Original Article

Oncologic outcome of breast reconstruction after mastectomy in breast cancer: a systematic review and meta-analysis

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Background: We conducted a comprehensive systematic review of the literature and meta-analysis of the oncologic outcomes of breast reconstruction (BR) after mastectomy and mastectomy only. This study aimed to analyze the impact of BR on the prognosis of patients with breast cancer.

Methods: A systematic search of MEDLINE and EMBASE databases was performed using the following keywords: breast cancer, mastectomy, and BR. Inclusion criteria were studies reporting the survival data of patients after mastectomy only and mastectomy with BR. Event-free survival (EFS), breast cancer-specific survival (BCSS), and overall survival (OS) were considered the indicators of oncological outcomes. As all the included studies were non-randomized trials, we used the Newcastle-Ottawa Scale (NOS) for risk of bias assessment. The effect of BR on survival was measured using the effect size of the hazard ratio (HR). Data from each study were analyzed using the Review Manager.

Results: Fifteen studies with 20,948 cases of BR and 63,358 cases of mastectomy were included. The pooled HRs for EFS and BCSS were 1.07 [95% confidence interval (CI): 0.78–1.47, P=0.65] and 0.84 (95% CI: 0.64–1.11, P=0.22), respectively. The patients who underwent BR after mastectomy had similar EFS and BCSS scores. Furthermore, patients who received BR had better OS (HR =0.73; 95% CI: 0.61–0.88, P=0.001) than those who underwent mastectomy only.

Conclusions: The data showed that BR after mastectomy had similar EFS and BCSS and better OS than mastectomy alone. Our meta-analysis suggests that BR is a practicable and safe treatment option for patients with breast cancer.

Keywords: Breast cancer; mastectomy; breast reconstruction (BR); prognosis

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Introduction

Breast cancer is the most common cancer worldwide as per the World Health Organization, 2022, and has a fairly favorable prognosis, with a 5-year survival rate of 90% as reported by American Cancer Society. As breast cancer is diagnosed at an early stage in many women, the survival rate of patients receiving appropriate treatment is improving. For patients with breast cancer, quality of life,

including body image after breast cancer surgery, is also becoming an important part of treatment and management. In recent years, treatment strategies for breast cancer, such as surgery, radiation therapy, chemotherapy, endocrine therapy, targeted therapy, and immunotherapy, have greatly improved. However, for operable breast cancer, surgical treatment, such as mastectomy, breast-conserving surgery, and breast reconstruction (BR) after mastectomy, is considered the most important treatments (1). In particular, radiation therapy following breast-conserving surgery has proven to be the preferred therapy for early breast cancer because the survival rates are equivalent to mastectomy, and surgeons can safely maintain the natural breast shape after surgery (2). However, mastectomy is recommended in cases of inflammatory breast cancer, large tumors, multiple lesions, early pregnancy, or contraindication of radiation therapy (1).

In particular, it is difficult to perform breast conserving surgery (BCS) if the breast cancer is multicentric or contraindication of radiation treatment or persistently positive margins. In these cases, BR after mastectomy is considered instead of BCS. Moreover, studies have shown that BR after mastectomy helps improve esthetic outcomes and quality of life without compromising oncological safety, and the demand for therapeutic mastectomy followed by reconstruction is increasing (3,4). In addition, as an important part of current breast cancer treatment, neoadjuvant chemotherapy (NACT) is widely used early-stage breast cancer, as well as locally advanced and inflammatory breast cancer. If breast-conserving surgery is not possible after NACT, breast cancer patients undergo mastectomy as a surgical treatment. In this case, BR after mastectomy may be an important alternative surgical option (3). Although many studies have demonstrated the oncological safety of BR after mastectomy, concerns remain regarding the delay in adjuvant therapy or impaired detection of local recurrence due to complications from reconstruction.

Therefore, this study aimed to conduct a systematic meta-analysis based on several studies on the oncological prognosis of BR after mastectomy from early breast cancer to locally advanced and inflammatory breast cancers. We present this article in accordance with the MOOSE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-706/rc).

Highlight box

Key findings

- Breast reconstruction (BR) does not affect the oncological outcomes of breast cancer patients.

What is known and what is new?

- Many studies have demonstrated the oncological safety of BR after mastectomy, concerns remain regarding the delay in adjuvant therapy or impaired detection of local recurrence due to complications for reconstruction.
- We analyzed systematic reviews of the oncologic outcome of BR after mastectomy and BR is a safe treatment option for breast cancer patients.

What is the implication, and what should change now?

- Since BR does not affect the oncological outcomes of breast cancer patients, BR after mastectomy can be recommended for patients who require mastectomy.

Methods

Search strategy

We performed systematic searches of MEDLINE and EMBASE (from 2008 to 2021) for English language publications using keywords such as “breast cancer”, “mastectomy” and “breast reconstruction (BR)”. All the searches were limited to human studies.

Study selection

We included studies that met the following criteria: (I) we include female patients diagnosed with *in situ* breast cancer or invasive breast cancer; (II) we include a BR as an experimental group; (III) we include a mastectomy only as a control group; (IV) we examine the main outcome indicators of oncologic prognosis [i.e., event-free survival (EFS), breast cancer-specific survival (BCSS), overall survival (OS)] and (V) the study design was retrospective, and the publication language can be English. Studies were excluded from our meta-analysis for the following reasons: (I) the study had insufficient or inadequate data; (II) the article was review, abstract, editorial, or duplicate publication.

Data extraction

The authors performed an initial screening by independently reviewing titles and abstracts according to inclusion and exclusion criteria. Discrepancies were resolved through

consensus or consultation with a third author. We also extracted the following data from the publications: first author, year of publication, country of origin, study design, follow-up duration, number of patients, and endpoints.

The primary outcome was EFS, defined as the time from the initiation of treatment until recurrence or progression. We obtained data on disease-free survival (DFS), relapse-free survival (RFS), recurrence or progression-free survival, and redefined the primary outcomes as EFS. If available, the secondary endpoints were BCSS and OS. BCSS and OS were defined as the time interval from the initial diagnosis until breast cancer-related death and death from any cause, respectively. Publication bias was evaluated using funnel plots.

Quality assessment

As all the included studies were non-randomized trials, we used the Newcastle-Ottawa Scale (NOS) for risk of bias assessment (5). The NOS tool assesses the risk of bias by dividing it into three different domains: selection, comparability, and exposure for case-control or outcome for cohort studies respectively. Studies could be scored from 0 to 9 points each study (5). While not obvious expressed in the NOS rating guidance, we used the following score ranges to qualitatively classify the overall quality of the included studies: 0 to 4 = poor quality, 5 to 7 = moderate quality, 8 to 9 = high quality.

Statistical analysis

The effect of BR on survival was measured using the effect size of the hazard ratio (HR). Data from each study were analyzed using the Review Manager.

The pooled HR was estimated using a random-effects model according to the results of heterogeneity. HR >1 and <1 indicated a worse and a better prognosis in patients with BR after mastectomy, respectively. Statistical significance was set at $P<0.05$, except for heterogeneity.

Results

Study characteristics

An electronic search identified 1,807 articles. After reviewing titles and abstracts, 127 potentially eligible articles left. After reviewing the full-text versions of these articles, 112 were excluded because they had insufficient data (n=51), inadequate data (n=54), or duplicated data (n=7). Finally, 15 eligible studies with a total of 84,306 patients were included in our meta-analysis and the BR and mastectomy alone groups (*Figure 1*).

The selected studies were published between 2008 and 2021. The study sample size available for analysis ranged from 474–35,126 and characterized a broad global patient population, including Europe, the United States, Canada, China, and Korea. All 15 studies had a retrospective design. Most of the included studies were of moderate to high quality (*Table 1*). The studies included a total of 20,948 cases and 63,358 controls. The follow-up duration varied from 39.6–280.8 months (median 106.61 months). Patients with histologically confirmed diagnosis of invasive breast cancer were included. All studies reported oncological outcomes: 8 studies with EFS, 9 studies with OS, and 7 studies with BCSS. *Table 1* presents a review of the summary information. Reconstruction type was defined as autologous-based reconstruction, implant-based reconstruction, or mixed reconstruction after mastectomy. The main characteristics of the 15 included studies are listed in *Table 1*.

BR and mastectomy comparative analyses

Eight studies, including 10,730 patients (4,417 BR and 6,313 mastectomy alone), assessed the EFS outcome. The pooled HR for EFS was 1.07 [95% confidence interval (CI): 0.78–1.47]. This difference was not statistically significant (P=0.65). The Forest plot illustrates the correlation between BR and EFS in *Figure 2*.

Seven studies (62,650 patients, 15,859 BR and 46,791 mastectomy alone) were included in the assessment of the correlation between BR and BCSS, and the HR for BCSS was 0.84 (95% CI: 0.64–1.11). BCSS was reported in seven studies that enrolled a total of 15,859 cases and 46,791 controls. No significant differences were observed between the two groups (P=0.22). The Forest plots illustrate the correlation between BR and BCSS in *Figure 3*.

Nine studies (70,285 patients, 17,755 BR and 52,530 mastectomy alone) analyzed the association between BR and OS. Patients who underwent BR had better OS (HR =0.73; 95% CI: 0.61–0.88) than that of those who underwent mastectomy only. This difference was statistically significant and favored BR (P=0.001). The Forest plots illustrate the correlation between BR and OS in *Figure 4*. All studies carried out sensitivity analysis and publication bias analysis. Funnel plot demonstrated no presence of publication bias in

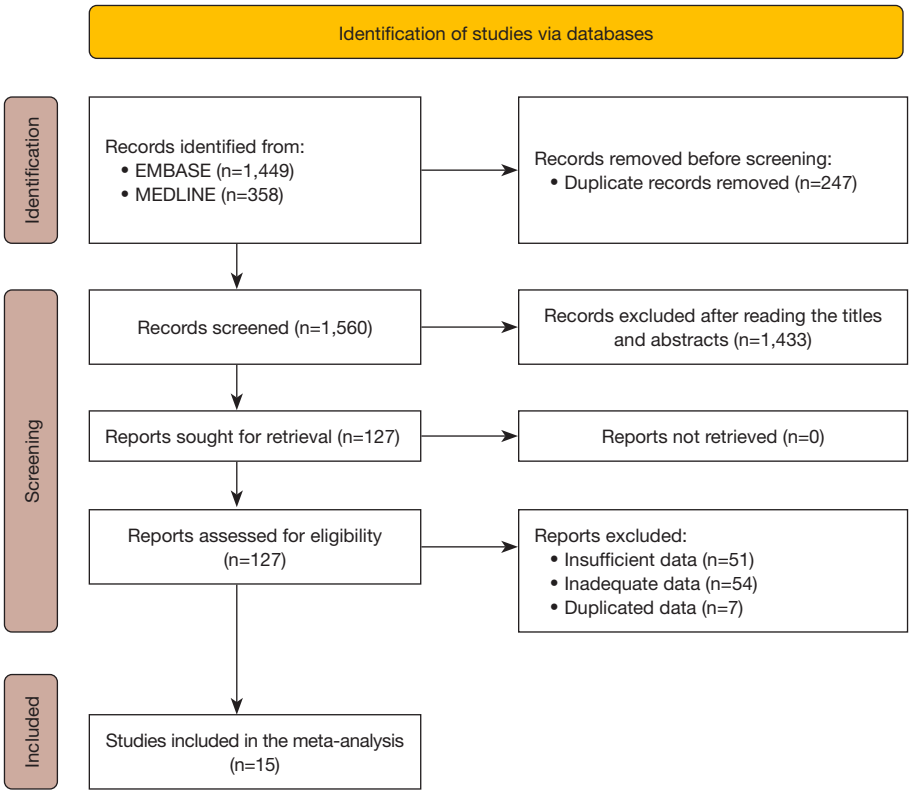

Figure 1 Flowchart of the study selection process.

Figure 5. No significant heterogeneity was statistical in this study.

Discussion

There is increasing popularity of mastectomy and BR as part of the therapeutic strategy for breast cancer (18-21). This seems to be due to the advantage of BR, which results in good esthetic results, reduces damage to women's self-esteem, increases postoperative quality of life, and does not require additional surgery. However, there are still concerns about the delay of follow-up radiotherapy or adjuvant chemotherapy due to surgical infection and detection of local or regional recurrence. Therefore, the effect of BR on survival after mastectomy has been largely investigated, with controversial results. This meta-analysis evaluated the oncological outcomes of EFS, BCSS, and OS in BR after mastectomy and mastectomy alone in patients with breast cancer.

Compared to mastectomy alone, BR after mastectomy did not increase the incidence of local recurrence, distant metastasis, or mortality. From early-stage breast cancer to locally advanced breast cancer treated with NACT, no significant difference was observed in oncologic outcomes among patients who underwent BR.

In previous studies, the results of EFS between the BR and mastectomy alone groups varied for each study, but in our meta-analysis, it was found that BR was not significantly different from the mastectomy alone group (3,6-12). Although Lee *et al.* (6) reported that mastectomy alone was superior to BR after mastectomy from an oncological standpoint, most of the studies we reviewed reported no differences in BCSS (1,7,13-16). In addition, our meta-analysis showed no significant differences between the two groups (BR and mastectomy alone). Several studies have also shown that BR was superior to mastectomy only, which also demonstrated its oncological safety in our study (1,3,7,8,10,12,15-17). Jiang and colleagues (15) demonstrated that patient family income has effect on improved survival outcomes. A possible explanation for this was that with higher the family income, the more likely the patients were to undergo reconstruction and had better access to medical service (e.g., neoadjuvant or adjuvant chemotherapy, adjuvant hormonal therapy,

Table 1 Studies included in meta-analysis

Study number	Author	Year	Country	Institution	Study design	Duration	Patients				Endpoint	Quality assessment
							BR	Mastectomy alone	Stage	BR type		
1	Zhang J (1)	2021	China	SEER database	Retrospective	2004–2016	7,501	7,418	>0, I, II, III	Mix	BCSS, OS	6
2	Baker JL (2)	2013	USA	UCSD-MCC	Retrospective	2002–2011	340	134	I, II, III, IV	Mix	OS	7
3	Wu ZY (3)	2020	Korea	Asan Medical Center	Retrospective	2010.1–2016.11	526	740	I, II, III (neoadjuvant)	Mix	DFS, OS	8
4	Lee SB (6)	2019	Korea	Asan Medical Center	Retrospective	2003.01–2008.12	675	2,124	I, II, III	Autologous	CSS, LR	8
5	Eriksen C (7)	2011	Sweden	Karolinska University Hospital	Retrospective	1990–2004	300	300	I, II, III	Implant	LR, OS, CSS	8
6	Hölmich LR (8)	2008	Denmark	Danish National Hospital Register	Retrospective	1978–1992	580	1,158	I, II, III	Implant	OS, DFS	6
7	Ryu JM (9)	2017	Korea	Samsung Medical Center	Retrospective	2008.01–2014.12	580	878	I, II, III	Mix	OS, DFS, LR	8
8	Petit JY (10)	2008	Italy	European Institute of Oncology	Retrospective	1997.04–2001.12	518	159	I, II, III	Mix	DFS, OS	5
9	Siotos C (11)	2019	USA	Johns Hopkins Hospital	Retrospective	2003–2015	1,013	504	0, I, II, III	Mix	OS, RFS	7
10	Svee A (12)	2018	Sweden	Uppsala University	Retrospective	2000.01–2009.12	225	450	I, II, III	Autologous	OS, RFS	7
11	Adam H (13)	2018	Sweden	Karolinska University Hospital	Retrospective	1999.01–2013.12	254	729	0, I, II, III	Autologous	DFS, OS, CSS	8
12	Bezuhly M (14)	2015	Canada	Canadian Institute for Health Information + Nova Scotia	Retrospective	1989.04–2007.03	331	6,459	I, II, III, IV	Mix	CSS	4
13	Jiang YZ (15)	2013	China	Shanghai SEER Database	Retrospective	1998.01–2002.12	6,123	29,003	I, II, III	Mix	CSS, OS	8
14	Platt J (16)	2015	Canada	Toronto (Ontario Cancer Registry)	Retrospective	1980–1990	758	758	I, II, III	Mix	OS, CSS	7
15	Karadsheh MJ (17)	2021	USA	National Cancer Database	Retrospective	2004–2016	1,307	12,544	Inflammatory cancer (T4)	Mix	OS	6

SEER, Surveillance, Epidemiology, and End Results; UCSD-MCC, The University of California San Diego Moores Cancer Center; BR, breast reconstruction; BCSS, breast cancer-specific survival; OS, overall survival; DFS, disease-free survival; CSS, cancer-specific survival; LR, local recurrence; RFS, recurrence-free survival.

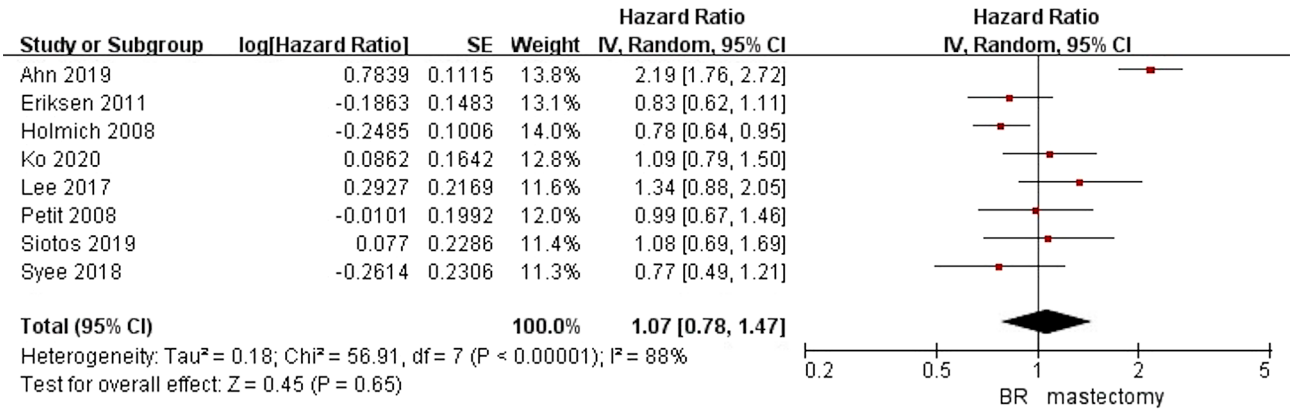

Figure 2 Forest plot of EFS, BR and mastectomy. SE, standard error; CI, confidence interval; EFS, event-free survival; BR, breast reconstruction.

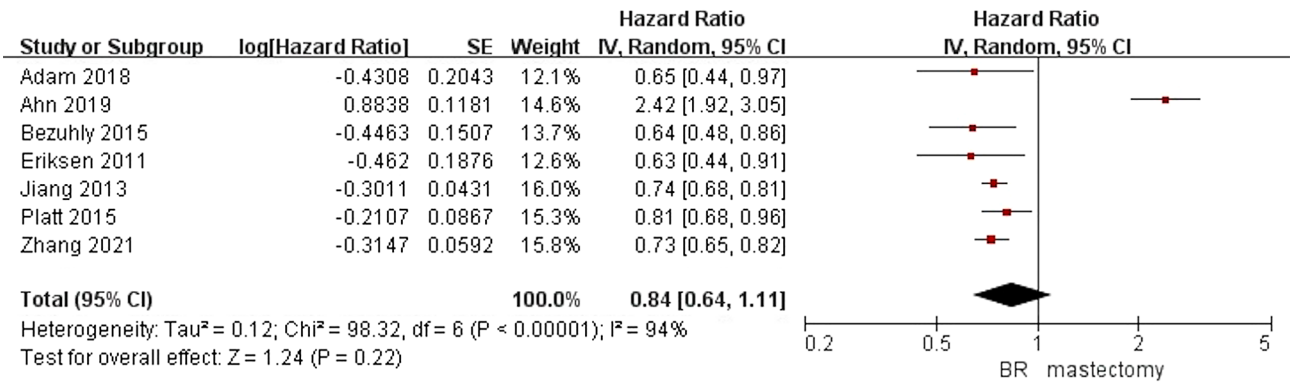

Figure 3 Forest plot of BCSS, BR and mastectomy. SE, standard error; CI, confidence interval; BCSS, breast cancer-specific survival; BR, breast reconstruction.

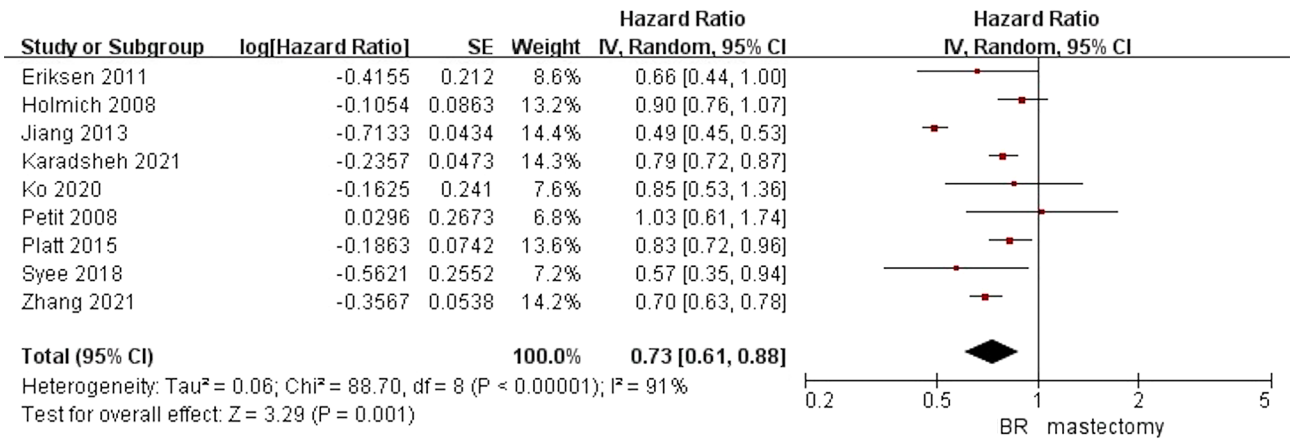

Figure 4 Forest plot of OS, BR and mastectomy. SE, standard error; CI, confidence interval; OS, overall survival; BR, breast reconstruction.

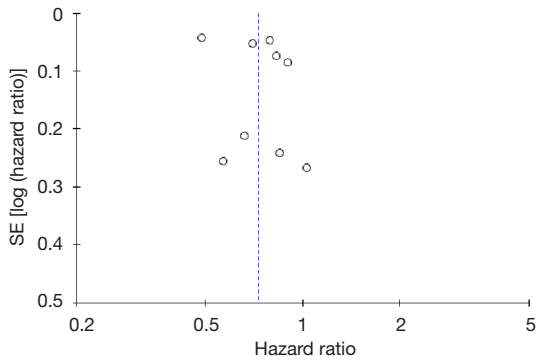

Figure 5 Funnel plot of OS, BR and mastectomy. SE, standard error; OS, overall survival; BR, breast reconstruction.

molecularly targeted therapy), which had significant impact on survival (15). Also, Zhang *et al.* (1) explained that reasons for a better prognosis for married breast cancer patients included greater financial resources, more timely treatments and more psychological support. It has also been documented that married patients express less depression and anxiety than unmarried patients after diagnosis of breast cancer, since a spouse can share the emotional burden and provide appropriate social support (1). Moreover, at long-term follow-up of >20 years, BR is comparable to mastectomy alone in terms of oncological safety (8). Our meta-analysis showed better OS with BR after mastectomy than with mastectomy alone. Similar to our results, another meta-analysis comparing the BR and mastectomy alone groups from an oncological point of view reported that no significant difference between EFS and OS (22-24).

The underlying reasons for these results may be physiological, immunological, and unmeasurable social influences. Patients in the BR group were more likely to be younger, lower Charlson comorbidity scores and had clinically or pathologically the early cancer, and had hormone-positive disease than those in the mastectomy alone group. Socioeconomic factors include access to medical institutions, family income and education level, private insurance benefits, and marital status. Women who meet the above conditions are more likely to receive medical treatments have a wide range of options for reconstruction counseling, education, and treatment, and have a high chance of survival due to the early detection of cancer recurrence. BR somewhat maintained patients' body image and improved their psychosocial life. This unmeasurable social influence may be supported by reports that patients with low psychological stress and high psychosocial support were less likely to have tumor progression and immune dysfunction (25) and may be a factor in improving survival outcome. In addition to, reconstruction did not influence the start of oncological treatment or given dosages and furthermore, tumor biology and systemic treatment rather than the surgical approach, may be more important factors in determining a patient's prognosis (1,3,7,8,12-17).

Our study was a systematic review of the available literature that examined EFS, BCSS, and OS in patients undergoing mastectomy with or without BR. This meta-analysis has several limitations. First, as non-English articles were excluded, the potential impact of language bias should also be considered. Second, all included studies were retrospective; therefore, a selection bias could not be ruled out. Lastly, only published studies were included when we searched the electronic databases, so potential publication bias in the studies could not be clearly ruled out, even though funnel plots did not show clear evidence.

Conclusions

We analyzed systematic reviews of the oncological prognosis of BR and mastectomy alone in patients with breast cancer. Our results suggest no significant difference between BR and mastectomy, even from early breast cancer to locally advanced breast cancer, after NACT for inflammatory breast cancer requiring multidisciplinary treatment. In the long-term follow-up of patients with breast cancer, no significant difference was observed in the oncological stability of BR after mastectomy compared with mastectomy alone. Moreover, BR after mastectomy has better OS than that of mastectomy alone. This finding implies that BR is a practicable and safe treatment option for patients with breast cancer.

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Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-706/rc

Peer Review File: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-706/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-706/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.

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