Prognostic Impact of Surgical Margin Status on Overall Survival of Patients with Early Breast Cancer: A Retrospective Analysis from the Department for Women's Medicine at Charité – University Hospital Berlin

Prognostische Auswirkung des Schnittrand-Status auf das Gesamtüberleben von Patientinnen mit Brustkrebs im Frühstadium: eine retrospektive Analyse aus der Abteilung für Frauenheilkunde an der Charité – Universitätsmedizin Berlin

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ABSTRACT

Introduction

The impact of surgical margins on the prognosis of early breast cancer remains uncertain, particularly in the context of modern treatment approaches. This study aimed to investigate whether involved margins after surgery for early breast cancer affect overall survival.

Methods

We conducted a retrospective analysis of 3767 patients who underwent surgery for primary breast cancer or carcinoma in situ between 2006 and 2022 at Charité – University Hospital Berlin. Survival analysis based on margin status and a subsequent multivariate Cox regression analysis were conducted.

Results

With a median follow-up of 72.2 months, clear margins were achieved in 81.4% of patients (n = 3068) after primary surgery, while 16.2% (n = 610) required re-excision. Only 2.4% of patients (n = 89) had definitively involved margins. Margin involvement was more common in hormone receptor-positive disease, lobular subtype, carcinoma in situ, or locally advanced tumors, but less frequent in patients with previous neoadjuvant chemotherapy or triple-negative breast cancer. The Kaplan–Meier survival curves showed a significant separation with worse outcomes for patients with definitive R1 resections. However, the multivariate Cox regression analysis detected no statistically significant difference in overall survival based on margin status. Breast conserving surgery (HR 0.66; 95% CI 0.54–0.81) and HER2 overexpression (HR 0.65; 95% CI 0.48–0.89) were associated with improved survival.

Conclusion

Patients who underwent breast-conserving surgery in our study demonstrated favorable outcomes compared to patients after mastectomy. Although margin status did not significantly affect overall survival, larger multicenter studies are needed to evaluate the prognostic implications of margin involvement in breast cancer treatment in different tumor stages, tumor subtypes and local and systemic treatments.

ZUSAMMENFASSUNG

Einleitung

Die Auswirkung des Schnittrand-Status auf die Prognose von Brustkrebs im Frühstadium ist immer noch unklar, insbesondere in Rahmen moderner Behandlungsansätze. Ziel der Studie war es, zu untersuchen, wie sich positive Schnittränder nach einer Operation zur Behandlung vom Mammakarzinom im Frühstadium auf das Gesamtüberleben auswirken.

Methoden

Es wurde eine retrospektive Analyse von 3767 Patientinnen, die wegen primärem Brustkrebs oder Carcinoma in situ zwischen 2006 und 2022 in der Charité – Universitätsmedizin Berlin operiert wurden, durchgeführt. Dazu wurde eine Überlebensanalyse hinsichtlich des Schnittrand-Status sowie eine multivariate Cox-Regressionsanalyse durchgeführt.

Ergebnisse

Die mediane Verlaufskontrolle betrug 72,2 Monate. Bei 81,4% der Patientinnen (n = 3068) waren die Schnittränder nach der primären Operation negativ, wohingegen 16,2% (n = 610) der Patientinnen eine Nachexzision benötigten. Nur 2,4% der Patientinnen (n = 89) hatten definitiv befallene Schnittränder. Befallene Schnittränder traten häufiger in Verbindung mit hormonrezeptorpositiver Erkrankung, lobulärem Subtyp, Carcinoma in situ oder lokal fortgeschrittenen Tumoren auf und weniger oft bei Patientinnen nach vorheriger neoadjuvanter Chemotherapie oder triple-negativem Mammakarzinom. Die Kaplan-Meier-Überlebenskurven zeigten deutliche Unterschiede und schlechtere Outcomes bei Patientinnen mit definitiver R1-Resektion. Dagegen ermittelte die multivariate Cox-Regressionsanalyse keinen statistisch signifikanten Unterschied im Gesamtüberleben basierend auf den Schnittrand-Status. Eine brusterhaltende Therapie (HR 0,66; 95%-KI 0,54–0,81) sowie HER2-Überexpression (HR 0.65; 95%-KI 0,48–0,89) waren mit einem besseren Überleben assoziiert.

Schlussfolgerung

Patientinnen, die sich in unserer Studie einer brusterhaltenden Operation unterzogen hatten, wiesen bessere Outcomes auf als Patientinnen nach einer Mastektomie. Obwohl der Schnittrand-Status keine signifikante Auswirkung auf das Gesamtüberleben hatte, werden große multizentrische Studien benötigt, um die prognostischen Auswirkungen von negativen Schnitträndern nach einer Brustkrebstherapie hinsichtlich verschiedener Tumorstadien, Tumor-Subtypen und lokalen bzw. systemischen Behandlungen zu evaluieren.

Introduction

Breast cancer remains the most prevalent malignancy among women worldwide and continues to be the leading cause of cancer-related mortality in women [1]. The implementation of effective screening programs has markedly increased the detection of early-stage breast cancer [2]. For the treatment of early breast cancer and ductal carcinoma in situ, breast-conserving surgery is widely regarded as the surgical modality of choice due to its oncologic safety, the preservation of breast tissue and favorable oncoplastic outcomes [3]. Nevertheless, mastectomy, with or without reconstruction, is still performed in up to 27% of patients with early breast cancer in Germany due to various clinical considerations, including patient preference, tumor characteristics, and genetic predispositions [4]. According to current guidelines, surgical margins for invasive carcinoma must be free of tumor cells ("no ink on tumor"), while a minimum margin of 2 mm is recommended for pure carcinoma in situ [3, 5]. These guidelines are based on evidence linking involved margins to higher rates of local recurrence [6] and an increased risk of distant recurrence [7]. Reported rates of margin involvement after breast-conserving surgery and oncoplastic surgery vary considerably across the literature, ranging from 3% to 20% in most studies [8, 9, 10, 11]. As a result, re-excision rates after breast-conserving surgery are nowadays considered as a key quality indicator in breast cancer treatment [12]. To minimize the risk of margin involvement, a range of intraoperative diagnostic techniques are utilized, including intraoperative margin assessment [13], intraoperative ultrasound [14] or intraoperative specimen radiography [15, 16].

In recent decades, the therapeutic landscape for early breast cancer has seen significant advancements [17]. There is a paucity of recent data on the impact of involved surgical margins on overall survival, with much of the existing evidence derived from older retrospective studies [18, 19, 20]. Given the complexity of modern multimodal therapeutic strategies, the impact of margin involvement on long-term outcomes remains unclear. This single-center retrospective analysis of prospective collected patient data seeks to determine the effect of involved margins on overall survival.

Methods

Objectives and end points

We conducted a retrospective analysis in the interdisciplinary breast center of the Charité – University Hospital Berlin to determine the prognostic impact of involved margins after surgery for early breast cancer.

Patients and data collection

The analysis included data of patients who underwent breast surgery for primary invasive carcinoma or carcinoma in situ at the breast center of Charité University Hospital in Berlin, with a documented margin status, follow-up and survival status. The study period extended from January 2006 to December 2022. Patients without known date of death were required to have a minimum follow-up of 6 months. Follow-up data on patient survival were obtained from the respective German residents' registration office ("Einwohnermeldeamt"). There were no restrictions on the histologic subtype, type, or extent of surgery. Surgical procedures included breast-conserving techniques, skin- or nipple-sparing mastectomy, and total mastectomy. Patients with secondary malignancies or multiple breast malignancies were excluded from this analysis. Patient characteristics and information about the disease and treatment specifics were retrospectively collected from the electronic medical records (EMR).

The present study was approved by the local ethics committee of the Charité – Universitätsmedizin Berlin.

Data analysis

Statistical analyses were conducted using IBM SPSS Statistics (version 29.0.0, IBM Corp., USA) and GraphPad Prism (version 10.2.2, GraphPad Software Inc., USA). The significance level for all tests was set at alpha < 0.05, with significance thresholds of * < 0.05, ** < 0.01, *** < 0.001, and **** < 0.0001. No adjustments were made for multiple comparisons. Data is presented as mean with standard deviation, median with interquartile range, or absolute and relative frequencies, depending on scale.

Subgroup analyses were conducted based on margin status, categorizing patients into those with clear surgical margins after primary surgery (primary R0), clear margins after additional secondary surgery (secondary R0), and definitive margin involvement after completed surgical treatment. Further stratifications were made for patients with hormone receptor-positive disease (defined by the expression of estrogen and/or progesterone receptors), HER2 overexpressing disease (determined by immunohistochemical staining with a score of 3+, or 2+ with positive in-situ hybridization), triple-negative disease (estrogen and progesterone receptor expression below 10 % and HER2 overexpression), type of surgery, tumor size, tumor grading, histologic subtype, nodal involvement and history of neoadjuvant treatment.

Group differences were assessed using one-way ANOVA with post-hoc Tukey multiple comparison tests. Survival analyses were limited to patients with invasive breast cancer and complete datasets. Overall survival was estimated using the Kaplan–Meier method, and differences between the respective Kaplan–Meier curves were assessed using log-rank testing. Hazard ratios were calculated using a stratified multivariate Cox regression model.

Results

Clinical characteristics

A total of 3767 patients were included in this retrospective analysis, with a median follow-up of 72.2 months. In most cases (81.4 %, n = 3068), clear margins were achieved after primary surgery, while 16.2 % (n = 610) required re-excision to obtain clear margins. A small percentage of patients (2.4 %, n = 89) had definitively involved margins after the completion of surgical therapy. Most patients (90.9 %, n = 3426) were treated for invasive breast cancer of no specific type (NST). The majority (78.0 %, n = 2938) had hormone receptor-positive disease, 11.7 % (n = 442) had HER2 overexpressing tumors, and 17.7 % (n = 668) were treated for triple-negative breast cancer. Approximately two thirds of the patients underwent breast-conserving surgery (69.1 %, n = 2604). For a detailed overview of the patients' characteristics, please refer to ▶ **Table 1**.

Patients were divided in three subgroups: The first group included patients with clear surgical margins after the initial surgery, categorized as primary R0 (resection). The second group consisted of patients whose initial surgery revealed involved margins but who achieved clear margins after secondary surgery, categorized as secondary R0 (resection). The third group comprised patients who had involved margins after the completion of all surgical treatments, with or without additional surgeries, categorized as definitive R1. Clinical characteristics for the three subgroups are displayed in ▶ **Table 1**.

Clinical differences between margin status subgroups

The patients' ages did not differ significantly between the respective margin subgroups. Patients with primary R0 resection were significantly more often treated for invasive carcinoma (91.9 %, n = 2820) compared to patients with secondary R0 resection (Δ = 4.5 %; 87.4 %, n = 533; p = 0.001) or definitive R1 resection (Δ = 9.9 %; 82.0 %, n = 73; p = 0.004) (▶ **Fig. 1**). The latter subgroups, conversely, were treated more frequently for carcinoma in situ. There was no significant difference in mastectomy rates between secondary R0 resection and definitive R1 resection. Breast-conserving surgery was more common among patients with primary R0 resection (70.6 %, n = 2166), while mastectomy was more frequent among patients with secondary R0 resection (Δ = 7.3 % for BCS; 63.3 %, n = 386; p = 0.0009) or definitive R1 resection (Δ = 12.2 % for BCS; 58.4 %, n = 52; p = 0.0361). Patients with primary R0 resection were significantly more likely to have received neoadjuvant treatment (20.0 %, n = 615) compared to patients with secondary R0 resection (Δ = 10.2 %; 9.8 %, n = 60; p < 0.001) or definitive R1 resection (Δ = 2.1 %; 7.9 %, n = 7; p = 0.009) (▶ **Fig. 1**). For detailed information on the clinical characteristics of the respective subgroups, please refer to ▶ **Table 1**.

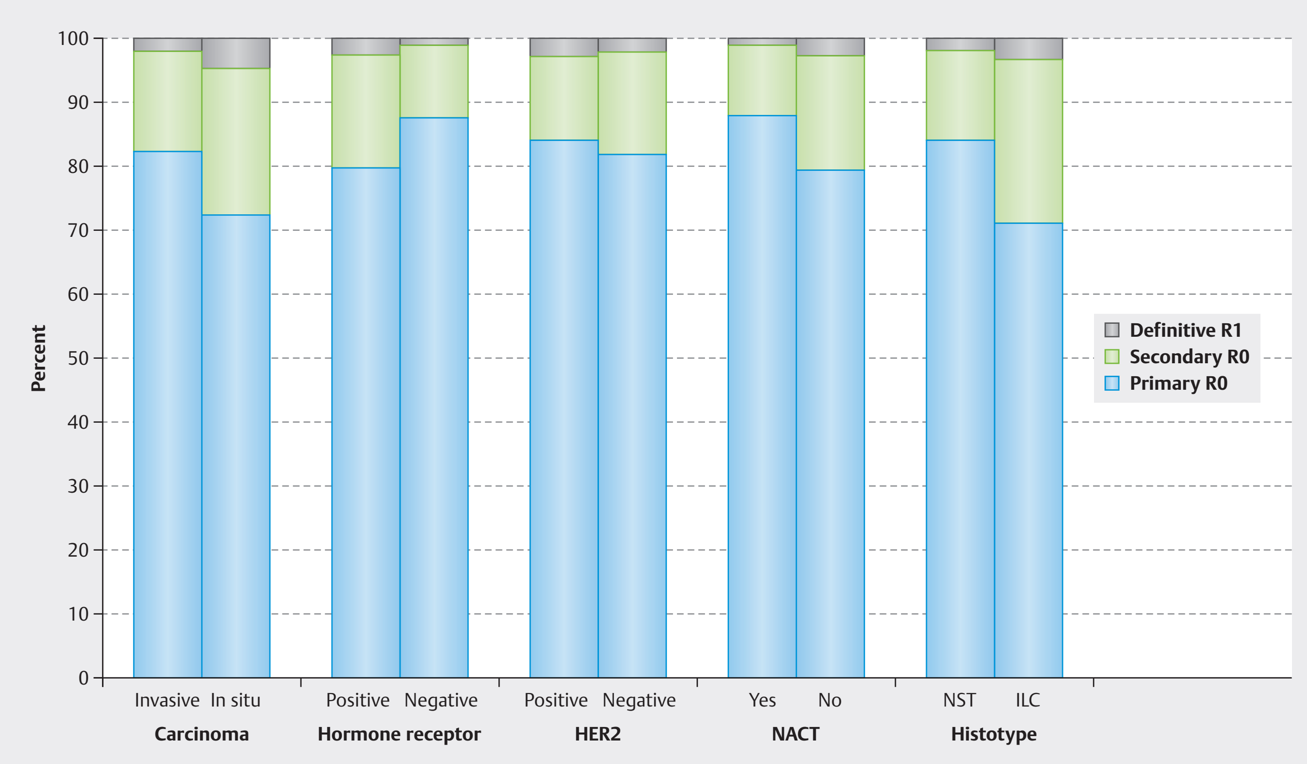
▶Table 1 Patient's characteristics for the overall population and the respective subgroups: primary R0 resection, secondary R0 resection, definitive R1 resection. If not indicated otherwise data is presented as number (percentage).

Patient's characteristics		Primary R0 (n = 3068)	Secondary R0 (n = 610)	Definitive R1 (n = 89)	Overall (n = 3767)
Age (years) [Mean (SD)]		57.5 (13.1)	57.0 (12.4)	60.1 (14.9)	57.5 (13.1)
Invasive disease	Invasive	2820 (91.9)	533 (87.4)	73 (82.0)	3426 (90.9)
	Carcinoma in Situ	248 (8.1)	77 (12.6)	16 (18.0)	341 (9.1)
Histotype	NST (ductal)	2389 (77.9)	393 (64.4)	57 (64.0)	2839 (75.4)
	Lobular	316 (10.3)	113 (18.5)	15 (16.9)	444 (143)
	Other	115 (3.7)	27 (4.4)	1 (1.1)	143 (3.8)
Tumor size (TNM)	pT1	1391 (45.3)	232 (38.0)	22 (24.7)	1645 (43.7)
	pT2	899 (29.3)	209 (34.3)	31 (34.8)	1139 (30.2)
	pT3	150 (4.9)	79 (13.0)	14 (15.7)	243 (6.5)
	pT4	39 (1.3)	2 (0.3)	6 (6.7)	47 (1.2)
Nodal involvement	yes	778 (26.3)	209 (34.3)	32 (36.0)	1019 (27.1)
Grading	G1	475 (15.5)	93 (15.2)	15 (16.9)	583 (15.5)
	G2	1478 (48.2)	350 (57.4)	47.2 (42)	1870 (49.6)
	G3	808 (26.3)	119 (19.3)	23 (25.8)	949 (25.2)
	Gx	307 (10.0)	49 (8.0)	9 (10.1)	365 (9.7)
Hormone receptor	Positive	2346 (76.5)	515 (84.4)	77 (86.5)	2938 (78.0)
	Negative	615 (20.0)	79 (13.0)	8 (9.0)	702 (18.6)
	Missing	107 (3.5)	16 (2.6)	4 (4.5)	127 (3.4)
HER2	Positive	372 (12.1)	58 (9.5)	12 (13.5)	442 (11.7)
	Negative	2394 (80)	468 (76.7)	61 (68.6)	2923 (75.6)
	Missing	302 (9.8)	84 (13.8)	16 (18.0)	402 (10.7)
TNBC	Yes	584 (19.0)	76 (12.5)	8 (9.0)	668 (17.7)
NACT	Yes	615 (20.0)	60 (9.8)	7 (7.9)	682 (18.1)
Type of Surgery	BCS	2166 (70.6)	386 (63.3)	52 (58.4)	2604 (69.1)
	Mastectomy	902 (29.4)	224 (36.7)	37 (41.6)	1163 (30.9)
OS (months)	Median [IQR]	63.5 [3.00, 211]	65.2 [3.00, 174]	58.6 [5.10, 181]	63.7 [3.00, 211]

BCS = Breast Conserving Surgery; IQR = Interquartile Range; NACT = Neoadjuvant Chemotherapy; NST = No Special Type; OS = Overall Survival; SD = Standard deviation; TNBC = Triple-Negative Breast Cancer

Hormone receptor-positive tumors were less frequently observed in patients with primary R0 resection (76.5 %, n = 2346) compared to individuals with secondary R0 resection (Δ = 7.9 %; 84.4 %, n = 515; $p < 0.0001$) or definitive R1 resection (Δ = 10.0 %; 86.5 %, n = 77; p = 0.0237) (▶ **Fig. 1**). In contrast for triple-negative breast cancer primary R0 resections were more frequently reported (19.0 %, n = 584; vs. secondary R0 resection [Δ = 6.5 %; 12.5 %, n = 76; p = 0.0002] and definitive R1 resection [Δ = 10.0 %; 9.0 %, n = 8; p = 0.0396]) (▶ **Fig. 1**). No significant differences were found between the subgroups regarding HER2 expression (▶ **Fig. 1**).

Lobular carcinomas were more frequently observed in patients with secondary R0 (18.5 %, n = 113) resection compared to those with primary R0 resection (Δ = 8.2 %; 10.3 %, n = 316; $p < 0.001$). However, no significant differences were observed for patients with definitive R1 resection. Compared to patients who achieved clear margins after primary surgery, significantly larger tumors and higher tumor stages were observed in patients with secondary R0 resection ($p < 0.001$). Additionally, cases with definitively involved margins showed significantly higher tumor stages compared to patients with primary R0 resection ($p < 0.001$) or secondary R0 resection ($p < 0.001$). Nodal involvement was more frequently observed in cases of secondary R0 resection (Δ = 8.1 %; 34.3 %, n = 209; $p < 0.001$) or definitive R1 resection (Δ = 9.7 %; 36.0 %, n = 32; p = 0.044) compared to patients with primary R0 resection (26.3 %, n = 778).



▶ **Fig. 1** Margin involvement displayed for tumor type, hormone receptor status, HER2 status, neoadjuvant chemotherapy and type of surgery in percentage. Margin involvement is color coded: Blue: free margins after primary surgery (Primary R0); Green: free margins after primary surgery (Secondary R0); Grey: definitively involved margins (Definitive R1). Corresponding actual numbers and percentages are displayed in ▶ **Table 1**. ILC = Invasive Lobular breast Cancer; NACT = Neoadjuvant Chemotherapy; Neg. = Negative; NST = No Special Type; Pos. = Positive.

Overall survival

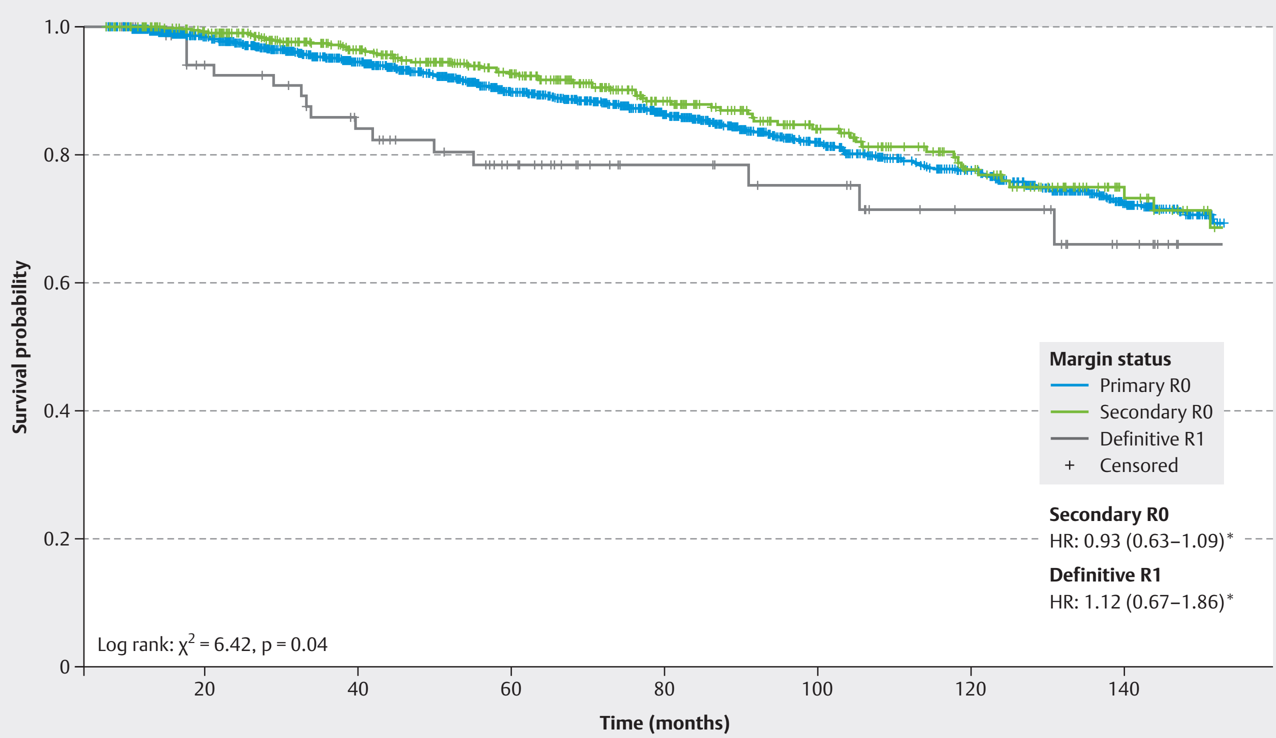
Patients with carcinoma in situ were excluded from the subsequent survival analysis due to the significantly better prognosis of non-invasive lesions. A median overall survival (OS) of 63.0 months (n = 2820) was observed in cases with clear margins after primary surgery, while a median OS of 64.0 months (n = 533) was observed in cases with free margins after secondary surgery. Patients with definitively involved margins experienced a shorter median OS of 57.9 months (n = 73).

Kaplan–Meier curves on overall survival are displayed in ▶ **Fig. 2**. A log-rank test was performed to evaluate possible differences in the Kaplan–Meier estimates for the different margin subgroups. The log-rank test showed significant differences between the respective margin subgroups ($\chi^2 = 6.42$, $p = 0.04$). The pairwise comparison revealed that patients with primary clear margins after both primary ($\chi^2 = 5.60$, $p = 0.018$) and secondary ($\chi^2 = 6.10$, $p = 0.013$) surgery had significantly longer overall survival compared to patients with definitively involved margins.

A multivariate Cox regression analysis on overall survival was applied to test if margin status, age, type of surgery, neoadjuvant chemotherapy, hormone receptor status, HER2 expression, presence of TNBC, tumor grading, tumor size, nodal involvement or histologic subtype could predict overall survival. Detailed results are presented in ▶ **Table 2**. The overall model was statistically significant ($\chi^2 = 479.329$, $p < 0.001$). Margin status had no significant impact on overall survival. In contrast increasing tumor size, nodal involvement, higher tumor grading, increasing age and previous neoadjuvant chemotherapy were associated with adverse overall survival, while breast-conserving surgery, lobular histologic subtype and HER2 overexpression were associated with better survival outcomes.

Discussion

In this single-center retrospective analysis of 3767 patients with a median follow-up of 72.2 months, the impact of surgical margin status on overall survival in breast cancer patients was evaluated. Higher rates of margin involvement were observed in patients with hormone receptor-positive disease, lobular subtype, carcinoma in situ, or locally advanced tumors, while lower rates were detected in patients who had undergone neoadjuvant chemotherapy and in individuals with triple-negative breast cancer. The multivariate survival analysis showed no statistically significant difference in overall survival based on margin status. However, the significant separation of the Kaplan–Meier survival curves suggests that involved margins after completed surgical therapy might be associated with reduced overall survival. Primary and secondary R0 resections appear to be oncologically equivalent. Factors linked to worse outcomes included older age, previous neoadjuvant chemotherapy, increasing tumor size, nodal involvement, and higher tumor grading, whereas breast-conserving surgery, lobular subtype, and HER2 expression were associated with better survival.



▶ **Fig. 2** Kaplan–Meier estimates on overall survival for patients with invasive breast cancer. Tick mark indicate data censored at the last time when the patient was known to be alive. Hazard ratio (HR) and confidence interval were calculated with the use of a multivariate Cox regression model. * Hazard ratios are corrected for age, tumor size, nodal involvement, neoadjuvant surgery, HER2-expression, hormone receptor expression, histologic subtype and type of surgery.

Consistent with previously published reports, hormone receptor-positive tumors, lobular histologic subtype, larger tumor size, nodal involvement and the presence of carcinoma in situ were associated with margin involvement [21, 22, 23]. Other well-known risk factors for margin involvement include mammographic microcalcifications and multifocality [21, 22, 23]. However, these factors were not specifically evaluated in this study. Conversely, patients with triple-negative tumors and previous neoadjuvant treatment exhibited reduced rates of margin involvement. Neoadjuvant chemotherapy was associated with adverse outcomes in our analysis. This could be attributed to the confounding factor that more aggressive tumors with poorer prognosis are treated with neoadjuvant chemotherapy. In contrast, tumors overexpressing HER2 showed a more favorable prognosis. While this may seem surprising given that HER2 overexpression is typically associated with more aggressive tumor behavior, it can be explained by the increased availability of highly effective HER2-directed modern treatment regimens [24].

Our Cox regression analysis revealed that breast-conserving surgery was the most significant predictor of improved overall survival. This could be partly explained by the fact that smaller tumors with a more favorable prognosis are more likely to be treated with breast-conserving surgery. Still, prognosis is mainly driven by tumor biology. Several analyses have shown similar distant and overall survival outcomes for breast-conserving surgery followed by irradiation compared to mastectomy [18, 25, 26]. Some newer analyses even suggest that breast-conserving surgery might be associated with superior survival outcomes [5, 27, 28]. In this context, our analysis underscores the oncologic safety of breast-conserving approaches for the treatment of early breast cancer. The improved outcomes observed in patients who undergo breast conserving surgery compared to mastectomy may largely be attributed to the additional radiotherapy administered to nearly all patients.

The question of whether patients undergoing re-excision due to involved margins experience the same local and distant recurrence rates as patients with primary clear margins remains inconclusive. Some studies suggest similar rates of local and distant recurrence after re-excision with clear margins [29], while others report increased local recurrence rates [30]. In our analysis, similar survival outcomes were found for patients with free margins after primary or secondary surgery. The prognostic impact of margin involvement after completed surgical therapy in the light of modern adjuvant treatment strategies has not been conclusively clarified. A recent meta-analysis demonstrated that involved or close margins after breast-conserving surgery for early breast cancer are not only associated with an increased risk of local recurrence [6] but also of distant recurrence [7]. Likewise, increased rates of local recurrence and distant recurrence have been reported for involved margins after mastectomy [31]. For patients with carcinoma in situ, margin involvement is associated with a higher risk of local recurrence and ipsilateral breast cancer [32]. Evidence on the im-

▶**Table 2** Cox regression analysis on overall survival for patients with invasive carcinoma: Results for clinical covariates are shown.

Covariates	Cox Regression Analysis	
	HR (95 %CI)	p value
Age	1.06 (1.05–1.06)	< 0.001
Margin status		
Primary R0	1 (Reference)	
Secondary R0	0.93 (0.63–1.09)	0.179
Definitive R1	1.12 (0.67–1.86)	0.670
Therapeutic approach		
Breast Conserving Surgery	0.66 (0.54–0.81)	< 0.001
Neoadjuvant Chemotherapy	2.08 (1.54–2.79)	< 0.001
Tumorbiology		
Hormone Receptor positive	0.70 (0.23–2.21)	0.548
HER2 positive	0.65 (0.48–0.89)	0.007
TNBC	1.56 (0.50–4.93)	0.447
Grading		
G1	1 (Reference)	
G2	1.16 (0.85–1.59)	0.356
G3	1.51 (1.06–2.14)	0.023
Tumor size (TNM)		
T1	1 (Reference)	
T2	1.71 (1.36–2.15)	< 0.001
T3	2.19 (1.57–3.06)	< 0.001
T4	3.69 (2.38–5.74)	< 0.001
Nodal Involvement	1.64 (1.34–2.00)	< 0.001
Histologic subtype		
NST	1 (Reference)	
ILC	0.69 (0.52–0.93)	0.016
Other	1.16 (0.70–1.90)	0.570

CI = Confidence Interval; G = Grading; HR = Hazard Ratio; ILC = Invasive Lobular Breast Cancer; NST = No Special Type; TNBC = Triple-Negative Breast Cancer

pact of margin involvement on overall survival remains limited. In our analysis, there was no significant difference in overall survival based on margin status in the multivariate analysis, although the Kaplan–Meier curves showed a significant separation for patients with definitive R1 resection. This might suggest a possible impact on survival, but larger cohorts are needed to confirm this observation. So far, several studies offer conflicting results regarding the impact of margin status on survival. An Italian study reported poorer disease-free survival in patients with T1 to T2 tumors and involved margins [19], in line with that a British analysis showed shorter distant disease-free survival rates for early breast cancer patients with involved margins [18]. In contrast, American and Canadian studies did not find any survival outcome differences based on margin status [20, 33].

In summary, evidence suggests that involved margins are associated with an increased risk of local and distant recurrences. Larger cohort studies are needed to clarify the prognostic impact of margin involvement on overall and disease-free survival in different clinical scenarios.

The present study has several limitations. Firstly, the retrospective design may affect the reliability of the results. Additionally, we lack data on local recurrence and disease-free survival. Moreover, systematic information on postoperative adjuvant treatment in all patients, which significantly influences breast cancer outcomes, is not available. With a median follow-up of 72.2 months, the present analysis offers a solid follow-up period. However, this duration may not be sufficient for low-risk and low-grade carcinomas, and longer follow-up periods should be considered in subsequent analyses. Furthermore, the relatively small number of patients with definitive R1 resection in our cohort may limit the statistical power of our findings. Notably, 58 % (n = 52) of patients with definitive R1 resection underwent breast-conserving surgery, yet our analysis lacks a definitive explanation for why secondary mastectomy was not performed in these cases. One possible reason could be that the tumor size was underestimated in these cases, and secondary mastectomies were not performed due to different possible clinical scenarios. Future studies should aim to determine why some patients with definitive R1 resection do not undergo secondary surgery, examining factors such as patient health status, patient choice, and more aggressive tumor characteristics. Despite these limitations, this report provides additional valuable evidence on the prognostic impact of involved margins in patients with breast cancer.

Conclusion

The analysis showed no statistically significant difference in overall survival based on margin status in patients treated for early breast cancer. Notably, patients who underwent breast-conserving therapy exhibited more favorable outcomes in our analysis, underscoring the oncologic safety of this procedure. Further larger multicentric analysis are needed to evaluate the prognostic value of margin involvement for different tumor types, stages and local and systemic treatment.

Availability of Data

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest

The authors declare that they have no conflict of interest.

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