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Breast Conserving Surgery Compared to Mastectomy in Male Breast Cancer: A Systematic Review

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Abstract

Background: Current surgical guidelines for male breast cancer (MBC) are predominantly influenced by clinical trials consisting of only female participants. As no clinical trial has been conducted for the surgical treatment of MBC, we sought to perform a systematic review to compare disease-free (DFS), disease-specific (DSS), and overall survival (OS) between MBC patients undergoing breast conserving surgery (BCS) versus mastectomy and to evaluate radiotherapy compliance among male BCS patients.

Methods: We performed a systematic search of electronic databases, including MBC cohort studies reporting at least one survival outcome (DFS, DSS, or OS) by surgical treatment (BCS and/or mastectomy) and/or radiotherapy compliance with BCS.

Results: One prospective and nine retrospective cohort studies were included, with the number of patients ranging from 7 to 6,039. Among BCS patients, compliance with postoperative radiotherapy was low (rates ranged from 27–46%), with the exception of one single institution prospective study that reported 86% (n=6) compliance. Pooled estimates for all MBC patients was 83% (95%CI 78–88%) for 5-year DSS and 66% (95%CI 63–70%) for 5-year OS. Most studies reported no difference in DFS, DSS, or OS for BCS and mastectomy.

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CAMS: study conception and design; performed article search, reviewed titles, abstracts, and full-text articles; performed data abstraction and interpretation of data; initial manuscript writing, revisions, and final approval of manuscript;

SBB: study conception and design; performed article search, reviewed titles, abstracts, and full-text articles; performed data abstraction, statistical analysis, and interpretation of data; initial manuscript writing, revisions, and final approval of manuscript;

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Conclusions: BCS is a reasonable treatment approach in MBC as it was associated with similar oncologic outcomes to mastectomy. However, low rates of radiotherapy compliance among male BCS patients is concerning and highlights the importance of shared decision-making with MBC patients when selecting a surgical treatment strategy.

Introduction

Male breast cancer (MBC) is a rare and understudied cancer, accounting for less than 1% of all breast cancers.(1) Thus, no single institution can comprise enough patients to guide therapy. Current National Comprehensive Cancer Network Guidelines recommend clinicians treat men similar to postmenopausal women, implying that breast conservative surgery (BCS) and mastectomy are equivalent local therapy based on the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-06 data.(2, 3) However, NSABP B-06, and the majority of breast cancer trials, include only female patients. Therefore, the primary objective of this study was to perform a systematic literature review to determine if BCS is associated with equivalent survival to mastectomy in MBC patients. Secondary objectives were to evaluate compliance with BCS and survival rates among MBC patients.

Methods

We performed this systematic review according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. MEDLINE/Pubmed, Cochrane Library, and ClinicalTrials.gov, searches were performed, with the last search performed April 2017, using the combination of terms: *male*, *invasive ductal carcinoma* and *breast* or *breast cancer*, and *breast conserving therapy* or *treatment* or *surgery*. We also reviewed reference titles from review articles, which were incorporated into our review. Two reviewers performed the article search, reviewed titles, abstracts, and full-text articles, and performed data abstraction. Discrepancies were resolved by a third reviewer and discussion with consensus.

Inclusion criteria consisted of retrospective and prospective cohort studies and clinical trials with >5 adult male patients (≥18 years of age) with breast cancer reporting either BCS compliance with radiotherapy and/or survival outcomes (disease-free (DFS), disease-specific (DSS), or overall survival (OS)). To be included, survival outcomes were either stratified by surgical approach or the entire cohort only underwent one surgical approach. We included only studies with patient cohorts from Western countries due to differences in breast cancer screening, surgical treatment, and prognosis between Eastern and Western countries.(4) We excluded case reports with ≤5 MBC patients and studies with only in-situ disease, lobular carcinoma, or Paget's disease cohorts and/or the only surgery performed was radical mastectomy. Articles in non-English languages, review articles, editorials, letters, commentaries, and conference abstracts were excluded. Articles with study periods occurring entirely prior to 1985 (year NSABP B-06 results were first published) were also excluded.(3)

Quality assessment was performed using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (https://www.nhlbi.nih.gov/health-topics/

study-quality-assessment-tools). Five studies were rated of good quality, while the remaining five were rated fair.

Statistical Analyses

Pooled estimates of 5-year DSS and OS wit 95% confidence intervals were calculated using the meta-analytic random effects model. Statistical heterogeneity was assessed with I^2. We were unable to compare survival by treatment as only two heterogeneous studies reported this data. Statistical analysis was performed using Stata 13.1 (College Station, TX).

Results

As shown in Figure 1, we identified 2,507 articles from the database search and 106 articles from review articles. After excluding duplicates, 2,555 titles/abstracts were screened. Most (n=2,403) were not relevant and excluded. The remaining 152 articles underwent full-text review, of which 142 were excluded based on inclusion/exclusion criteria. Data extraction was performed on the remaining 10 articles. As two articles included the same patient cohort from the same data source and time-period, they were reported as one study.(5, 6) The final qualitative analysis of these 10 articles consisted of 9 studies.

The 9 included studies with corresponding cohort characteristics are described in Table 1. The articles were published from 1995 to 2016, with 5 from the US and 4 from western Europe. Study periods, from which patients were diagnosed and/or treated, ranged from 10- to 50-years (median 25 years), with sample sizes ranging from 7 to 6,039 patients. All studies with patient cohorts ≥1000 (n=4) were from Surveillance, Epidemiology, and End Results (SEER).(5–9)

Postoperative radiotherapy was reported in 8 studies, ranging from 14–86%.(5–13) Among BCS patients, most studies reported low rates of radiotherapy compliance ranging from 27–46%, with the exception of a single institution prospective cohort study (n=7) reporting 86% compliance.(5, 6, 9, 11, 13) Post-mastectomy radiotherapy rates ranged from 8–61%.(5, 6, 9, 11, 12)

As shown in Figure 2, pooled estimates for all MBC patients was 83% (95%CI 78–88%) for 5-year DSS and 66% (95%CI 63–70%) for 5-year OS. Cloyd et al. reported 5-year DSS of 87% for BCS and 88% for mastectomy, while Zaenger et al., which included only stage I & II disease, reported 97% 5-year DSS for BCS and 95% for mastectomy.(5, 6, 9) After adjusting for age, race, stage, histologic grade, and radiotherapy, Cloyd et al. observed no significant differences in DSS for BCS and mastectomy (aHR 1.09, 0.87–1.37). Madden et al. also found no difference in DSS for BCS and mastectomy in an unadjusted SEER analysis.(7) Interestingly, O'Malley et al., also using patients abstracted from SEER, stratified their survival analyses by race and was the only study to observe worse DSS among both Caucasian and Black patients who underwent BCS compared to mastectomy (although BCS was compared to only modified radical mastectomies) after adjusting for age, year of diagnosis, stage, histology, and radiotherapy (Caucasian: aHR 1.6, 95%CI 1.2–3.0; Black aHR 3.9, 95%CI 1.6–9.7).(8)

Cloyd et al. was the only study to report 5-year OS for BCS, which was 66%, while 5-year OS for mastectomy, reported by Cloyd and Yu et al., ranged from 70–74%.(5–7, 12) Cloyd observed worse OS for BCS compared to mastectomy in univariate analysis (HR 1.18, 95%CI 1.04–1.33), which was no longer significant on multivariable analysis after adjusting for age, race, stage, grade and radiotherapy (aHR 1.12, 0.98–1.27). Interestingly, Madden and Ribeiro et al. found no differences in OS for BCS and mastectomy in their unadjusted analyses.(7, 14) However, O'Malley et al. described worse OS among both Caucasian and Black patients who underwent BCS compared mastectomy (specifically modified radical mastectomy) in their multivariate analyses controlling for age, stage, histology, year of diagnosis, and radiotherapy (Caucasian: aHR 1.9, 95%CI 1.4–2.5; Black aHR 2.2, 95%CI 1.1–4.4).

Local recurrence or DFS were reported in three studies.(10, 11) Cutuli et al. observed no difference in local recurrence rates for BCS and mastectomy, with local recurrence rates of 16% and 6% for BCS and mastectomy patients respectively (p=0.06). Stierer et al. also reported no difference in local recurrence for BCS and mastectomy (p=0.09). For stage I disease, Ribeiro et al. observed greater 5-year DFS for BCS (all underwent radiotherapy) patients (78%) compared to simple mastectomy alone patients (45%), although the DFS for mastectomy with radiotherapy patients (77%) was similar (p=0.0002).

Discussion

In this systematic review of MBC cohort studies, the 5-year DSS and OS survival were equivalent for mastectomy and BCS. These findings suggest BCS is a reasonable treatment approach in MBC. However, low rates of radiotherapy compliance among male BCS patients is concerning and highlights the importance of shared decision-making with MBC patients when selecting the most optimal, realistic treatment strategy.

Importantly, this review highlights the need for a multicenter prospective evaluation of the MBC population as we identified lower rates of 5-year DSS and OS compared to female patients included in NSABP B-06.(3) This may signify distinct biological gender difference in breast cancer as shown in a recent study by Massarweh et al. who found higher 21-gene breast cancer recurrence risk scores and worse survival among men compared to women.(15) Therefore, based on these known gender differences, there is a present need for multicenter prospective clinical trials in men comparing surgical therapy to better understand if BCS and mastectomy may truly be considered equivalent in this population.

In conclusion, based on retrospective cohort analyses, BCS and mastectomy are comparable surgical treatments for MBC; however, further MBC trials are warranted.

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Availability of data and materials:

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

List of Abbreviations:

NIH	National Institute of Health
MBC	Male breast cancer
DFS	Disease Free Survival
DSS	Disease Specific Survival
OS	Overall Survival
BCS	Breast conserving surgery
NSABP B-06	National Surgical Adjuvant Breast and Bowel Project B-06
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
SEER	Surveillance, Epidemiology, and End Results
US	United States
UK	United Kingdom
VA	Veterans Affairs
IS	in situ
ER	estrogen receptor
PM	postmastectomy
PPM	post partial mastectomy
NR	Not reported
CI	Confidence interval

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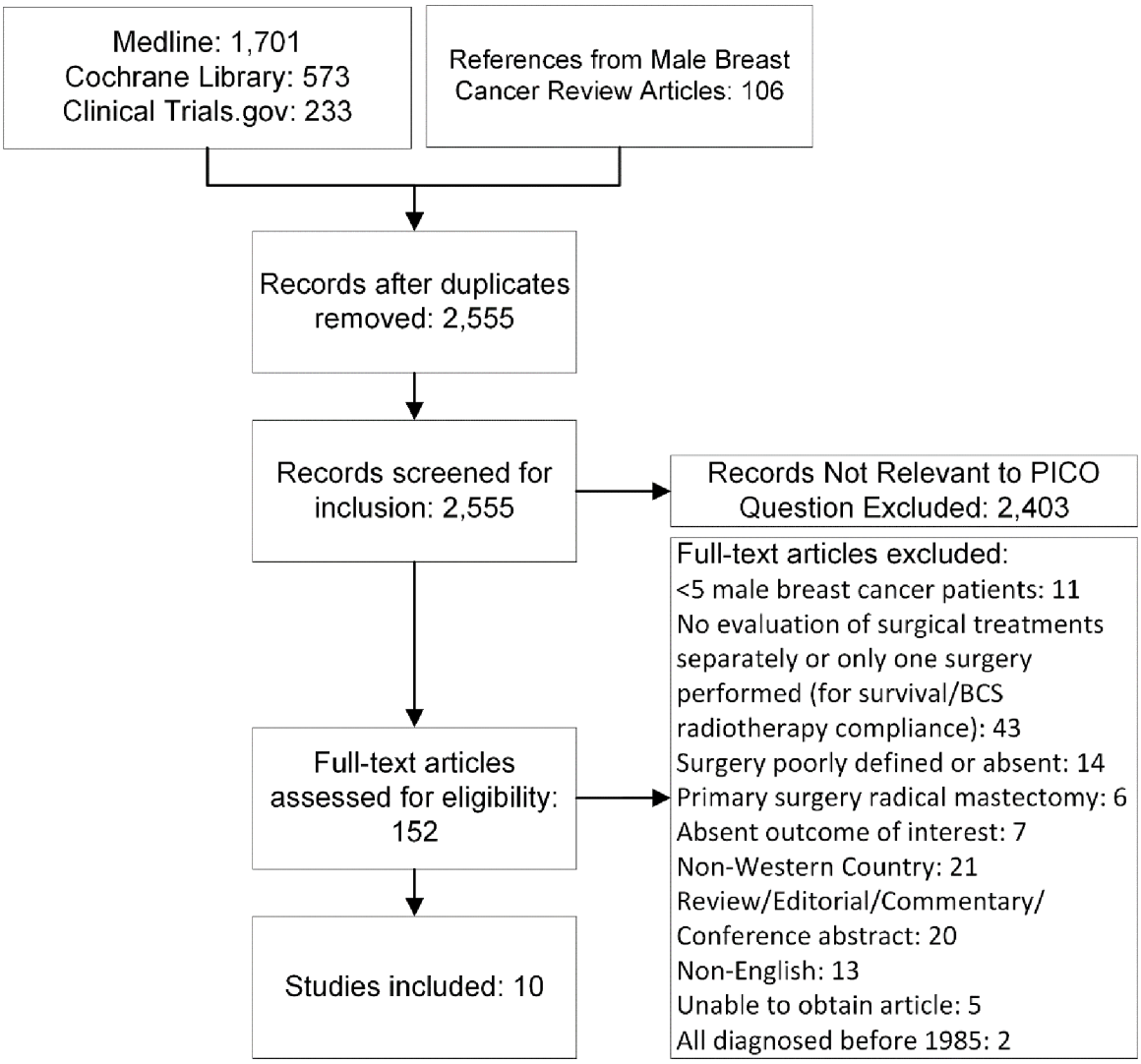

Figure 1.
Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Diagram.

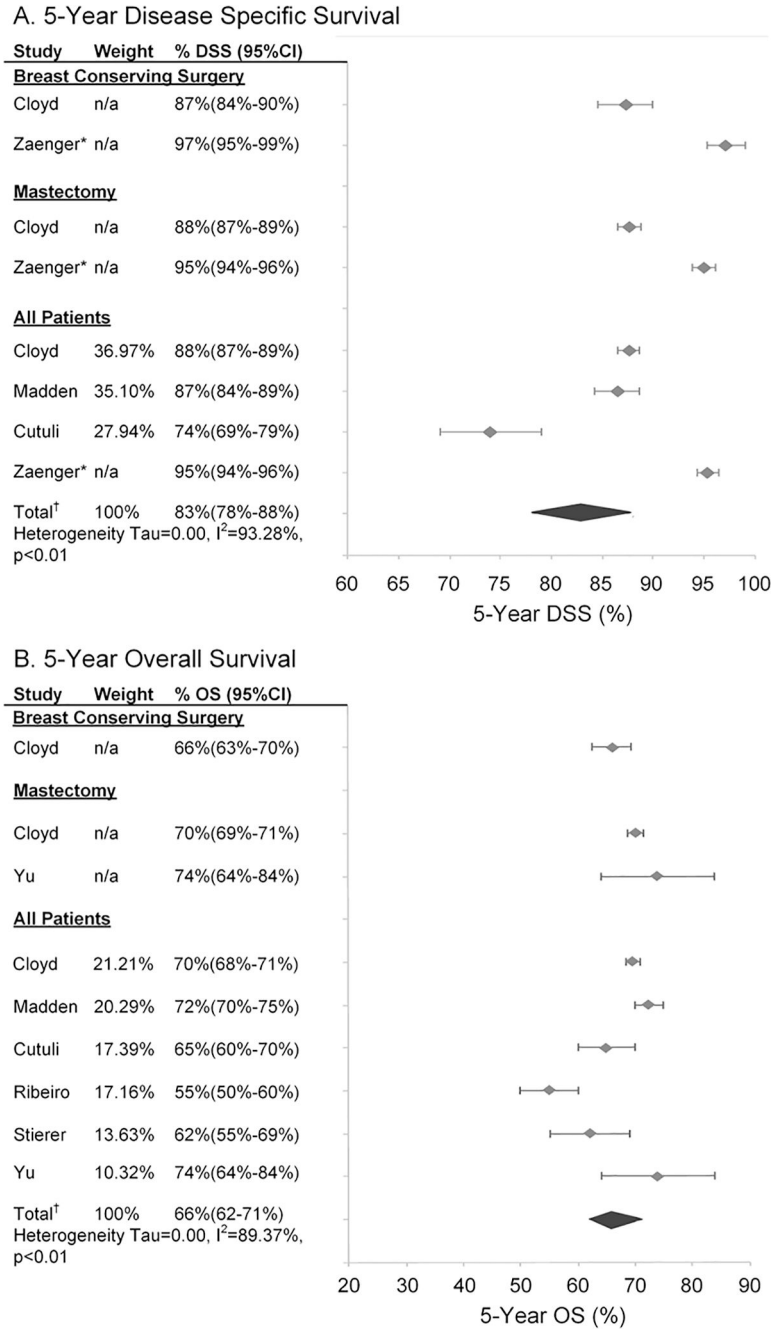

Figure 2A/B.

Disease specific (DSS, A) and Overall Survival (OS, B) at 5 years for breast conserving surgery, mastectomy, and all patients. *Patients only included stage I and II disease and therefore excluded from total estimated DSS. † Pooled survival estimates for all patients only.

Table 1.

Description of studies and patient cohorts.

Author	Country	Data Source	Study Period	Patients N	Age Range (years)	Stage Distribution N (%)	ER/PR Positive Status N (%)	BCT N	Mastectomy† N	Hormone N (%)	Radiation N	Chemo N
Madden et al. (7)	US	SEER	1983–2002	1,337	27–95	I 432 (34%) II 666 (53%) III 119 (10%) IV 36 (3%)	ER: 915 (94%) PR: 786 (83%)	113	1,205	NR	All: 329 (25%)	NR
Yu et al.(12)	UK	London Regional Cancer Program	1977–2006	81	35–87	I 15 (20%) II 49 (53%) III 20 (27%) IV 6 (8%)	ER: 62 (98%) PR: 53 (87%)	0	75	43 (57%)	PM: 46 (61%)	9 (12%)
O'Malley et al.(8)	US	SEER	1973–1997	1,979	10–103	N/a	ER: 399 (89%) PR: 343 (79%)	183	1,142	NR	All: 392 (20%)	NR
Cutuli et al. (10)	France	14 French Cancer Centers	1960–1986	397	25–93	N/a	ER: 83 (79%) PR: 81 (77%)	49	268	68 (17%)	All: 214 (54%)	71 (18%)
Golshan et al. (13)	US	Brigham and Women's and Massachusetts General Hospital	1996–2006	7	38–86	IS 1 (14%) I 1 (71%) II 5 (14%)	ER: 6 (100%) PR: 5 (83%)	7	0	6 (86%)	PPM: 6 (86%)	3 (43%)
Zaenger et al. (9)	US	SEER	1998–2011	1,777	N/a	I 1,165 (66%) II 612 (34%)	ER: N/a PR: N/a	296	1,481	NR	All: 254 (14%) PPM:135(46%) PM: 119 (8%)	NR
Cloyd et al.(5, 6)	US	SEER	1983–2009	5,425	N/a	IS 10 (0.2%) I 1,671 (36%) II 2,217 (47%) III 602 (13%) IV 196 (4%)	ER: 3,792 (94%) PR: 3,275 (83%)	718	4,707	NR	All:1,231 (23%) PPM:254(36%) PM:997 (21%)	NR
Stierer et al. (11)	Austria	36 Austrian Surgical Dept.	1970–1991	169	30–87	IS 8 (5%) I 39 (23%) II 59 (35%) III 43 (26%) IV 18 (11%)	ER: 46 (78%) PR: 37 (70%)	22	133	16 (9%)	All: 67 (40%) PPM: 6 (27%) PM: 61 (41%)	22 (13%)
Ribeiro et al. (14)	UK	Christie Hospital	1941–1991	420	27–95	I 210 (50%) II 49 (12%) III 122 (29%) IV 39 (9%)	ER: 75 (87%) PR: 64 (74%)	29	169	NR	NR	NR

US, United States; UK, United Kingdom; VA, Veterans Affairs; Dept, Department; SEER, surveillance, epidemiology, and end results program; IS, in situ; ER, estrogen receptor; PM, postmastectomy; PPM, post partial mastectomy; NR, Not Reported; *BCS patients only

†Modified radical and simple mastectomy only.