Original Article

Surgical reduction in chest wall disease to prolong survival in breast cancer patients: a retrospective study

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Background: Patients with breast cancer (BC) may develop locoregional recurrence alone or with distant metastases. Results of previous studies discussing the benefit of local surgery among patients with chest wall disease were controversial. Whether surgical reduction for chest wall disease could influence survival outcome is still a question. The objective of this study was to compare overall survival (OS) in patients with recurrence involving the chest wall who did or did not undergo surgical reduction after previous treatment of the primary BC to explore the role of surgical reduction.

Methods: We retrospectively reviewed BC patients with chest wall as the first recurrent/metastatic site selected between January 2012 and December 2018 to explore whether surgical reduction for chest wall disease could influence OS. Clinicopathological data, including age at initial diagnosis, TNM stage, the pathological parameters, and treatment were recorded and analyzed. OS was primarily described using the Kaplan-Meier estimator for each group, with the statistical significance between groups being tested by the log-rank test.

Results: A total of 198 patients with a median age of 48 years (range, 22–73 years) were analyzed. Chest wall as the only site of recurrence occurred in 139 patients (70.2%), and the other 59 (29.8%) patients had other metastatic sites. There were 88 patients who underwent surgical reduction for chest wall recurrence. The median OS was significantly longer for the patients who had chest wall disease reduction than for those who did not {194.2 months [95% confidence interval (CI): 140.4–247.9 months] *vs.* 102.7 months (95% CI: 79.7–125.7 months), respectively, P=0.001}. From multivariate analysis, surgical reduction was an independent factor significantly influenced OS (HR =0.52, 95% CI: 0.33–0.81, P=0.004). Subgroup analyses showed that OS was statistically longer in the chest wall disease surgical reduction group than in the no reduction group with respect to hormone receptor (HR) negative (–), human epidermal growth factor receptor 2 (HER2) negative (–), triple-negative breast cancer (TNBC), disease-free survival (DFS) >24 months, and chest wall disease only.

Conclusions: BC patients with chest wall recurrence could benefit from surgical reduction with a prolonged OS. In a certain selected group, surgical reduction may be warranted.

Keywords: Breast cancer (BC); chest wall recurrence; metastasis; surgery; survival

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Introduction

Female breast cancer (BC) was the most commonly diagnosed cancer worldwide in 2020, representing 11.7% of all cancer cases, with an incidence and mortality of 24.5% and 15.5%, respectively (1).

Approximately 5–35% of patients with BC develop locoregional recurrence alone or with distant metastases (2-5), and approximately 11% have persistent chest wall progression (6). Recurrent/metastatic BC in the chest wall is a significant problem and a very poor prognostic sign (7).

However, patients with chest wall recurrence often have heterogeneous characteristics, and not all present poor prognosis (8). A study revealed that local therapy including surgery resection of the chest wall lesion may benefit certain patients (9). A systematic review from Wakeam *et al*. revealed that, in selected chest wall recurrence patients undergoing chest wall resection, long-term survival approached 40–50% at 5 years and included some patients in whom long-term remission and even cure can be achieved (10). Although surgery is suggested for patients with chest wall recurrence (11), many such as who with multiple lesions or in sites that are not suitable for surgery cannot undergo complete chest wall surgery.

For metastatic breast cancer (MBC) patients with not only chest wall disease and who have already undergone curative treatment for the primary disease, systemic methods should be the first to be considered. However, for patients suffering from compression, ulceration, and pain of the chest wall disease, palliation could be considered when other metastatic sites are not immediately life-threatening.

Although previous studies have discussed the benefit of local surgery among a fraction of patients with chest wall disease (12,13,20-23), the results were controversial. The inconsistent results may due to heterogeneous characteristics among patients received surgical resection. Whether surgical reduction for chest wall disease to reduce tumor burden influences survival outcome for this group of patients is still a question that clinical doctors face frequently. Therefore, the main objective of the present retrospective study was to examine the overall survival (OS) of patients who progressed firstly to the chest wall with or without surgical tumor reduction after previous treatment of primary BC. We present the following article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-246/rc).

Methods

Study design and participants

The current study retrospectively reviewed the medical data of Chinese female patients with the chest wall as the first recurrent/metastatic site after treatment for the primary disease at the Department of Breast Oncology, Peking University Cancer Hospital & Institute between January 2012 and December 2018. Patients meeting all of the following criteria were included: non-stage IV BC at initial diagnosis, undergone curative surgery for primary disease, and chest wall was the only site of disease progression or as one of the sites of metastasis. Patients were excluded from the study if they were male, had a serious systemic disorder, and had a second primary malignancy.

Characteristics and follow-up

For all included patients, clinicopathological data, including age at initial diagnosis, TNM stage, the pathological parameters, and treatment of the primary disease as well as of the progressed disease were recorded and analyzed. Estrogen receptor (ER), progestogen receptor (PR) and HER2 status were determined by immunohistochemistry (IHC). Positivity was established at least 1% of cells staining positive for ER or PR. Hormone receptor (HR) positivity was defined as positivity of either the ER or PR. The HER2 status was considered positive if the IHC score was 3+ or if an IHC score of 2+ was confirmed by fluorescence in situ hybridization (FISH). Triple-negative breast cancer (TNBC) was defined as ER negative, PR negative and HER2 negative. The primary endpoint was the OS, defined as the time from the diagnosis date of breast cancer until death from any cause or the last follow-up date, whichever occurred first. The disease-free survival (DFS) was defined as the time from the diagnosis date of breast cancer until the first diagnosis of tumor progression.

The primary aim of the study was to compare the OS between patients with and without surgical reduction for chest wall tumor.

All included patients were followed up regularly until death or study data cutoff (31 July 2021). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Peking University Cancer Hospital & Institute (No. 2016YJZ19) (Beijing, China). Individual

consent for this retrospective analysis was waived.

Statistical analysis

Categorical variables are presented as frequency and percentage, while continuous variables are presented as mean (SD) or median (IQR), wherever appropriate. The statistical significance for categorical variables was tested by the χ^2 test and for continuous variables was tested by the unpaired *t*-test [for mean (SD)] or the Mann-Whitney U test [for median (IQR)]. OS was primarily described using the Kaplan-Meier estimator for each group, with the statistical significance between groups being tested by the log-rank test. The hazard ratios (HRs) for OS and 95% confidence interval (CI) were estimated using the Cox proportional-hazards model. Missing data was excluded from the analysis. Specifically, variables with imbalance distributions at baseline or statistically significant associations (P<0.05) in univariate analysis were included in the multivariate Cox model. All statistical analyses were conducted with SPSS 22.0 statistical software (SPSS, Chicago, IL, USA). All reported P values are two-sided, with P<0.05 being considered statistical significance.

Results

Patient information

A total of 198 female BC patients from the Department of Breast Oncology, Peking University Cancer Hospital & Institute between January 2012 and December 2018 (median age 48 years; range, 22–73 years) were enrolled. All those with the chest wall as one of the first metastatic sites were analyzed. The median follow-up after the initial diagnosis of BC was 93.3 months, and the median follow-up after recurrence/metastasis was 49.0 months.

The patients' characteristics and treatment are presented in *Table 1*. All patients had primary tumor surgery and there were none with *de novo* stage IV. As the molecular type of primary BC, 36 patients (18.2%) were diagnosed with triple-negative breast cancer (TNBC), 138 (69.7%) had hormone receptor positive (HR+) BC and 54 patients (27.3%) had human epidermal growth factor receptor 2 (HER2) positive BC. Furthermore, a total of 106 patients (53.5%) had stage I–II disease and 73 patients (36.9%) had stage III disease. Tumors >2 cm were detected in 58.6% (n=116) of the patients. A total of 129 (65.2%) patients had axillary lymph node (LN) metastasis. A total of 174 (87.9%) patients received adjuvant chemotherapy. Patients who were eligible (n=70, 35.4%) received radiotherapy after primary surgery. There are 101 (51.0%) patients on hormone therapy, and 25.9% of patients (14/54) with positive HER2 amplification received standard anti-HER2 therapy. A total of 117 patients (59.1%) had a DFS >24 months following diagnosis.

The chest wall as the only site of recurrence occurred in 139 patients (70.2%), and the other 59 (29.8%) patients not only had chest wall recurrence but also other sites of metastasis, the most common being the LNs (50/59, 84.7%), both regional and distant. Other metastatic sites included the bone (12/59, 20.3%), lung (8/59, 13.6%), liver (11.9%, n=7), pleura (5.1%, n=3), contralateral breast (3.4%, n=2) and adrenal (1.7%, n=1). A total of 17 patients (28.8%) had ≥3 metastatic sites.

As treatment for disease progressions, the patients received a median of three lines of systematic therapy, including chemotherapy, hormonal therapy and targeted therapy. There were 88 (44.4%) patients who underwent surgical reduction for chest wall. While, 75/139 (54.0%) patients with the chest wall as the only recurrent site had surgical reduction, compared with 13/59 (22.0%) of those with multiple metastatic sites. After recurrence/metastasis, a total of 88 (44.4%) patients had radiotherapy as local treatment; most of the patients (93.9%) had systematic treatment at first line. There were 19.7% (39/198) patients treated with antiangiogenesis therapy.

Survival

Patients undergoing surgical reduction for chest wall disease had better OS compared with patients without. The median OS was significantly longer for patients who had surgical reduction of chest wall disease (n=88) than for those who did not (n=110) [194.2 months (95% CI: 140.4–247.9 months) *vs.* 102.7 months (95% CI: 79.7–125.7 months), respectively, P=0.001, *Figure 1*].

Univariate analysis of the correlation between characteristics as well as treatment and OS was performed. The results showed significant prolongation of median OS in patients with surgical reduction of chest wall disease (P=0.001), HR+ status (P=0.000), non-TNBC (P=0.001), negative axillary LN metastasis (LNM) of the primary tumor (P=0.020), TNM stage I–II (P=0.000), chest wall recurrence only (P=0.014) and DFS >24 months (P=0.000) (*Table 2*).

Variables with imbalance distributions at baseline or

Table 1 Patients' characteristics and treatment

Characteristic	n (%)	Surgical reduction (n=88), n (%)	No surgical reduction (n=110), n (%)	P value
Age (years)				0.313
Median [range]	48 [22–73]			
≤50	113 (57.1)	54 (61.4)	59 (53.6)	
>50	85 (42.9)	34 (38.6)	51 (46.4)	
Hormone receptor				0.088
Negative	60 (30.3)	21 (23.9)	39 (35.5)	
Positive	138 (69.7)	67 (76.1)	71 (64.5)	
HER2				0.422
Negative	144 (72.7)	67 (76.1)	77 (70.0)	
Positive	54 (27.3)	21 (23.9)	33 (30.0)	
TNBC				0.194
No	162 (81.8)	76 (86.4)	86 (78.2)	
Yes	36 (18.2)	12 (13.6)	24 (21.8)	
Histopathologic grade				0.353
I–II	73 (36.9)	30 (34.1)	43 (39.1)	
III	53 (26.8)	17 (19.3)	36 (32.7)	
Unknown	72 (36.3)	41 (46.6)	31 (28.2)	
Tumor size (cm)				1.000
≤2.0	53 (26.8)	23 (26.1)	30 (27.3)	
>2.0	116 (58.6)	51 (58.0)	65 (59.1)	
Unknown	29 (14.6)	14 (15.9)	15 (13.6)	
Axillary lymph node metastasis				0.757
Positive	129 (65.2)	56 (63.6)	73 (66.4)	
Negative	61 (30.8)	28 (31.8)	33 (30.0)	
Unknown	8 (4.0)	4 (4.5)	4 (3.6)	
TNM stage				0.444
I–II	106 (53.5)	49 (55.7)	57 (51.8)	
III	73 (36.9)	29 (33.0)	44 (40.0)	
Unknown	19 (9.6)	10 (11.4)	9 (8.2)	
Chemotherapy for primary tumor				0.015
Yes	174 (87.9)	83 (94.3)	91 (82.7)	
No	24 (12.1)	5 (5.7)	19 (17.3)	
Hormonal therapy for primary tumor				0.776
Yes	101 (51.0)	46 (52.3)	55 (50.0)	
No	97 (49.0)	42 (47.7)	55 (50.0)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristic	n (%)	Surgical reduction (n=88)	No surgical reduction (n=110)	P value
Anti-HER2 therapy for primary tumor				0.406
Yes	14 (7.0)	8 (9.1)	6 (5.5)	
No	184 (93.0)	80 (90.9)	104 (94.5)	
Radiotherapy for primary tumor				0.553
Yes	70 (35.4)	29 (33.0)	41 (37.7)	
No	128 (64.6)	59 (67.0)	69 (62.7)	
DFS				0.309
≤24 months	81 (40.9)	32 (36.4)	49 (44.5)	
>24 months	117 (59.1)	56 (63.6)	61 (55.5)	
Chest wall recurrence only				0.000
Yes	139 (70.2)	75 (85.2)	64 (58.2)	
No	59 (29.8)	13 (14.8)	46 (41.8)	
Radiotherapy for chest wall after progression				0.000
Yes	88 (44.4)	54 (61.4)	34 (30.9)	
No	110 (55.6)	34 (38.6)	76 (69.1)	
Systemic therapy at first line				0.100
CT only	74 (37.4)	32 (43.2)	42 (56.8)	
Contain HT	77 (38.9)	32 (41.6)	45 (58.4)	
Contain anti-HER2 therapy	28 (14.1)	10 (35.7)	18 (64.3)	
Contain HT + anti-HER2	7 (3.5)	5 (71.4)	2 (28.6)	
None	12 (6.1)	9 (75.0)	3 (25.0)	
Lines of systemic treatment after chest wall recurrence				0.079
≤3	106 (48.5)	44 (50.0)	62 (56.4)	
>3	92 (46.5)	44 (50.0)	48 (43.6)	
Antiangiogenesis therapy				0.282
Yes	39 (19.7)	14 (15.9)	25 (22.7)	
No	159 (80.3)	74 (84.1)	85 (77.3)	

HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; DFS, disease-free survival; CT, chemotherapy; HT, hormone therapy.

statistically significant associations (P<0.05) in univariate analysis were included in the multivariate Cox model. The results showed that DFS >24 months and surgical reduction of disease remained independent predictive factors of OS (*Table 3*).

A total of 88 patients had surgical reduction and there was no significant difference between patients who did (54/88) or did not (34/88) receive radiation therapy for the chest wall after surgical reduction [197.7 months (95% CI: 143.5–251.9 months) *vs.* 194.2 months (95% CI: 73.1–315.3 months), respectively, P=0.483].

In a subgroup analysis of patients with only chest wall recurrence, those who had surgical reduction (n=75) had a longer median OS [203.6 months (95% CI:

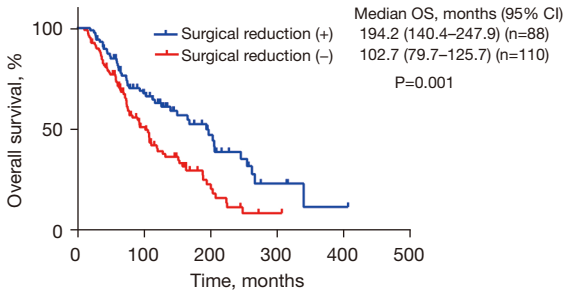

Figure 1 Kaplan-Meier curve of OS in patients who did or did not have surgical reduction. OS, overall survival.

159.5–247.7 months) *vs.* 82.8 months (95% CI: 47.6–117.9 months), respectively, P<0.001, *Figure 2*].

Univariate analysis of the correlation between characteristics as well as treatment and OS was performed in patients with only chest wall recurrence. The results showed a significant prolongation of median OS in those with surgical reduction of chest wall disease (P=0.000), HR+ status (P=0.000), non-TNBC (P=0.003), TNM stage I–II (P=0.000) and DFS >24 months (P=0.000) (*Table 4*).

Multivariate analysis performed with the factors with P value <0.05 in the univariate analysis showed that TNM stage I–II, DFS >24 months and surgical reduction of chest disease remained independent predictive factors of OS in patients with chest wall metastasis only (*Table 5*).

In patients with only chest wall disease as BC progression, a total of 75 underwent surgical reduction. There was no significant difference between patients who did (49/75) or did not (26/75) receive radiation therapy for the chest wall after surgical reduction [203.6 months (95% CI: 101.0–306.2 months) *vs.* 205.8 months (95% CI: 110.5–301.1 months), respectively, P=0.711]. Additionally, in patients who had both adjuvant radiation therapy and surgical reduction for the chest wall, there was no significant difference between patients who did (14/26) or did not (12/26) receive radiation therapy for local recurrence after surgical reduction [246.1 months (95% CI: 133.5–358.8 months) *vs.* 206.4 months (95% CI: 0.0–445.7 months), respectively, P=0.623].

However, whether patients did or did not have surgical reduction of chest wall disease did not influence survival outcome among patients with multiple metastatic sites.

Subgroup analyses (*Figure 3*) showed that OS was statistically longer in the chest wall disease surgical reduction group than in the no reduction group with respect to HR(–) (hazard ratio 0.32; 95% CI: 0.15–0.71;

Table 2 Univariate analysis of median OS between patients with different characteristics

Variable	OS (months), median (95% CI)	P value
Hormone receptor status		
Positive	163.8 (114.2–213.5)	0.000
Negative	74.5 (55.9–93.1)	
HER2		
Positive	111.6 (72.2–151.0)	0.283
Negative	128.8 (84.6–173.1)	
TNBC		
Yes	66.0 (43.6–88.3)	0.001
No	151.7 (112.5–190.9)	
Tumor size (cm)		
≤2	163.8 (100.6–227.1)	0.427
>2	119.9 (92.2–147.6)	
Axillary LNM of primary tumor		
Negative	168.4 (93.4–243.3)	0.020
Positive	99.4 (75.3–123.5)	
TNM stage		
I–II	158.3 (100.8–215.9)	0.000
III	75.7 (64.3–87.1)	
Chest wall recurrence only		
No	106.3 (89.3–123.3)	0.014
Yes	153.6 (114.0–193.2)	
Chest wall disease surgical reduction		
No	102.7 (79.7–125.7)	0.001
Yes	194.2 (140.4–247.9)	
Radiotherapy for chest wall after progression		
No	111.6 (97.4–125.9)	0.372
Yes	150.5 (107.0–194.0)	
Antiangiogenesis therapy		
No	132.4 (101.0–163.9)	0.106
Yes	78.4 (37.2–119.6)	
DFS (months)		
≤24	58.8 (46.9–70.7)	0.000
>24	189.1 (154.3–223.9)	

OS, overall survival; CI, confidence interval; DFS, disease-free survival; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; LNM, lymph node metastasis.

Table 3 Multivariate Cox proportional hazard models of OS

Variable	Hazard ratio (95% CI)	P value
Hormone receptor (–/+)	0.74 (0.39–1.40)	0.360
TNBC (no/yes)	1.53 (0.77–3.04)	0.224
Axillary LNM of primary tumor (no/yes)	1.40 (0.80–2.44)	0.236
TNM stage (I–II/III)	1.64 (1.00–2.70)	0.050
Chest wall recurrence only (no/yes)	0.74 (0.47–1.17)	0.204
DFS (≤24/>24 months)	0.28 (0.17–0.45)	0.000
Surgical reduction (no/yes)	0.52 (0.33–0.81)	0.004
Chemotherapy for primary tumor (no/yes)	1.45 (0.77–2.72)	0.251
Radiotherapy for chest wall after progression (no/yes)	1.26 (0.81–1.95)	0.303

+, positive; –, negative. OS, overall survival; TNBC, triple-negative breast cancer; LNM, lymph node metastasis; DFS, disease-free survival.

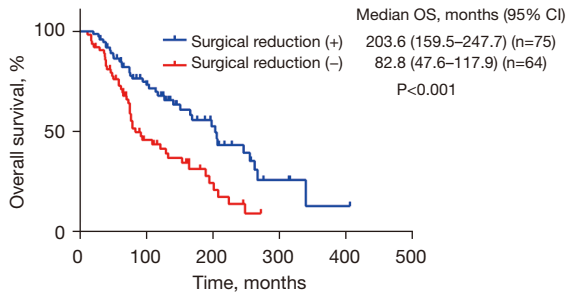

Figure 2 Kaplan-Meier curve of OS comparing patients with chest wall recurrence only who did or did not have surgical reduction. OS, overall survival.

P=0.005), HER2(–) (hazard ratio 0.45; 95% CI: 0.29–0.69; P=0.000), TNBC (hazard ratio 0.23; 95% CI: 0.07–0.78; P=0.003), DFS >24 months (hazard ratio 0.47; 95% CI: 0.28–0.78; P=0.004), and chest wall disease only (hazard ratio 0.46; 95% CI: 0.29–0.72; P=0.001). Patients in the surgical reduction group had better OS whether or not they received adjuvant radiation therapy.

Discussion

This retrospective study mainly focused on whether surgical reduction of chest wall tumor burden could affect survival in patients with chest wall metastasis in real clinical practice. All the patients enrolled had chest wall lesions, and some of them had multiple metastatic sites.

We found that OS was significantly prolonged in patients who had chest wall disease partly or fully removed, which means local surgical burden reduction should be considered when allowed.

In this study, most of the patients had chest wall recurrence only, which was totally removed or reduced surgically according to the indication.

Previous studies have focused mainly on surgery of chest wall recurrence (12,13) or primary breast tumor in *de novo* metastatic patients (14-20). So we chose treatment of patients with only chest wall recurrence as our study topic. In the National Comprehensive Cancer Network (NCCN) consensus (11), patients with only local recurrence should be considered for surgical resection with radiation therapy in mastectomy-treated and mastectomy in breast-conserving patients, respectively. But the NCCN still emphasizes the importance of individual treatment in this group of patients.

Our study found that in patients with only chest wall recurrence, the median OS was significantly improved in the surgical reduction group in compared with the nonsurgical group, which was consistent with the NCCN recommendation that surgical treatment of locally recurrent disease is of great importance (11). In our subgroup analysis, we did not find any difference of OS whether patients had radiation therapy or not after surgical reduction, but this result may be limited by the sample size.

For chest wall recurrent disease, previous research on whether patients should undergo chest wall surgical resection has been mostly retrospective. From small-sample research concerning the benefits of chest wall resection, the overall 5-year survival was 18–25% (13,21). However, results from studies with two comparative groups are controversial. In the study by Shen *et al.* (22), the difference

Table 4 Univariate analysis of OS in subgroup of patients with only chest wall recurrence

Variable	n (%)	OS (months), median (95% CI)	P value
Hormone receptor status			
Positive	98 (70.5)	194.7 (148.0–241.5)	0.000
Negative	41 (29.5)	75.2 (32.5–117.8)	
HER2			
Positive	35 (25.2)	132.4 (59.2–205.7)	0.086
Negative	104 (74.8)	165.8 (107.0–224.5)	
TNBC			
Yes	24 (17.3)	74.5 (21.2–127.8)	0.003
No	115 (82.7)	189.1 (141.8–236.4)	
Tumor size (cm)			
≤2	39 (28.1)	189.1 (144.1–234.1)	0.700
>2	75 (54.0)	140.0 (97.7–182.3)	
Axillary LNM of primary tumor			
Negative	45 (32.4)	189.1 (122.9–255.3)	0.089
Positive	87 (62.6)	103.3 (51.6–155.0)	
TNM stage			
I–II	73 (52.5)	168.4 (118.3–218.4)	0.000
III	49 (35.3)	75.2 (58.8–91.5)	
Chest wall disease surgical reduction			
No	64 (46.0)	82.8 (47.6–117.9)	0.000
Yes	75 (54.0)	203.6 (159.5–247.7)	
Radiotherapy for chest wall after progression			
No	66 (47.5)	126.5 (26.0–227.0)	0.486
Yes	73 (52.5)	153.6 (119.1–188.1)	
Antiangiogenesis therapy			
No	121 (87.1)	153.6 (97.7–209.5)	0.150
Yes	18 (12.9)	78.4 (17.9–138.9)	
DFS			
≤24 months	54 (38.8)	58.0 (43.9–72.1)	0.000
>24 months	85 (61.2)	203.6 (184.3–222.9)	

CI, confidence interval; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; LNM, lymph node metastasis; DFS, disease-free survival; OS, overall survival.

Table 5 Multivariate Cox proportional hazard models of OS in patients with only chest wall recurrence

Variable	Hazard ratio (95% CI)	P value
Hormone receptor (–/+)	0.96 (0.44–2.12)	0.919
TNBC (no/yes)	2.03 (0.90–4.61)	0.090
TNM stage (I–II/III)	2.11 (1.28–3.47)	0.003
Surgical reduction (no/yes)	0.44 (0.27–0.73)	0.001
DFS (≤24/>24 months)	0.25 (0.14–0.44)	0.000

+, positive; –, negative. TNBC, triple-negative breast cancer; DFS, disease-free survival; OS, overall survival.

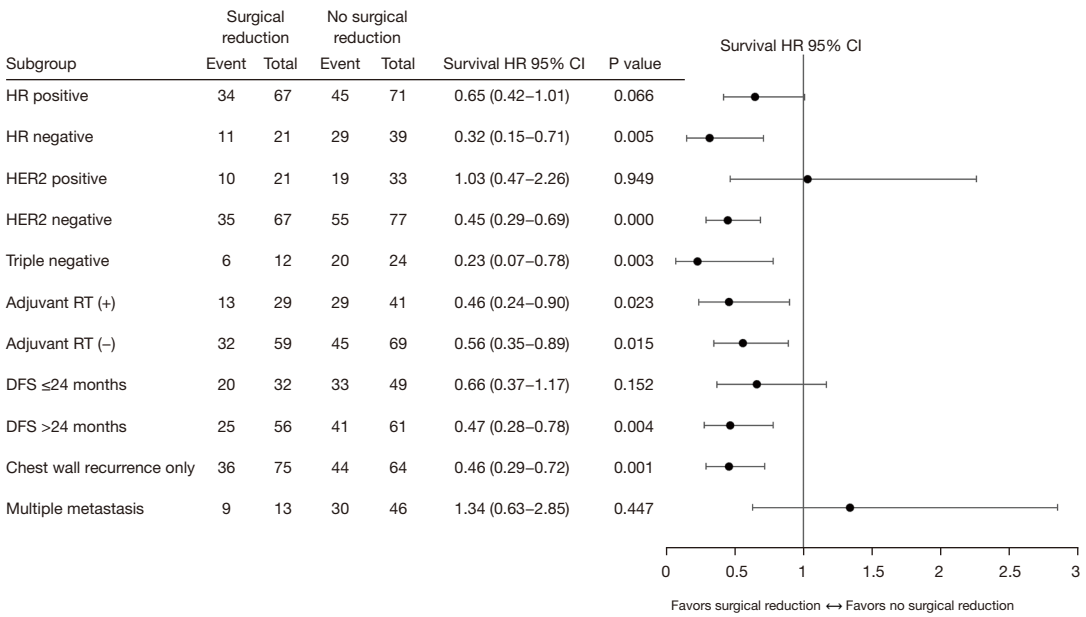

Figure 3 Forest plot of OS subgroup analyses with hazard ratios. HR, hormone receptor; HER2, human epidermal growth factor receptor 2; RT, radiotherapy; DFS, disease-free survival; OS, overall survival.

in 5-year survival was not statistically significant between the surgical group (30.6%) and nonsurgical group (49.6%), with a nearly 20% decrease in patients who underwent surgery. This relatively big difference might due to the aggressive characteristics of their surgical group with mainly TNBC patients. In the latest research from Shanghai (23), Wu *et al.* retrospectively developed a nomogram based on clinicopathological factors, dividing patients with local recurrence into low- and high-risk subgroups. They found that local treatment, especially surgery, after local recurrence was the optimal choice for patients with lower risk, whereas systemic treatment should be considered for patients with higher risk. This finding reminds us of the great importance of individual patient selection for surgery.

In our subgroup analysis exploring patients who could benefit from surgical reduction, we found those with DFS >24 months could gain longer survival outcome. This finding was consistent with Wakeam *et al.* (10) who systematically reviewed the literature on chest wall resection for recurrent BC. From the 48 studies they searched, a disease-free interval (DFI) >24 months was one of the factors consistently associated with improved outcomes after resection of recurrence (13,24-26). These findings challenge the impression that all chest wall recurrences portend a uniformly poor prognosis. In a certain selected group, resection or surgical reduction may be warranted (9).

Our study group included stage IV patients with multiple metastases besides the chest wall after treatment of the primary tumor. Because this patient population is still considered incurable, the primary goal of treatment is to

extend life expectancy and improve quality of life. Systemic therapy is the current standard of care, and surgery is not recommended except for those patients requiring palliation of symptoms or with impending complications such as skin ulceration and bleeding (11).

But what about the role of local tumor burden release by surgery in multi-site metastasis patients? In the subgroup analysis (n=59), we did not find any relationship between lesion removal and OS. However, tumor burden reduction (27) did indeed have something to do with OS. From the limited number of previous prospective studies, research from Turkey reported that the initial surgery group showed a statistically significant improvement in 5-year survival of *de novo* stage IV BC (20). Meanwhile, they found that patients in several groups could benefit from surgery. So, combined with the results from the largest meta-analysis concerning locoregional therapy of primary tumor in *de novo* stage IV BC, the local therapeutic option should be considered in selected patients after multidisciplinary discussion (28).

Because of the sample size, there were only 13 multi-site metastasis patients who had undergone tumor burden reduction in our study. It was difficult to determine the benefit for clinical outcome from this study. Besides, a potential bias may have been created by the choice of systemic treatment, which was dependent on the site of recurrence/metastasis.

In conclusion, the present study in patients with chest wall disease found that OS was significantly prolonged in patients who had surgical reduction, especially in patients with only chest wall recurrence. Breast cancer patients with chest wall recurrence could benefit from surgical reduction with a prolonged OS. In a certain selected group, such as patients with DFS >24 months, resection or surgical reduction may be warranted in real clinical practice.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-22-246/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Peking University Cancer Hospital & Institute (No. 2016YJZ19) (Beijing, China). Individual consent for this retrospective analysis was waived.

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