-1676. doi:10.1001/jama.2017.2836
20. Donker M, van Tienhoven G, Straver ME, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol*. 2014;15(12):1303-1310. doi:10.1016/S1470-2045(14)70444-8
21. Ling DC, Iarrobino NA, Champ CE, Soran A, Beriwal S. Regional recurrence rates with or without complete axillary dissection for breast cancer patients with node-positive disease on sentinel lymph node biopsy after neoadjuvant chemotherapy. *Adv Radiat Oncol*. 2020;5(2):163-170. doi:10.1016/j.adro.2019.09.006