Research Article ISSN 2639-8478

Cancer Science & Research

Mastectomy Wound Infections Increase with Advanced Age

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Received: 21 November 2018; **Accepted:** 18 December 2018

Citation: Tammy Ju MD, Cecilia Rossi BS, Andrew Sparks MS, et al. Mastectomy Wound Infections Increase with Advanced Age. Cancer Sci Res. 2018; 1(4); 1-6.

ABSTRACT

Objectives: *The purpose of this study is to determine if there is an increased risk of complications following mastectomies associated with advanced age.*

Materials and Methods: *The ACS-NSQIP database was queried from 2010 to 2015 using a CPT code for mastectomy and complications were identified as defined by the database. Univariate analyses were performed using a binary outcome variable (complication present or not) by age decade. Multivariable logistic regression analysis was performed using decade 6 (age 60-69) as the reference group. P-value<0.05 was considered statistically significant.*

Results: *4,854 patients met inclusion criteria, ages 18 to 90+. Univariate analyses for the presence of a postoperative complication by age decade showed no statistical difference except for wound infections (p<0.01). On multivariable analysis, the odds of having a postoperative complication is 1.4 times higher in obese patients (p<0.01,95%CI:1.1-1.8) and 1.4 times higher in smokers (p<0.01,95%CI:1.1-1.9). Complications are 3.5 times higher in patients who are not of fully independent functional status (p<0.0001,95%CI:2.3-5.8) and 5.9 times higher for dialysis patients (p<0.001,95%CI:2.3-15). Non-fully independent functional status also increased risk for mortality (p<0.05,OR=8.7,95%CI:1.5-49.6). Patients ages 90 or older were 3.4 times more likely to have a wound infection (p<0.05,95%CI:1.3-9.0).*

Conclusion: *There is no increased overall risk of a postoperative complication within 30 days of mastectomy due to the age of the patient. However, patients 90 years of age or older are at higher risk for wound infections. Our study suggests elderly breast cancer patients should not be excluded from undergoing a mastectomy solely based on their age.*

Keywords

Advanced age, Post-mastectomy complications, Wound infection.

Background

Due to the rapid aging population in the U.S. it is anticipated there will be a 67% increase in cancer incidence by 2030 for patients over the age of 65, compared to an 11% increase in cancer incidence in patients under 65 [1,2]. Breast cancer is not only the most common cancer among women, but elderly breast cancer patients are known to have increased mortality and are largely undertreated for their cancer compared to their younger counterparts [3-6]. Due to the paucity of data related to elderly breast cancer patients, complications related to breast cancer surgery are also not well elucidated at these age extremes.

As elderly breast cancer patients are often undertreated, mastectomy is sometimes avoided because the risk of postoperative complications may outweigh the benefit. Some studies have shown that while elderly patients undergo breast conservation therapy more often than mastectomy, it is not clear that less aggressive treatment results in comparable survival [4,5]. Recent studies have investigated complications for the elderly breast cancer patient and have found overall complications to be low (approximately 4%) and similar to those in younger patients [4,7]. However, these studies

have not investigated mastectomy alone and often group breast conserving surgery with patients treated with mastectomy with reconstruction, which has been known to increase complications [8,9]. Furthermore, there is no consensus on the age cut off of an older woman, with some studies citing 70 or 80 years of age as defining geriatric breast cancer patients [4,7].

Given the anticipated increase in the older breast cancer population in the near future, and lack of data investigating the postoperative risk of complications in this population, our study aims to identify the short-term outcomes after mastectomy using a large national surgical database to examine whether there is an increased risk of complications in elderly patients.

Materials and Methods

Following IRB exemption, a retrospective analysis was performed from 2010 - 2015 using the American College of Surgeon's National Surgical Quality Improvement Program Participant User File (ACS-NSQIP PUF) database. Adult patients age 18 or older were identified who underwent mastectomy using CPT code 19303 with or without sentinel lymph node biopsy (SLNB, CPT code 38525) for a primary diagnosis of invasive breast cancer defined by ICD-9 code. Patients were excluded from this study if they had disseminated cancer, bleeding disorders, underwent reconstruction, or underwent emergency surgery. Further information regarding the ACS-NSQIP database can be found at: https://www.facs.org/quality-programs/acs-nsqip.

Preoperative patient variables and 30-day morbidity and mortality were investigated across age quintiles. Preoperative patient variables were defined using the ACS-NSQIP definitions which include gender, BMI, diabetes, smoking status, dyspnea, functional status, history of chronic obstructive pulmonary disease (COPD), hypertension (HTN), dialysis, American Society of Anesthesiologists (ASA) classification, and steroid use. Outcomes of interest defined as "postoperative complications" include wound infection, superficial wound infection, wound dehiscence, deep vein thrombosis (DVT), pulmonary embolism (PE), bleeding requiring transfusion, return to the operating room (OR), myocardial infarction (MI), cardiac arrest, stroke, urinary tract infection (UTI), renal insufficiency, fail to wean from the ventilator, deep organ space infection, pneumonia (PNA), reintubation, sepsis, and septic shock. A binary score was compiled for presence of any of these complications. Complications were then stratified by age decade (decade 2 = age 18-29, 3 = 30-39, 4 = 40-49, etc) using patients within decade 6 (ages 60-69) as the reference group due to the largest amount of patients in that age range, to determine the association between age and risk of postoperative complication.

Univariate analyses using chi-squared tests were then performed using age decade by comorbidities and demographic data. Univariate analyses using chi-squared tests were performed using the binary outcome variable (complication present or not) by age decade. The 30-day mortality was also investigated independently using a chi-squared test by age decade. A multivariable logistic regression analysis was performed on incidence of postoperative complications compared by age decade using decade 6 (ages 60-69) as the reference group. Comorbidities of interest were controlled for and entered into the multivariable model if the univariate test produced a p-value less than 0.1 ($\alpha = 0.1$). A p-value <0.05 was considered statistically significant. All statistical analysis was performed using SAS version 9.3 (Cary, NC).

Results

There were 4,854 patients who met inclusion criteria. Age range was 18 to over 90. On univariate analyses, there was a significant association between age decade and female gender (p=0.05*), BMI (p <0.0001), diabetes (p <0.0001), smoker (p <0.0001), dyspnea (p <0.0001), non-independent functional status (p <0.0001), COPD (p <0.0001), HTN (p <0.0001), dialysis (p=0.08*), and ASA class other than 1 (p <0.0001) (Table 1).

On univariate analysis, there was no statistically significant difference found between age decade and presence of a complication (p=0.69) or with 30-day mortality (p=0.23). However, there was a difference between wound infection across decades (p<0.01) (Table 2). No other complications had a significant difference individually on univariate analysis. On multivariable logistic regression analysis, there was no statistically significant difference between age decade and presence of a postoperative complication (p = 0.98) and no difference between age decade and 30-day mortality (p = 0.66) (Table 3, Table 4).

The odds of having a postoperative complication was 1.42 times higher in patients with obesity (p<0.01, 95% CI: 1.12-1.8) and 1.4 times higher in current smokers (p<0.01, 95% CI: 1.1-1.9). The odds of having complications was 3.5 times higher in patients who are not of a fully independent functional status compared to those who are fully functional (p <0.0001, 95% CI: 2.3-5.3) and 5.9 times higher in those on dialysis (p<0.001, 95% CI: 2.3-15) (Table 3). Female gender had a protective effect with regards to 30-day mortality (p<0.05, OR = 0.07 95% CI 0.01-0.62) while not being of fully independent functional status increased risk for 30-day mortality (p<0.05, OR = 8.7, 95% CI: 1.5-49.6) (Table 4). Patients age 90 or older were 3.4 times more likely to have a wound infection (p<0.05 95% CI: 1.3-9.0) (Table 5).

Discussion

Due to the paucity of data and limited randomized control trials looking at age extremes, the risk of complications after mastectomy for elderly patients is unclear. This is one of the few studies addressing risk of complications specifically after simple mastectomy in elderly breast cancer patients. Post-mastectomy complications continue to have a low overall morbidity and mortality for patients of all ages in our dataset. Our study shows that age is not an independent risk factor for complications after mastectomy, whereas comorbid conditions such as obesity, smoking, dialysis, and non-independent functional status are significant predictors of 30-day morbidity and mortality [10,11]. However, patients over the age of 90 are at an increased risk for wound infections, even after adjusting for comorbid conditions.

Age Decade		18-29 (2) N=20	30-39 (3) N=172	40-49 (4) N=638	50-59 (5) N=1049	60-69 (6) N=1271	70-79 (7) N=1014	80-89 (8) N=599	90+ (9) N=91	All N=4854	p-value * = sig. at α=0.1
Variable		N (%)									
Female Gender		18 (90)	169 (98.3)	627 (98.3)	1030 (98.2)	1245 (98)	999 (98.5)	594 (99.2)	87 (95.6)	4769 (98.3)	0.05*
BMI	Underweight <18.5	1 (5)	5 (2.9)	16 (2.5)	22 (2.1)	17 (1.3)	30 (3)	30 (5)	8 (8.8)	129 (2.7)	<0.0001*
	Normal 18.5–24.9	8 (40)	73 (42.4)	253 (39.7)	308 (29.4)	340 (26.8)	289 (28.5)	230 (38.4)	46 (50.6)	1547 (31.9)	
	Overweight 25.0–29.9	5 (25)	42 (24.4)	162 (25.4)	299 (28.5)	364 (28.6)	331 (32.6)	181 (30.2)	28 (30.8)	1412 (29.1)	
	Obese >/= 30	6 (30)	52 (30.2)	207 (32.45)	420 (40)	550 (43.3)	364 (35.9)	158 (26.4)	9 (9.9)	1766 (36.4)	
Diabetes		0 (0)	5 (2.9)	22 (3.5)	100 (9.5)	197 (15.5)	201 (19.8)	91 (15.2)	8 (8.8)	624 (12.9)	<0.0001*
Smoker		5 (25)	41 (23.8)	132 (20.7)	187 (17.8)	187 (14. 7)	84 (8.3)	16 (2.7)	3 (3.3)	655 (13.5)	<0.0001*
Dyspnea		0 (0)	5 (2.9)	29 (4.6)	69 (6.6)	125 (9.8)	129 (12.7)	67 (11.2)	11 (12.1)	435 (9)	<0.0001*
Not fully independent functional status		0 (0)	0 (0)	5 (0.78)	18 (1.7)	20 (1.6)	25 (2.5)	48 (8)	25 (27.5)	141 (2.9)	<0.0001*
COPD		0 (0)	0 (0)	1 (0.16)	24 (2.3)	54 (4.3)	49 (4.8)	33 (5.5)	2 (2.2)	163 (3.4)	<0.0001*
Hypertension		1 (5)	11 (6.4)	120 (18.8)	372 (35.5)	709 (55.8)	674 (66.5)	428 (71.5)	67 (73.6)	2382 (49.1)	<0.0001*
Dialysis		0 (0)	0 (0)	3 (0.47)	3 (0.29)	10 (0.79)	0 (0)	4 (0.67)	0 (0)	20 (0.41)	0.08*
ASA class >1		18 (90)	137 (79.7)	561 (87.9)	999 (95.2)	1231 (96.9)	1000 (98.6)	589 (98.3)	91 (100)	4626 (95.3)	<0.0001*
Steroid use		0 (0)	2 (1.2)	9 (1.4)	15 (1.4)	27 (2.1)	18 (1.8)	11 (1.8)	3 (3.3)	85 (1.8)	0.78

Table 1: Pre-operative patient characteristics by age decade.
BMI: Body Mass Index, COPD: Chronic Obstructive Pulmonary Disease, ASA: American Society of Anesthesiologists.

Age Decade	18-29 (2) N=20	30-39 (3) N=172	40-49 (4) N=638	50-59 (5) N=1049	60-69 (6) N=1271	70-79 (7) N=1014	80-89 (8) N=599	90+ (9) N=91	All N=4854	p-value * = sig. at α=0.05
Variable	N (%)									
Any post-op complication	1 (5)	13 (7.6)	54 (8.5)	98 (9.3)	124 (9.8)	91 (9)	57 (9.5)	13 (14.3)	451 (9.3)	0.69
30 Day mortality	0 (0)	0 (0)	1 (0.16)	1 (0.10)	1 (0.08)	1 (0.10)	4 (0.67)	0 (0)	8 (0.16)	0.23
Wound infection	0 (0)	2 (1.2)	4 (0.63)	14 (1.3)	16 (1.3)	13 (1.3)	15 (2.5)	9 (9.9)	73 (1.5)	<0.01*
Superficial Wound infection	0 (0)	2 (1.2)	8 (1.3)	28 (2.7)	37 (2.9)	25 (2.5)	15 (2.5)	1 (1.1)	116 (2.4)	0.42
Wound dehiscence	0 (0)	4 (2.3)	2 (0.31)	4 (0.38)	3 (0.24)	3 (0.30)	1 (0.17)	0 (0)	17 (0.35)	0.08
DVT	0 (0)	0 (0)	2 (0.31)	2 (0.19)	2 (0.16)	5 (0.49)	1 (0.17)	0 (0)	12 (0.25)	0.77
PE	0 (0)	0 (0)	0 (0)	1 (0.10)	1 (0.08)	1 (0.10)	1 (0.17)	0 (0)	4 (0.08)	0.93
Bleeding	1 (5)	0 (0)	2 (0.31)	7 (0.67)	4 (0.31)	8 (0.79)	0 (0)	0 (0)	22 (0.45)	0.07
Return to the OR	0 (0)	5 (2.9)	37 (5.8)	53 (5.1)	67 (5.3)	38 (3.8)	18 (3)	3 (3.3)	221 (4.6)	0.14
MI	0 (0)	0 (0)	1 (0.16)	0 (0)	1 (0.08)	2 (0.20)	2 (0.33)	0 (0)	6 (0.12)	0.50
Cardiac arrest	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.08)	1 (0.10)	1 (0.17)	0 (0)	3 (0.06)	0.71
Stroke	0 (0)	0 (0)	1 (0.16)	0 (0)	1 (0.08)	2 (0.20)	2 (0.33)	0 (0)	6 (0.12)	0.50
UTI	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.24)	4 (0.39)	4 (0.67)	0 (0)	11 (0.23)	0.13
Renal insufficiency	0 (0)	0 (0)	0 (0)	1 (0.1)	0 (0)	0 (0)	1 (0.17)	0 (0)	2 (0.04)	0.38
Fail to wean from the ventilator	0 (0)	0 (0)	1 (0.16)	0 (0)	1 (0.08)	1 (0.10)	4 (0.67)	0 (0)	7 (0.14)	0.10
Deep organ space infection	0 (0)	0 (0)	3 (0.47)	1 (0.10)	3 (0.24)	2 (0.20)	1 (0.17)	0 (0)	10 (0.21)	0.79
Pneumonia	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.16)	2 (0.20)	4 (0.67)	0 (0)	8 (0.16)	0.13
Reintubation	0 (0)	0 (0)	1 (0.16)	0 (0)	2 (0.16)	2 (0.20)	4 (0.67)	0 (0)	9 (0.19)	0.21
Sepsis	0 (0)	0 (0)	1 (0.16)	2 (0.19)	4 (0.31)	3 (0.30)	1 (0.17)	0 (0)	11 (0.23)	0.98
Septic shock	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.08)	3 (0.30)	2 (0.33)	0 (0)	6 (0.12)	0.31

Table 2: Presence of postoperative complication by age decade.
Note: VIF analysis performed to analyze multicollinearity in multivariable models below. All independent variables are good, no variance inflation factors >= 1.4.

Variables	Adjusted OR (95% CI)	p-value (* if significant at α=0.05)
Age Decade (Overall)	N/A	0.98
Age Decade 2	0.52 (0.07 – 3.9)	0.53
Age Decade 3	0.81 (0.44 – 1.5)	0.49
Age Decade 4	0.89 (0.64 – 1.3)	0.51
Age Decade 5	0.97 (0.73 – 1.3)	0.81
Age Decade 7	0.97 (0.72 – 1.3)	0.82
Age Decade 8	0.96 (0.68 – 1.4)	0.82
Age Decade 9	1.22 (0.63 – 2.4)	0.56
BMI obese vs normal	1.42 (1.12 – 1.8)	<0.01*
BMI overweight vs normal	1.09 (0.84 – 1.4)	0.53
BMI underweight vs normal	1.03 (0.54 – 2.0)	0.93
Smoker	1.4 (1.1 – 1.9)	<0.01*
Non-independent functional status	3.5 (2.3 – 5.3)	<0.0001*
Dialysis	5.9 (2.3 – 15.0)	<0.001*

Table 3: Logistic regression model for presence of postoperative complications by age decade (reference group = decade 6).

Variables	Adjusted OR (95% CI)	p-value (* if significant at α=0.05)
Age Decade (Overall)	N/A	0.66
Age Decade 2	0 (0 – 1000)	0.99
Age Decade 3	0 (0 – 1000)	0.99
Age Decade 4	2.2 (0.13 – 34.7)	0.59
Age Decade 5	1.2 (0.08 – 19.6)	0.89
Age Decade 7	1.3 (0.08 – 20.3)	0.87
Age Decade 8	7.0 (0.72 – 67.1)	0.09
Age Decade 9	0 (0 – 1000)	0.98
Female gender	0.07 (0.01 – 0.62)	<0.05*
Non-independent functional status	8.7 (1.5 – 49.6)	<0.05*

Table 4: Logistic regression model of 30-day mortality by age decade (reference group = decade 6).

Variables	Adjusted OR (95% CI)	p-value (* if significant at α=0.05)
Age Decade (Overall)	N/A	0.21
Age Decade 2	0 (0 – 1000)	0.98
Age Decade 3	1.1 (0.26 – 5.1)	0.86
Age Decade 4	0.52 (0.17 – 1.6)	0.26
Age Decade 5	1.1 (0.53 – 3.0)	0.80
Age Decade 7	1.04 (0.49 – 2.2)	0.92
Age Decade 8	1.4 (0.65 – 2.9)	0.40
Age Decade 9	3.4 (1.3 – 9.0)	<0.05*
Non independent functional status	10.6 (5.7 – 19.6)	<0.0001*
Dialysis	8.4 (2.3 – 31.0)	<0.01*

Table 5: Logistic regression model of wound infection by age decade (reference group = decade 6).

According to the U.S. census, the median age continues to rise with those age 65 and older increasing from 35 million in 2000 to nearly 50 million in 2016 [1]. It is anticipated that by 2030, the geriatric population will be near 70 million, with a similar trend of increasing cancer incidence [12]. Studies have shown that with regards to breast cancer, not only is the incidence higher in elderly women but elderly women are generally undertreated with recent trends showing older patients undergoing less invasive or no surgery [3-5,7]. Studies have suggested that elderly patients may omit multimodal treatment due to reasons such as not being fit for surgery, intolerance to chemotherapy or radiation, or poor overall life expectancy [3]. Previous studies have reported mixed results citing age as a predictor of complications while more recent studies have shown otherwise [4,5,12]. A recent study using the ACS-NSQIP database by Pettke et al. investigated short-term morbidity for patients greater than 80 years of age compared to those less than 80 years and found higher rates of mortality and complications due to comorbidities. However, this dataset

included less invasive procedures such as partial mastectomy which inherently carry less morbidity than total mastectomies [4,13]. Similarly, another study using the ACS-NSQIP database by Angarita et al. compared women aged 70 and over to women aged 40-69 and found no difference in overall morbidity although older women were more likely have complications related to cardiac, pulmonary or neurological issues [7]. Again, this study pooled partial mastectomy with mastectomy. Our data suggests that a more aggressive surgical operation such as mastectomy if indicated may be performed with no increased risk of overall short-term complication compared to younger patients, however those at age extremes such as greater than 90 are different.

Increased BMI, smoking, and diabetes are established risk factors for post-surgical complications and specifically for those undergoing mastectomy for breast cancer [10,11,13]. Our study also found increased BMI and smoking status to be predictive of increased morbidity across all age quintiles, as well as dialysis. Functional status has not been previously described to be predictive of complications in this cohort. Our study found a strong correlation between any non-independent functional status as a risk factor for short term postoperative complication and mortality following mastectomy. Functional status was defined as any non-independent status (such as partially or fully dependent). The clinical implications of our study suggest that in addition to these well-established predictors of short-term complications, functional status should also be included during preoperative assessment of breast cancer patient. Our results show that physiological age is more important than chronological age in determining short-term morbidity and mortality after mastectomy. Other studies have recommended preoperative evaluations such as the comprehensive geriatric assessment (CGA) to help predict short term surgical outcomes [14,15].

Our study found that the most common complication was return to the OR (Table 2) while other studies have cited wound infection complications as the most common after breast surgery [2]. The FOCUS study analysis performed in the Netherlands in 2013 by de Glas et al. looked at postoperative complications for partial mastectomy and mastectomy and found complications of bleeding were as common as wound infections [13]. On multivariable analysis, patients in their nineties were 3.4 times more likely to have a wound infection while dialysis and functional status also persisted to be independent risk factors for wound infection (Table 5). There was however no difference among any other complication between age decade. Recent studies using the ACS-NSQIP database have reported that breast surgery patients older than 70 or 80 do not have an increased risk of wound infections, but did not specifically examine the subgroup aged 90 and over. This finding has been proposed to be due to the lack of smokers and decreased amount of breast reconstruction in this elderly population [4,8]. While those in their 70s and 80s may not have an increased risk of any complication including wound infection compared to their younger patients, those over age 90 appear to be at increased risk for complications.

With regards to dialysis, it is well established that long term dialysis is a risk factor for perioperative complications, including mortality, among a variety of general surgery procedures such as emergent and non-emergent abdominal surgery, cardiac surgery, and any major general surgery [16,17]. Patients on dialysis also have been found to be at increased risk for wound infection after surgery which has been proposed to be due a variety of reasons including increased blood transfusions, central line access, and uremia with associated malnutrition [16-18]. Our study also found that dialysis increased the risk of postoperative complications in mastectomy patients.

The ACS-NSQIP database is a nationally validated and risk adjusted database, however our study is not without limitations. Due to the retrospective nature of a large database study, we are subject to coding errors and limitations secondary to the database's definitions. In addition, we are unable to assess outcomes past 30 days. Oncologic staging, including tumor characteristics and prior history of breast cancer could not be accounted for in the database. Additionally, chemotherapy and radiation performed could not be assessed as over 75% if the variables were missing. It is known that elderly patients are undertreated for breast cancer, and thus there may be a selection bias present for those patients being treated with mastectomy especially at the extremes of age in our study. However, our study is one of the few to use the ACS-NSQIP database to specifically look at mastectomy only in age extremes and investigate physiologic status vs chronological status as a predictor of complications.

Conclusion

Our results show that age is not an independent risk factor for overall risk of a post-mastectomy complication. However, patients over the age of 90 are at increased risk for wound infections. Non-independent functional status is a strong predictor of complications in the postoperative period including 30-day mortality. Established risk factors such as increased BMI, smoking, and dialysis continue to be predictive of morbidity. Further studies are needed to establish the long-term morbidity and oncologic outcomes in these patient populations.

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