

Trends in Breast-Conserving Surgery in Male Breast Cancer in the United States

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Abstract

Background: Male breast cancer (MBC) is a rare disease, comprising only 1% of all incidents of breast cancer diagnosed in the United States. Most of the treatment strategies for male breast cancer are based on the studies of female breast cancer and modified radical mastectomy (MRM) remains the standard of care for virtually all the MBC cases. Breast-conserving surgery (BCS) in MBC has been coming to the forefront as a reasonable treatment option. We elected to compare surgical outcomes between BCS and MRM in male breast cancer.

Methodology: National Surgical Quality Improvement Program (NSQIP) database was analyzed for the year 2015. We reviewed all male breast surgical patients. Mastectomy for gynecomastia, simple mastectomy, and radical mastectomy was excluded from analysis. Partial mastectomy (with and without) axillary lymph node biopsy were compared to MRM. Chi-square and independent t-tests were used to compare the two variables for demographics, comorbidities, and postoperative complications.

Results: A total of 175 patients underwent breast surgery for MBC in 2015. BCS was performed on 101 males (57.7%) and MRM was performed on 74 (42.3%). Patients that underwent MRM were older than the patients that underwent BCS (57 versus 66 years, respectively) ($P < 0.0001$). Comorbidities were overall similar in both groups. Postoperative complications were overall not statistically different. Patients that underwent BS had shorter length of hospital stays ($P < 0.0001$) and were more likely to have been operated on under MAC or IV sedation (14.85% vs 0%) ($P < 0.0001$).

Conclusion: BCS in male breast cancer is frequently performed in the United States with similar surgical outcomes and shorter length of stay as MRM.

Keywords: Male Breast Cancer (MBC); Modified Radical Mastectomy (MRM); Breast-Conserving Surgery (BCS); National Surgical Quality Improvement Program (NSQIP)

Introduction

Breast cancer in males is rare comprising of less than 1% of all breast cancers and less than 1% of all male cancers [1]. Over the past 25 years, there has been a 26% increase in male breast cancer (MBC) cases. The median age at diagnosis is typically 67, compared to 62 in females [1]. The cases of male breast cancer reported, indicates that the disease is highly related to the progressing age i.e. it increases slowly from 0.1% at the age of 35 - 39 to 11.1% at the age of 85 and above, further studies showed that it is extremely rare in male children [2].

MBC has many similarities to female breast cancer (FBC). The MBC and FBC have shown a similar rate of incidence with almost similar risk factors, indicating a common etiology. Incidence rates are higher in North America and Europe and lower in Asia, Japan, and Finland [2,3]. Just like in FBC, MBC is associated with an endocrine component, family history of breast and ovarian cancer, bone fractures, obesity, and genetic mutations. Prostate cancer treatment in males and hormone replacement therapy for transsexual males have been associated with higher incidence of breast cancer [4,5]. The differences in breast cancer between two genders are tumor size, age at diagnosis, delay in the result of the treatment and number of lymph nodes affected [6]. However, this is likely due to rarity of the disease and no screening procedures established for breast cancer in males.

Incidence rate of MBC increases linearly with age, while FBC has a bimodal distribution with peaks at early onset before the age of 40 and late-onset breast cancer [7]. The tumor suppressor gene, BRCA2, is more commonly associated with MBC, while BRCA1 is more commonly associated with FBC [8-13]. BRCA2 mutations in men as compared to BRCA1 mutations, leads to an increased risk of breast cancer (up to 10%), prostatic cancer, and pancreatic cancer [14]. It is more common in black men than white men and presents more aggressively with a larger tumor size and higher rates of nodal involvement [7].

Klinefelter syndrome, which consists of an extra X chromosome in a male, increases the risk of MBC 20-50 times [15,16]. The syndrome is characterized by testicular dysgenesis, gynecomastia, low testosterone, and elevated gonadotrophin levels. Other risk factors include testicular abnormalities from mumps orchitis, undescended testicles, congenital inguinal hernia, lack of exercise, infertility, exposure to radiations at the workplace, working in a perfume or cosmetic industry where men are exposed to estrogen-containing creams and products, or a high-temperature working environment experienced by steel mills, rolling mills, and blast furnace workers [2,17,18].

Clinical assessment, imaging, and biopsy are the standard to diagnose MBC. MBC typically presents as a unilateral painless palpable mass in a central sub-areolar location with early nipple involvement [19]. The left breast is more commonly involved, as is the case in FBC [1]. However, the location varies i.e. in men palpable mass is present directly beneath the nipple whereas in women it is present in the upper quadrant. This clinical presentation is by far the most common indication for the male breast cancer [2]. Ultrasound and mammography are the imaging tests of choice because they can detect the presence of carcinoma in early stages especially in men with discharge (blood) producing nipples and it also helps in avoiding invasive techniques and biopsies [20]. Cytologic techniques, such as fine needle, core or excision biopsies, have high specificity and sensitivity and help in staging the disease. Similar to FBC, the most common histopathology is invasive ductal carcinoma 85 - 90% of the time [21,22]. Tumor biology studies for Estrogen receptor, Progesterone receptor, HER2 and genetic testing for BRCA mutations have all become standard workup for MBC. Similarly, genetic testing should be performed on most patients to screen mutations in tumor suppressor genes like BRCA1 and BRCA2.

Standard treatment for localized MBC involves surgery. Surgical approach depends on the degree of tumor size and chest wall invasion. Options include radical mastectomy, modified radical mastectomy (MRM), simple mastectomy with sentinel lymph node biopsy (SLNB) and breast conserving surgery (BCS) with SLNB. MRM involves complete removal of the breast and axillary levels 1 and 2. In BCS, also known as lumpectomy, only cancer-containing breast tissue is removed; and SLNB is used for axillary nodal assessment. BCS is less commonly used because there is less breast tissue in males and diagnosis usually occurs at an advanced age. Since, MBC usually presents with larger tumors and higher rates of the chest wall and retro-areolar infiltration that necessitate MRM [23]. Some studies have reported lower rates of recurrence with MRM, which remains the standard treatment of choice. However, new data has emerged that breast conserving surgery in MBC should be considered an option in patients without overt nipple/areolar involvement. No study exists that depicts trends in breast conserving surgery in MBC in the United States.

Aims and Objectives

The aim of this study is to find out the trends in the United States with which male breast cancer is treated with breast conserving surgery. The secondary aim of this study is to compare the surgical outcomes of BCS vs MRM for the treatment of MBC.

Methodology

Data collection

The American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) is a national blinded, risk-adjusted database, containing data from participating hospital on morbidity and mortality and operative outcomes. A total of 517 hospitals participated in the NSQIP program in 2015 with 750,397 cases submitted. The data is populated directly from the patient's medical chart and not insurance claims. It provides the participating hospitals with the tools to improve their surgical care quality, reduce the number of complications and acts as a national benchmark for each participating hospital. The data collected involves different surgical specialties preoperative risk factors, intraoperative variables, and postoperative morbidity and mortality tracked over 30 days. ACS-NSQIP data is obtained by trained surgical clinical reviewers from the patient's electronic medical record and is risk-adjusted, and case-mix-adjusted. The database was deemed exempt from Institutional Review Board approval at our institution.

Our study focused on all male breast surgical patients and isolated postoperative diagnosis of breast cancer for all patients (ICD-9 code 174.9). Mastectomy for gynecomastia, simple mastectomy, and radical mastectomy were excluded from analysis. Breast Conserving Surgery or Partial mastectomy (with and without) axillary lymph node biopsy were compared to MRM. Two types of data set were collected - The first one comparing the demographical factors of the patients receiving the two surgeries and the second data set was based on the post-operative variables. Demographical factors such as age, race, weight, comorbidities (ESRD, CHF, DM-2 and more) and type of patients (in-patient or out-patient) were analyzed and compared. Similarly, postoperative factors including hospital stay after the surgery, operation time, open wound infections and superficial infections were compared.

Data analysis

Statistical analysis was performed utilizing IBM SPSS software, V.22.0 (SPSS, Armonk, New York, USA). Continuous variables were analyzed utilizing ANOVA. Whereas Independent T-Test and Chi-Square test were used to analyze categorical variables after accounting for homogeneity of data and removing missing data and outliers. Homogeneity was confirmed utilizing histogram plots. Statistical significance was set at p-value of 0.05. Breast Conserving Surgery (BCS) was compared to Modified Radical Mastectomy (MRM) which is a current standard of care for male breast cancer treatment.

Missing data analysis

SPSS was used to run a missing value analysis. No pattern to missing data was detected and a listwise deletion was performed. Data was also analyzed for homogeneity. It was found to be homogeneous with minimal outliers.

Results

A total of 175 patients underwent breast surgery for MBC in 2015. BCS was performed on 101 males (57.7%) and MRM was performed on 74 (42.29%). According to the data in the table 1, the average age of the patients was approximately 60 years old. Patients that underwent MRM were older than patient that underwent BCS (57 versus 66 years, respectively) ($P < 0.0001$).

No significant difference was found in the average weight of individuals undergoing BCS or MRM surgery, suggesting that none of the two surgeries are weight dependent. Caucasians comprised 70.3% of the population, followed by African-Americans (16%). Majority of the cases of BCS were done as an outpatient (81.1%) and under general anesthesia (91.4%). While majority of the cases of MRM were done as inpatient.

The number of smokers within one year before the surgery was almost same, indicating no significant difference. The most common comorbidity was hypertension requiring medication (49.1%). However, weight, race, and other comorbidities such as Diabetes Miletus

Type II, End Stage Renal Disease (ESRD) and Cardiac Heart Failure (CHF) were not found to be statistically different. Disseminated cancer diagnosis was more common in the MRM group, however one case was done with BCS (Table 1).

Variables	BCS (n = 101)	MRM (n = 74)	P-Value
	Mean (SD)	Mean (SD)	
Age	57.01 (16.50)	65.82 (12.92)	< 0.0001
Weight in lbs.	195.45 (71.60)	203.78 (50.75)	0.393
	n (%)	n (%)	
Asian	1 (1.00)	1(1.35)	0.155
Black or African American	11 (10.89)	17 (22.97)	0.155
Unknown/Not Reported	12 (11.88)	10 (13.51)	0.155
White	77 (76.24)	46 (62.16)	0.155
Inpatient	7 (6.9)	26 (35.14)	< 0.0001
Outpatient	94 (93.1)	48 (64.86)	< 0.0001
General Anesthetic	86 (85.15)	74 (100)	< 0.0001
MAC/IV Sedation	15 (14.85)	0 (0)	N/A
Current smoker within one year	13 (12.87)	12 (16.21)	0.34
DM2	7 (6.93)	7 (9.46)	0.119
CHF	2 (1.98)	2 (2.70)	0.556
HTN Requiring Medication	44 (43.56)	42 (56.75)	0.058
ESRD	0 (0.00)	1 (1.25)	N/A
Disseminated Cancer	1 (1.0)	5 (6.8)	0.05
Chronic Steroid Use	3 (2.97)	2 (2.70)	0.664
Bleeding Disorder	2 (1.98)	3 (4.1)	0.356

Table 1: Demographics of the male breast cancer patient population analyzed (n = 175).

*SSI: Surgical Site Infection; OR: Operating Room; ESRD: End Stage Renal Disease; HTN: Hypertension; CHF: Congestive Heart Failure; DM2: Type 2 Diabetes Mellitus; N/A: Not Applicable; lbs.: Pounds; Mins: Minutes; MAC: Monitored Anesthesia Care; IV: Intravenous.

The time it took to complete the procedure was longer on average by 45 minutes in the MRM group showing a significant difference as compared to BCS group (P < 0.001). Similarly, length of the total hospital stays after the surgery was significantly lower in the patients receiving BCS surgery (P < 0.0001) and were more likely to have been operated under MAC or IV sedation (14.85% vs 0%) (P < 0.0001). Wound infection rates, need for return to the operating room, rates of readmission and superficial surgical site infections were similar between the two groups. No postoperative complications were seen in the BCS group but overall the difference was not statistically significant (Table 2).

Variables	BCS (n = 101)	MRM (n = 74)	P-Value
Total Operation Time (mins)	60.96 (45.70)	106.69 (46.73)	<0.0001
Length of Total Hospital Stay (Days)	0.2 (0.68)	1.34 (1.8)	<0.0001
	n (%)	n (%)	
Open Wound Infection	1 (1.0)	3 (4.1)	0.204
Return to the OR Required	3 (2.97)	4 (5.4)	0.332
Any Readmission Required	3 (2.97)	3 (4.1)	0.504
Superficial SSI	2 (1.98)	5 (6.76)	0.115
Transfusion Intraoperative/Postoperative	0 (0.00)	1 (1.25)	N/A

Table 2: Patient outcomes in male breast cancer surgery comparing breast conservation surgery to modified radical mastectomy.

Discussion

Although rare, MBC has significant morbidity and mortality rates with the increasing number of cases over the years. Studies have shown similarities between the incidences and many other factors of MBC and FBC, suggesting common etiology for breast cancer in both the genders but there are still biological, etiological, anatomical, and physiological differences between the two. Due to the rarity of the disease, there is very little data that exists on treatment and outcomes of male breast cancer surgery. Therefore, the current standard of care for MBC is based on studies done for FBC, since data for MBC is lacking. We hypothesized that Breast Conserving Surgery, a less aggressive technique, occurs more frequently in the United States due to recent reported literature. We also wanted to compare the surgical outcomes of breast conserving surgery to modified radical mastectomy.

We found that in 2015, a higher percentage of patients with MBC in the United States underwent BCS than MRM. They were younger, mostly done outpatient, had shorter length of hospital stay, and were more likely to have been operated under MAC or IV sedation. Moreover, operation time was also lesser by the average of 45 minutes in the case of BCS.

Comorbidities and postoperative complications were similar for both BCS and MRM. Based on these results, BCS seems to be a better treatment option than MRM for appropriate surgical candidates. MRM is still the standard of care for breast cancer treatment in MBC, especially for older patients with advanced disease. We cannot yet recommend BCS without data on recurrence rates, negative margin information, and survival rates after the surgery. The data available on the efficacy of BCS is inconclusive and the scarcity of MBC related specific information makes research in this area more difficult. Although the data available from treatment outcomes of female breast cancer has been useful in male breast cancers too, there is still a need for further studies that target MBC for better treatment guidance.

There are several limitations of the study. The stage at which the patients presented with at the time of diagnosis is unclear. It is also unclear from the database whether cases were performed for palliation or treatment. Total follow-up time for the cases was 30 days which might not be sufficient. The major limitation of a large database is missing data and not all hospitals in the United States participate in the NSQIP program. These are some of the major limitations of this study. Efficacy rates and the rate of recurrence of the disease cannot be determined or compared in the BCS and MRM surgeries using this data, because no staging or long term follow up is included in the database. Therefore, institutions performing breast conserving surgery should attempt to publish data on survival rate, marginal information, and recurrence rates for breast conserving surgery in the future. In addition, no information was included on whether or not patients received radiation treatment after BCS. However, it is assumed that those patients received radiation treatment. Information on axilla management is also missing in the database. It is not clear whether or not patients that received BCS underwent a sentinel lymph node biopsy or axillary dissection. Further studies evaluating the efficacy and benefits of the BCS over MRM should be performed and more data about the MBC specific treatment should be gathered in order to improve the quality of life and survival rate in men suffering from breast cancer.

Conclusion

In conclusion, we found that there is an increasing trend of breast conserving surgery being performed in the United States for male breast cancer. Some surgical outcomes appear to be in the favor of breast conserving surgery. However, more information is needed regarding recurrence rates and survivability after breast conserving surgery in male breast cancer.

The data currently available is not sufficient to predict the long-term efficacy and survival rates, therefore, there is a huge scope of research on the benefits of BCS over MRM.

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