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REVIEW ARTICLE – BREAST ONCOLOGY

Saving the Male Breast: A Systematic Literature Review of Breast-Conservation Surgery for Male Breast Cancer

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ABSTRACT

Background. Male breast cancer (MBC) management is extrapolated from female BC. Mastectomy remains the most frequently used surgical procedure for male breast cancer (MBC). We performed a literature review to assess the use of breast-conservation (BCS) in MBC as well as outcomes following BCS.

Methods. A systematic literature was performed, and articles screened to identify studies that measured overall survival (OS), disease-free survival (DFS), or local recurrence (LR) in patients undergoing BCS. Weighted averages based on study size were performed for LR, DFS, and 5-year OS.

Results. Eight studies met the inclusion criteria with male breast surgery cases, and 859 (14.7%) underwent BCS. The mean follow-up time was 53 months, and mean age was 62.6 years, with stage II as the most common presentation. Two studies reported that 50–71.4% of patients underwent sentinel lymph node biopsy, and four studies reported axillary lymph node dissection in 14.3–100%. Five studies reported on adjuvant radiation therapy in 12.0–100% of total patients undergoing BCS. Four studies reported use of hormonal therapy in 73.8–100% of patients. Four studies reported use of chemotherapy in 25–66.7% of patients. Seven studies reported LR among 116 patients, with a weighted average of 9.9%. Three studies reported on DFS in 14 patients, with a weighted average 85.6%. Two studies report OS in 143 patients with a weighted average of 84.4%.

Conclusions. Breast conservation may be considered a safe alternative in the surgical treatment of MBC. Future research should focus on better standardization of local therapy for MBC and improved reporting of outcomes.

BACKGROUND

The American Cancer Society estimates that, in 2018, about 2550 men will be diagnosed with breast cancer and approximately 480 men will die from breast cancer.[1] Male breast cancer (MBC) is approximately 100 times less common than breast cancer in women, but an increase in incidence by approximately 26% has been observed in the past 30 years.[2] The lifetime risk of a man developing breast cancer is 1:1000, compared with 1 in 8 for a woman. This risk increases with age (with an average age of 67 years compared with 62 years for women), being twice as great in Afro-Caribbean men compared with Caucasians. The relatively low numbers of MBC have made large prospective trials challenging, and therefore understanding the management and surgical and oncologic outcomes is more difficult than breast cancer in women. There are no randomized controlled trials of male breast cancer, and much of what we know from male breast cancer is extrapolated from retrospective datasets. Men have limited involvement in breast cancer clinical trials.[3–5]

In the last 50 years, surgical management for breast cancer in women has evolved markedly from the Halsted mastectomy to less radical procedures including breast-

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conservation surgery (BCS). Numerous clinical trials for women with breast cancer have demonstrated no significant difference in survival between BCS and mastectomy.[4–6] In 2002, 20-year follow-up results for NSABP B-06 demonstrated no significant differences in disease-free survival, distant disease-free survival, or OS between the groups.[4] More recent 20-year follow-up data from the EORTC 10801 trial showed similar results in rates of time to distant metastasis and overall survival in patients with BCS versus mastectomy.[7] Surgical advances in breast cancer treatment for women have also evolved to include oncoplastic surgery and nipple-sparing mastectomy. In this setting, oncologic safety has been demonstrated in the setting of improved cosmesis and patient satisfaction.[8,9] Despite this strong evidence for women with breast cancer, this trend of breast conservation has not been seen in MBC. Most studies report rates of 3–12% of men undergoing BCS as surgical intervention for their breast cancer.[10–12]

In addition to the lower number of patients with this disease, this perceived lack of surgical "progression" may be in part due to the "perception" that male patients will develop breast cancer in an area of gynecomastia located in the retroareolar region, thereby necessitating mastectomy.[13] Whilst this is reasonable, no study has assessed the prevalence of nipple involvement in MBC. Breast-conservation surgery has been reported, albeit in smaller numbers, for men with breast cancer.

The purpose of this systematic review is to summarize the totality of evidence that evaluates oncologic outcomes for BCS for MBC. We performed a systematic literature review to assess overall survival (OS), disease-free survival (DFS), and local recurrence (LR) for MBC patients undergoing BCS.

METHODS

Study Selection

A search was conducted through the MEDLINE database using PubMed. Our search terms included "Breast Neoplasms, Male/analysis," "Breast Neoplasms, Male/statistics and numerical data," "Breast Neoplasms, Male/surgery." We filtered all articles from 1988 to 2018, selecting those containing the key terms "male," "breast'," "surgery," "operative surgical procedures," and/or "general surgery." A manual search of bibliographies of relevant articles was performed. All searches were conducted in January 2018. Abstracts were screened to identify studies that measured OS, DFS, or LR in patients undergoing BCS.

Data Extraction

Two investigators performed the search, independently screened articles pertaining to male breast surgery using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and extracted data from each study. Discrepancies in coding required agreement between authors in order to be considered resolved.

Definitions of Outcomes of Interest

Included studies reported at least one of the following outcomes:

- *Overall survival (OS)* Patients in the study who were alive from time of surgery to date of last follow-up.
- *Disease-free survival (DFS)* Patients in the study who were alive from time of surgery to date of last follow-up without development of local or distant disease recurrence or new breast tumor.
- *Local recurrence (LR)* Cancer that recurred in the ipsilateral breast, chest wall, or lymph nodes following surgery and prior to date of last follow-up.

Inclusion and Exclusion Criteria

Studies were selected based on the following inclusion criteria: (i) reporting on male patients undergoing breast-conservation surgery in the setting of breast cancer (invasive and ductal carcinoma in situ); (ii) reporting OS, DFS, and/or LR; and (iii) available in English or Spanish. Studies were excluded due to any one of the following criteria: (i) review articles; (ii) articles reporting only on mastectomy patients (i.e., radical, modified radical, or simple); (iii) articles reporting only on surgical technique; (iv) articles reporting on BCS that does not involve outcomes of interest; (v) articles describing studies that included fewer than five patients, and (vi) database studies could not overlap time period.

Statistical Analysis

For all studies, we report one or more of the primary outcomes of interest (OS, DFS, and LR). We further determined the weighted average, based on the number of patients in each study, thus placing greater emphasis on larger studies, to provide descriptive statistical analysis of OS, DFS, and LR. In addition, we extracted the study type (retrospective versus prospective), number of cases, mean age, mean follow-up time, stage, lymph node surgery, use of adjuvant radiotherapy, and use of adjuvant hormone therapy and chemotherapy.

RESULTS

The literature search yielded 4341 articles (Fig. 1). Eight studies published from 1998 to 2016 met the inclusion and exclusion criteria and were selected for systematic literature review.[12,14–20] All studies were prospective by study design. Table 1 provides the baseline characteristics of studies selected for systematic literature review.

Data were extracted from the eight studies that collectively evaluated 859 patients who underwent BCS out of a total cohort of 5864 patients (rate of BCS = 14.7%). The mean age of these patients was 62.6 years. Follow-up ranged from 23 to 74 months with mean of 53.0 months. The majority of patients had stage II breast cancer in four of the five studies that reported on clinical stage. Two studies reported that 50–71.4% of patients underwent sentinel lymph node biopsy, and four studies reported axillary lymph node dissection in 14.3–100%. Five studies reported that adjuvant radiation therapy was administered in 12.0–100% of 64 total patients undergoing BCS. Four studies reported use of hormonal therapy in 73.8–100% of patients. Four studies reported use of chemotherapy in 25–66.7% of patients.

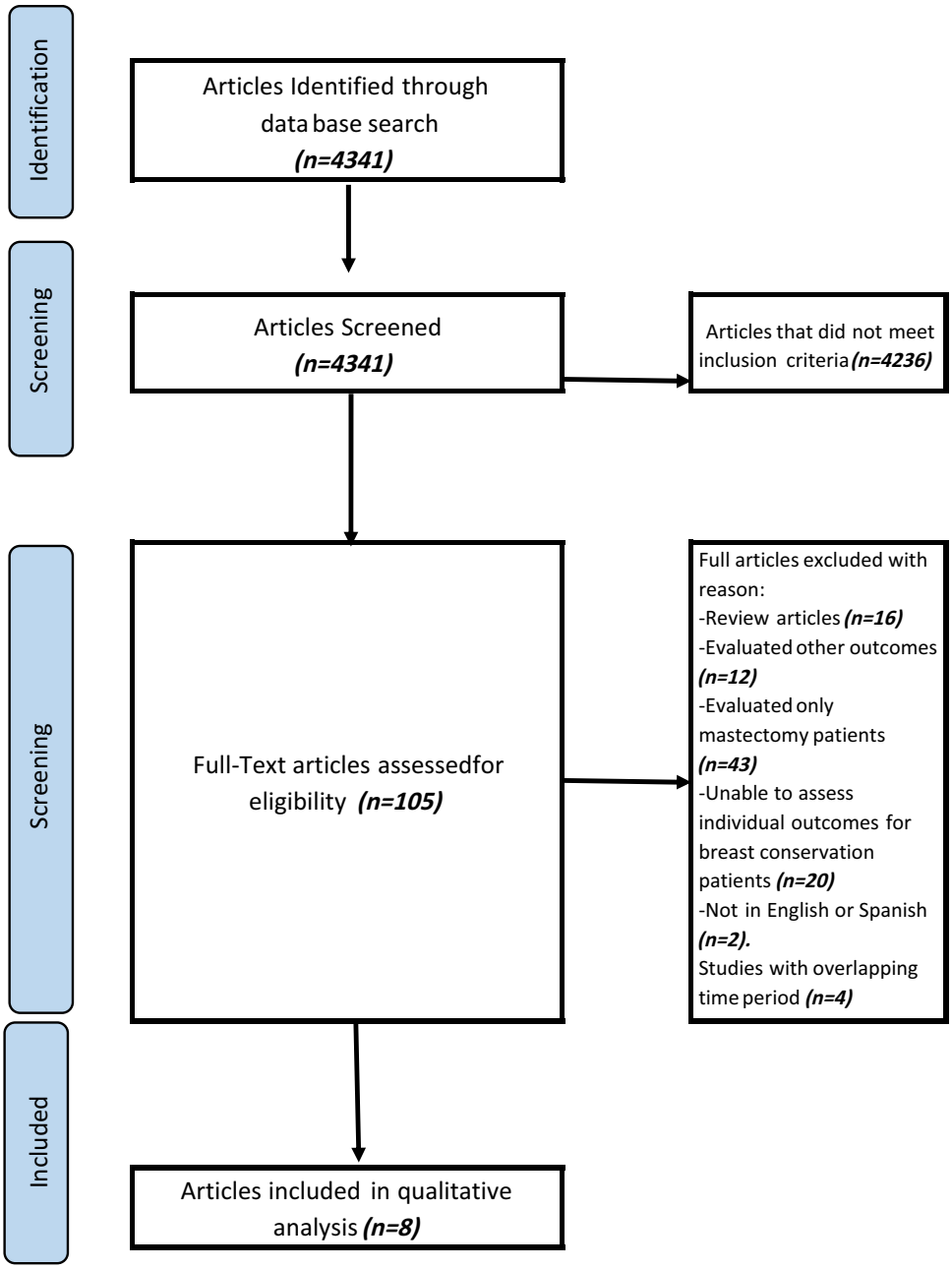

FIG. 1 Flow chart of literature review

TABLE 1 Baseline study characteristics

Study (year published)	Study years	Total no. of patients (*n*)	Number of BCS cases (*n*)	Mean age (years)	Mean follow-up (months)	Most common stage	Sentinel lymph node biopsy (*n*, %)	Axillary lymph node dissection (*n*, %)	Chemotherapy (*n*, %)	Radiation therapy *n* (%)	Hormonal therapy (*n*, %)
Bratman[14] (2012)	1960–2011	41	4 (9.8%)	65.5	23	I&II	2 (50%)	1 (25%)	1 (25%)	4 (100%)	3 (75%)
Cloyd[12] (2013)	1983–2009	4707	718 (15.3%)	–	54	I	–	–	–	–	–
Cutuli[15] (2010)	1990–2005	489	42 (8.6%)	66	58	–	–	–	–	–	31 (73.8%)
Cutuli[16] (1995)	1960–1986	397	49 (12.3%)	64	74	–	–	29 (59.2%)	–	49 (100%)	–
Golshan[17] (2007)	1996–2006	7	7 (100%)	61	67	II	5 (71.4%)	1 (14.3%)	3 (42.9%)	6 (85.7%)	6 (85.7%)
Selcukbiricik[18] (2013)	1973–2010	86	11 (12.8%)	62	66	II	–	11 (100%)	–	–	–
Serarslan[19] (2015)	1994–2014	16	3 (18.8%)	59.8	–	II	–	–	2 (66.7%)	2 (66.7%)	3 (100%)
Yildirim[20] (1998)	1972–1994	121	25 (20.7%)	60	29	–	–	–	12 (48%)	3 (12%)	–

TABLE 2 Oncologic outcomes of interest

Study (year published)	No. of BCS cases (*n*)	Local recurrence (%)	Disease-free survival (%)	5-Year overall survival (%)
Bratman[14] (2012)	4	0	100	–
Cloyd[12] (2013)	718	–	–	87.3
Cutuli[15] (2010)	42	5	–	–
Cutuli[16] (1995)	49	16.3	–	–
Golshan[17] (2007)	7	0	85.7	–
Selcukbiricik[18] (2013)	11	12.4	–	–
Serarslan[19] (2015)	3	0	66	–
Yildirim[20] (1998)	25	–	–	0
Weighted average		9.9	85.6	84.4

Table 2 demonstrates the oncologic outcomes of interest for this study. Seven studies reported LR among 116 patients, with a weighted average of 9.9%. Three studies reported DFS of 85.6% in 14 patients. Two studies reported on 5-year OS in 743 patients with a weighted average of 84.4%.

DISCUSSION

In the modern era of breast cancer treatment, it is increasingly apparent that oncologic safety is more strongly associated with factors inherent to the patient and tumor biology than surgical approach.[21] Likely secondary to low incidence and potential pathologic factors, the deescalation of breast surgical intervention in men has not materialized, with most men receiving a mastectomy for the treatment of their breast cancer. Given the data in female patients and push from MBC to preserve healthy tissue, we should reevaluate this surgical paradigm. Increased emphasis of this is evidenced by the EORTC 10085/Translational Breast Cancer Research Consortium/ Breast International Group/North American Breast Center Group International Male Breast Cancer Program, which reported on 1046 men with nonmetastatic breast cancer from 1990 to 2010 and noted a 4% rate of BCS.[22] The goal of this program/trial is to gather medical information and tumor samples from patients with MBC. With both a retrospective collection and prospective registry, the group hopes to alleviate some of the challenges of this low-incidence disease and provide better standardization of care.

Amongst the studies reported here, we found relatively high rates of DFS and relatively low rates of LR; of the two studies that reported OS, one reported an OS that was relatively high for MBC patients undergoing BCS. Furthermore, the LR and DFS rates demonstrated in our review are comparable to those found among women treated with BCS. The BCS rate was 14.7% in this selected group of patients. While still low, it does demonstrate feasibility of this approach in certain patients. Additionally, radiotherapy should be offered according to guidelines developed for women with breast cancer, but radiotherapy is often underused in men with breast cancer.[22,23]

The authors acknowledge that this review has inherent limitations. Many of the studies that were included had missing datasets with respect to tumor characteristics and use of adjuvant therapy that may impact oncologic outcomes such as use of radiation in BCS. In addition, there were no data on margins for evaluation of LR. The use of observational data also introduces confounding factors, including patient demographics, genetic predisposition, tumor size and location, nodal status, hormonal status, and neoadjuvant and/or adjuvant therapy, that may bias oncologic outcomes in certain studies but cannot be accounted for in a systematic review. Finally, the methodology utilized in a systematic review that includes many retrospective studies is not adequate to determine causality.

Our study has a number of strengths. Through rigorous literature review, we have identified, synthesized, and assessed all available evidence to demonstrate the totality of evidence and oncologic safety of BCS for MBC. The current study is the largest comprehensive literature review to date on BCS for MBC, evaluating a large representative sample of 859 patients in eight studies. These results are generalizable to males with breast cancer and highlight the importance of further discussion to assess the recommendations of BCS in this patient population.

Future work is required to improve the knowledge gaps in the treatment of MBC, and to prevent undertreatment in these patients. This is currently being done by groups such as the International Male Breast Cancer Program, a global consortium of investigators focused on MBC research. Our systematic literature review suggests that BCS is an oncologically safe treatment option in carefully selected patients, enabling breast conservation without compromising LR or DFS in patients with MBC. There remains a paucity of data highlighting the percentage of men that may be eligible for this procedure.

AUTHOR'S CONTRIBUTION L.C., C.F., and P.T. conceptualized and designed the project. L.C., S.J., and T.J. performed data acquisition. S.B. performed data analysis. L.C. performed interpretation and drafted the initial manuscript. L.C., C.F., S.J., T.J., and P.T. assisted in critical revision of the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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