



Original article

A comparison of patient-centered economic and clinical outcomes of post-mastectomy breast reconstruction between obese and non-obese patients



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ARTICLE INFO

Article history:

Received 25 April 2016

Received in revised form

18 August 2016

Accepted 8 September 2016

Keywords:

Breast cancer

Breast reconstruction

Obesity

Mastectomy

Health care costs

ABSTRACT

Background: The objectives of this study were to compare, by patient obesity status, the contemporary utilization patterns of different reconstruction surgery types, understand postoperative complication profiles in the community setting, and analyze the financial impact on health care payers and patients. **Methods:** Using data from the MarketScan Health Risk Assessment Database and Commercial Claims and Encounters Database, we identified breast cancer patients who received breast reconstruction surgery following mastectomy between 2009 and 2012. The Cochran-Armitage test was used to evaluate the utilization pattern of breast reconstruction surgery. Multivariable logistic regressions were used to estimate the association between obesity status and infectious, wound, and perfusion complications within one year of surgery. A generalized linear model was used to compare total, complication-related, and out-of-pocket costs.

Results: The rate of TE/implant-based reconstruction increased significantly for non-obese patients but not for obese patients during the years analyzed, whereas autologous reconstruction decreased for both patient groups. Obesity was associated with higher odds of infectious, wound, and perfusion complications after TE/implant-based reconstruction, and higher odds of perfusion complications after autologous reconstruction. The adjusted total healthcare costs and out-of-pocket costs were similar for obese and non-obese patients for either type of breast reconstruction surgery.

Conclusions: A greater likelihood of one-year complications arose from TE/implant-based vs autologous reconstruction surgery in obese patients. Given that out-of-pocket costs were independent of the type of reconstruction, greater emphasis should be placed on conveying the surgery-related complications to obese patients to aid in patient-based decision making with their plastic surgeons and oncologists.

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Introduction

Breast cancer is the most common malignancy in women, with an estimated 231,840 new cases diagnosed in the United States in 2015 [1]. Mastectomy, the standard of care before the

1980s, remains one of the most widely used breast cancer treatments today. Despite numerous studies documenting the equal effectiveness in cancer control between mastectomy and radiation therapy following breast conserving surgeries [2,3], an upward trend of mastectomy has been observed in the past decade [4,5]. Patients with breast cancer who choose to undergo breast reconstruction after mastectomy have the option between two techniques of breast reconstruction: autologous vs. implant-based reconstruction [6,7]. Each form of reconstruction has its distinctive advantages and disadvantages, making the selection process complex for patients, plastic surgeons, and oncologists.

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Studies in the U.S. have shown an increasing use of breast reconstruction surgery following the Women's Health and Cancer Rights Act of 1998, which was designed to remove the financial burden associated with reconstruction for breast cancer patients [8,9]. Two epidemiological trends suggest that obese patients will constitute a substantial proportion of breast reconstruction surgeries: a prevalent obesity rate of adult women in the U.S. as high as 36.5% [10] and a demonstrated association between obesity and increased risk of breast cancer in postmenopausal women [11–13]. While previous research has shown that patients with obesity experienced higher rates of complications with either autologous or implant-based reconstruction, information from the current literature is of limited use to breast cancer patients because of the relatively short duration of observations (i.e. 30 days) in these studies [14–20]. For many patients, information on intermediate- or long-term complications is equally, if not more, important than 30-day perioperative complications because patients need to factor in the long-lasting effects when selecting between different forms of breast reconstruction.

Another important factor for patients contemplating different methods of breast reconstruction is cost. Very few studies have evaluated costs of breast reconstruction and the associated post-operative complications. Further, most of these studies reported costs using service charge data obtained from university-affiliated hospitals [15,21–23]. Costs reported from these studies are of less relevance to patients because charges tend to be highly inflated. More importantly, none of the existing studies have estimated the out-of-pocket costs of surgery and postoperative care, factors which are of critical importance to patients. Indeed, it has been reported that sixty-three percent of patients wanted to know out-of-pocket costs from their physicians [24]. In light of the limited cost information available for patients faced with the choice between different reconstruction techniques, an understanding of the economic impact of the reconstruction methods is greatly needed.

In the present study we sought to characterize the type of reconstructive surgery with less risk and cost to obese patients to be able to guide treatment choice for this high-risk patient population. We started by describing the contemporary trend toward use of autologous reconstruction and TE/implant-based reconstruction for obese and non-obese patients, followed by examining the subsequent complications incurred within one year of undergoing each type of breast reconstruction. We then estimated and compared total, complication-related, and out-of-pocket costs between obese and non-obese patients.

Patients and methods

Datasets

Unlike many countries in the Organization for Economic Cooperation and Development (OECD), the United States doesn't have a single-payer health care system. Americans aged 65 and older as well as younger people with disabilities are covered by Medicare, an insurance program administered by US federal government. For most individuals younger than 65 with income above poverty level, they often obtain health insurance from their employers. MarketScan databases, data used in our study, were based on information collected from employment-based insurance. The MarketScan Health Risk Assessment (HRA) and Commercial Claims and Encounters (CC&E) databases (Truven Health Analytics, Ann Arbor, MI). The MarketScan HRA database includes self-reported information on biometrics, health status, health risks and behavioral change collected from risk assessment questionnaires of employees administrated by participating U.S. corporations and health plans. The MarketScan CC&E database is a large de-identified

health care claims database of civilian working populations, their spouses, and dependents in the United States [25]. The MarketScan HRA covers approximately 2% of enrollees from the MarketScan CC&E, and it can be linked with the CC&E via a unique identifier for each enrollee. This study was granted an exemption from review by the institutional review board at The University of Texas MD Anderson Cancer Center for use of de-identified data.

Ascertainment of study cohort

From the linked databases, we identified patients aged less than 65 years old and diagnosed with breast cancer (International Classification of Diseases, 9th revision [ICD-9] codes 174.XX) who had undergone mastectomy between January 1, 2009 and December 31, 2012. The date of mastectomy was considered the index date. We included patients who had at least two diagnosis codes on separate dates for breast cancer within 3 months of the index date. To ensure data completeness, we only included patients who had continuous medical insurance coverage for the duration from 3 months before to 12 months after the indexed mastectomy. To improve the specificity of the cohort, we excluded patients who had undergone radiation therapy within 3 months before mastectomy and those who had a diagnosis code of metastatic disease during the study period. To study the one-year complications after breast reconstruction surgery, we further limited the study sample to patients who had 12 months of continuous medical insurance coverage after breast reconstruction to ensure completeness of information in the one-year observational window. The cohort ascertainment criteria are summarized in [Appendix Material A](#). The final sample consisted of 1780 patients who had received either autologous or TE/implant-based reconstruction after mastectomy and who also satisfied the aforementioned criteria.

Identification of breast reconstruction

We used ICD-9 procedure codes and Healthcare Common Procedure Coding System (HCPCS) codes to identify autologous (transverse rectus abdominis myocutaneous flap, deep inferior epigastric artery perforator flap, superficial inferior epigastric artery flap, gluteal artery perforator flap, latissimus dorsi flap, and other free flap) or TE/implant-based reconstruction procedures that had been performed within one year after mastectomy ([Appendix Material B](#)). We applied the intent-to-treat approach and categorized patients who had received both autologous reconstruction and TE/implant-based reconstruction within the one-year study period according to the type of the first reconstruction procedure received after mastectomy.

Obesity status and other key variables

The primary independent variable of interest was BMI, which was reported as a continuous variable in the HRA database. Based on the World Health Organization (WHO) obesity classification system, we dichotomized this BMI variable as non-obese ($\text{BMI} \leq 29.9 \text{ kg/m}^2$) versus obese ($\text{BMI} \geq 30 \text{ kg/m}^2$) [26].

Other demographic and clinical variables included age at mastectomy, metropolitan statistical area (MSA), census region, insurance type, comorbid conditions, bilateral mastectomy, breast cancer lymph node surgery, chemotherapy, and radiation therapy ([Table 1](#)). We classified patients' breast reconstructions as immediate reconstruction if the reconstruction code was recorded on the same day as the mastectomy and as delayed reconstruction if the reconstruction code was recorded after the date of mastectomy. To capture the burden of comorbid conditions, we identified four common risk factors of surgical complications reported in the

Table 1
Demographic characteristics of study population stratified by body mass index classification.

Characteristics	Non-obese		Obese		P-value
	N	%	N	%	
Year of mastectomy					0.760
2009	265	21.4	122	22.4	
2010	290	23.5	132	24.3	
2011	309	25.0	140	25.7	
2012	372	30.1	150	27.6	
Age at mastectomy (years)					0.510
<40	142	11.5	51	9.4	
40–49	427	34.6	184	33.8	
50–59	504	40.8	230	42.3	
≥60	163	13.2	79	14.5	
Reconstruction					0.004
TE/Implant-based	949	76.8	383	70.4	
Autologous	287	23.2	161	29.6	
MSA					0.083
No	139	11.3	77	14.2	
Yes	1097	88.8	467	85.9	
Region					<0.001
Northeast	171	13.8	42	7.7	
Midwest	245	19.8	105	19.3	
South	635	51.4	334	61.4	
West	185	15.0	63	11.6	
HMO or PPO with capitation					0.982
No	998	80.7	439	80.7	
Yes	238	19.3	105	19.3	
Charlson Comorbidity Score					0.019
0	1218	98.5	527	96.9	
1+	18	1.5	17	3.1	
Cardiovascular disease					0.770
No	1183	95.7	519	95.4	
Yes	53	4.3	25	4.6	
Diabetes					<0.001
No	1205	97.5	494	90.8	
Yes	31	2.5	50	9.2	
Hypertension					<0.001
No	1076	87.1	389	71.5	
Yes	160	12.9	155	28.5	
Anemia					0.023
No	1178	95.3	504	92.7	
Yes	58	4.7	40	7.4	
Immediate reconstruction					0.146
No	157	12.7	83	15.3	
Yes	1079	87.3	461	84.7	
Bilateral mastectomy					0.259
No	1035	83.7	467	85.9	
Yes	201	16.3	77	14.2	
Breast cancer lymph node surgery					0.872
No	221	17.9	99	18.2	
Yes	1015	82.1	445	81.8	
Chemotherapy					0.236
No	667	54.0	277	50.9	
Yes	569	46.0	267	49.1	
Radiation therapy					0.103
No	994	80.4	419	77.0	
Yes	242	19.6	125	23.0	

literature [27,28], namely cardiovascular disease, diabetes, hypertension, and anemia recorded in the database 3 months before mastectomy, and we also calculated the Charlson comorbidity score using physician and hospital claims [29].

Complications and costs

The primary outcomes were complications at any time within one year after breast reconstruction, including: (I) skin or soft tissue infections, (II) wound complications (seroma, hematoma, skin dehiscence, and nonhealing surgical wounds), (III) perfusion complications (fat necrosis and flap necrosis), and (IV) breast pain. Each complication type was identified via ICD-9 diagnosis or procedure

codes within one year of breast reconstruction (Appendix Material B). The secondary outcomes were health care costs, which included complication-related, total, and out-of-pocket health care costs within 12 months of breast reconstruction. The costs of complications were estimated by using the amounts paid by insurers for inpatient and outpatient services, as well as prescription drugs that were incurred/prescribed on the same day of complications. Total health care costs were defined as the total amount paid by insurers for all health care services provided during the same period. The out-of-pocket costs included coinsurances, copayments and deductibles paid by the patients during the 12-month duration for all claims. All three cost estimates were normalized to 2014 U.S. dollar using the medical care component of the consumer price index [30].

Statistical analysis

Baseline patient demographic and clinical variables were described for non-obese and obese patients. The Pearson χ^2 test was used to assess the association between obesity status and reconstruction techniques, patient demographics, and clinical variables. To describe the utilization trend of each type of breast reconstruction, we calculated the percentage use of each reconstruction technique for non-obese and obese patients by year of mastectomy. Cochran-Armitage tests were conducted to evaluate the significance of the time trends. A multivariable logistic regression was performed to evaluate the factors associated with receipt of autologous reconstruction using TE/implant-based reconstruction as the reference group.

To investigate postoperative complications, we used the Pearson χ^2 test to assess the univariate association of obesity status with the occurrence of postoperative complications. Adjusted odds of each complication after breast reconstruction were determined using logistic regression models, and the goodness of fit of models were assessed using Hosmer and Lemeshow test. Finally, since cost data were not normally distributed, we performed Mann–Whitney test on unadjusted complication-related, total and out-of-pocket health care costs stratified by obesity status. We used generalized linear models (GLM) with a gamma family and log link function to assess the adjusted costs (complication-related, total, and out-of-pocket) for non-obese and obese patients stratified by reconstruction type. All analyses were conducted with SAS software version 9.4 (SAS Institute, Cary, NC) and Stata software version 12 (StataCorp, College Station, TX). Statistical significance was defined as a P value less than 0.05.

Results

Patient characteristics

Characteristics of the 1780 breast cancer patients in our study cohort are provided in Table 1. The mean ages were 52.3 years (standard deviation [SD], 7.9 years) for non-obese patients and 53.3 years for obese patients (SD, 7.8 years). In the bivariate analysis, the receipt of autologous reconstruction of non-obese patients (23.2%) was significantly lower than that of obese patients (29.6%; $P = 0.004$).

Selection of breast reconstruction

Over the study period, the use of autologous reconstruction decreased over time (Fig. 1). For non-obese patients, the rate decreased from 28.7% in 2009 to 19.4% in 2012 ($P_{\text{trend}} < 0.01$); for obese patients, while there was a significant reduction in the rate from 35.3% in 2009 to 26.0% in 2012 ($P = 0.003$), the downward

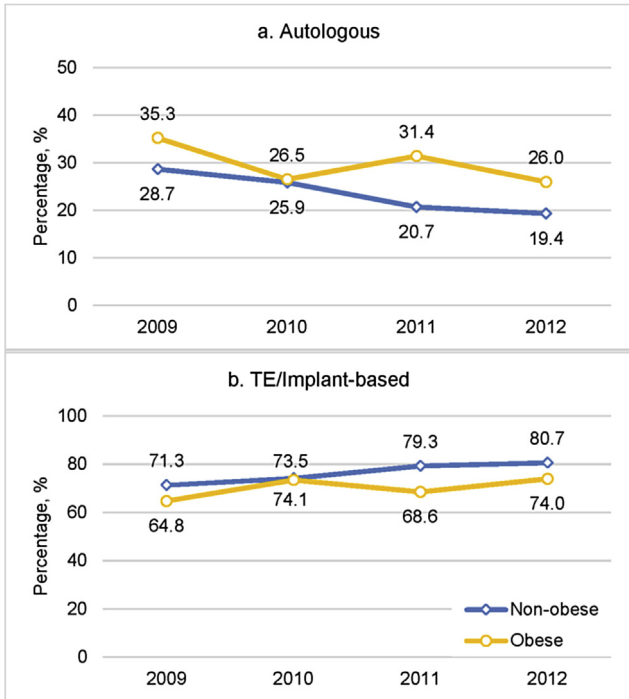


Fig. 1. Temporary trend of breast reconstruction type stratified by body mass index.

trend was not significant in trend test due to fluctuations in the rate over time ($P_{\text{trend}} = 0.20$). The rate of TE/implant-based reconstruction showed a significant upward trend among non-obese patients, from 71.3% in 2009 to 80.7% in 2012 ($P_{\text{trend}} < 0.01$), but no significant linear trend was observed among for obese patients ($P_{\text{trend}} = 0.20$).

Results from the multivariable logistic regression model are presented in Table 2. The list of covariates that significantly predict patients' receipt of autologous reconstruction vs TE/implant-based reconstruction included residing in the northeast region, treatment with radiation therapy after mastectomy, and a history of hypertension. Also, a significantly negative time trend for autologous reconstruction was observed. The association between obesity and autologous reconstruction was only marginally significant (OR = 1.28, 95% CI 0.97–1.57, $P = 0.09$).

Postoperative complications

Fig. 2 illustrates the rates of complications after breast reconstruction in non-obese and obese patients. Among patients who received autologous reconstruction, obese patients had a significantly higher rate of perfusion complications (16.8% of obese vs. 10.1% of non-obese patients, $P = 0.04$) but not infectious or wound complications (Appendix Material C). For patients who received TE/implant-based reconstruction, obesity was associated with significantly higher rates of infectious, wound and perfusion complications (infectious complications: 25.9% vs. 16.8%, $P < 0.01$; wound complications: 20.9% vs. 11.1%, $P < 0.01$; perfusion complications: 8.1% vs. 5.0%, $P = 0.03$). Of all the complications, the highest rate was found in wound complications. Within the subtypes of wound complications, seroma was the most common type, making up 52.4% and 47.0% of wound complications among patients who received autologous and TE/implant-based reconstruction, respectively. Obesity was associated with higher risk of seroma for patients with TE/implant-based reconstruction (11.4% of obese patients vs 4.7% of non-obese patients, $P < 0.01$).

Table 2

Logistic regression analysis of breast reconstruction choice for patients with breast cancer undergoing mastectomy.

(Base group: TE/Implant-based reconstruction)	Autologous reconstruction			P-value
	OR	95% CI		
Obesity group				
Non-obese	1.00			
Obese	1.23	0.97	1.57	0.089
Year of mastectomy				
2009	1.00			
2010	0.80	0.58	1.10	0.169
2011	0.74	0.54	1.01	0.059
2012	0.62	0.45	0.84	0.003
Age at mastectomy (years)				
<40	1.00			
40–49	1.14	0.78	1.68	0.496
50–59	0.82	0.56	1.21	0.316
≥60	0.72	0.45	1.16	0.172
MSA				
No	1.00			
Yes	0.90	0.64	1.26	0.530
Region				
Northeast	1.00			
Midwest	0.45	0.30	0.68	<0.001
South	0.73	0.52	1.03	0.071
West	0.44	0.28	0.69	<0.001
HMO or PPO with capitation				
No	1.00			
Yes	0.83	0.61	1.12	0.220
Bilateral mastectomy				
No	1.00			
Yes	0.89	0.64	1.23	0.466
Breast cancer lymph node surgery				
No	1.00			
Yes	0.86	0.64	1.16	0.337
Chemotherapy				
No	1.00			
Yes	0.93	0.72	1.19	0.550
Radiation therapy				
No	1.00			
Yes	2.29	1.72	3.04	<0.001
Charlson Comorbidity Score				
0	1.00			
1+	1.29	0.59	2.85	0.523
Cardiovascular disease				
No	1.00			
Yes	0.84	0.49	1.45	0.535
Diabetes				
No	1.00			
Yes	1.04	0.60	1.79	0.888
Hypertension				
No	1.00			
Yes	1.83	1.38	2.45	<0.001
Anemia				
No	1.00			
Yes	1.34	0.85	2.12	0.212

After controlling for patient demographics and clinical characteristics, the logistic regression model of patients who received autologous reconstruction indicated that obesity was associated with a higher risk of perfusion complications (OR = 1.97, 95% CI 1.07–3.61; $P = 0.03$) (Fig. 3, Appendix Material F). For patients who received TE/implant-based reconstruction, obesity was associated with significantly higher odds of infectious complications (OR = 1.68, 95% CI 1.24–2.27; $P < 0.01$), wound complications (OR = 1.93, 95% CI 1.38–2.70; $P < 0.01$), and perfusion complications (OR = 1.63, 95% CI 1.00–2.66; $P = 0.05$) (Fig. 3, Appendix Material D–F).

Costs and obesity status

Fig. 4 shows both unadjusted and adjusted costs by obesity status for three types of costs: complication-related, total, and

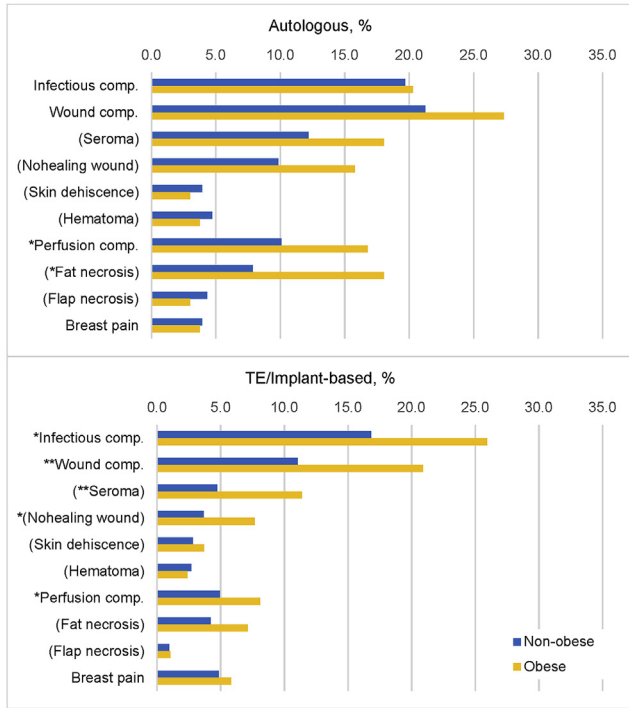


Fig. 2. Complication rate after breast reconstruction stratified by breast reconstruction type.

out-of-pocket costs. The adjusted complication-related costs were significantly higher for obese patients among those who received autologous reconstruction (excess costs: \$2948 [ERUO€: 2360], $P = 0.04$). For those with TE/implant-based reconstructions, while the unadjusted complication-related and total medical costs were higher for obese patients, the differences were no longer significant after adjusting for patients' demographic, socioeconomic and clinical covariates in GLM analysis. Out-of-pocket costs were similar for patients who received either reconstruction type regardless of obesity status.

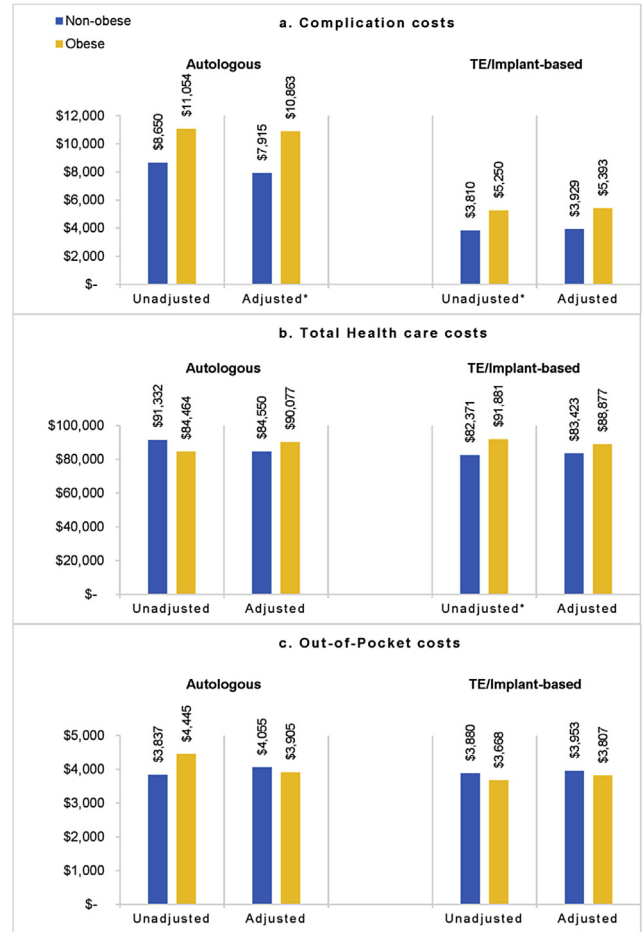


Fig. 4. Unadjusted and adjusted 1-year complication-related costs, total health care costs, and out-of-pocket costs among non-obese and obese patients stratified by breast reconstruction type. (Adjusted complication-related costs, total health care costs, and out-of-pocket costs are calculated from generalized linear models with a gamma family and log link function controlling for year of mastectomy, age at mastectomy, MSA, region, timing of reconstruction, bilateral mastectomy, breast cancer lymph node surgery, chemotherapy, radiation therapy, Charlson comorbidity score, cardiovascular disease, diabetes, hypertension, and anemia).

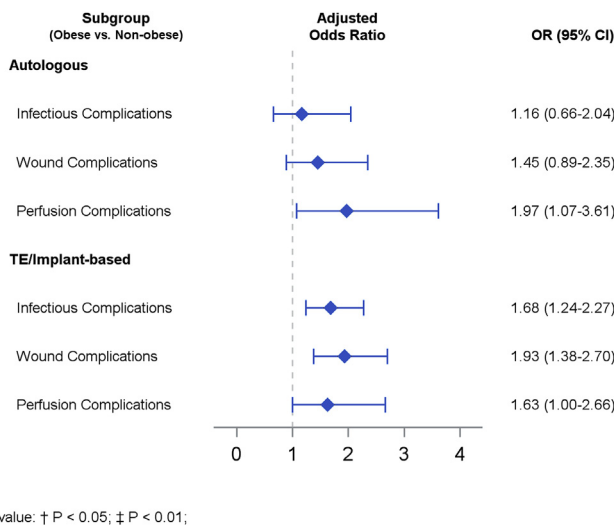


Fig. 3. Adjusted odds ratio for complications between non-obese and obese patients. (Adjusted odds ratios are calculated from logistic regression models controlling for year of mastectomy, age at mastectomy, MSA, region, timing of reconstruction, bilateral mastectomy, breast cancer lymph node surgery, chemotherapy, radiation therapy, Charlson comorbidity score, cardiovascular disease, diabetes, hypertension, and anemia).

Discussion

To the best of our knowledge this is the first study focusing on one-year complication rates after breast reconstruction in the community setting, and it is also the only study to examine the financial impact of post-mastectomy breast reconstruction from both the payers and patients perspective. In this study, we have shown a decreasing trend in autologous reconstruction between 2009 and 2012, with the trend most pronounced among non-obese patients. We also found higher rates of infectious and wound complications for obese patients with TE/implant-based reconstruction, but not with autologous reconstruction. Moreover, the adjusted total health care and out-of-pocket costs did not differ significantly based on obesity status with either type of reconstruction surgery.

Although several studies reported that patients who had undergone autologous reconstruction had overall higher satisfaction rates, better aesthetic outcomes, and better quality of life in the long-term [31–33], our study showed that these well-established benefits did not necessarily promote the adoption of autologous reconstruction for either obese or non-obese breast cancer patients. Instead, we found a decreasing trend of autologous reconstruction

surgeries from 2009 to 2012, a pattern that mimics the gradual decline of this procedure in the past two decades [9,21].

A recently published study found that obesity is a common risk factor for a variety of complications after breast reconstruction [34]. Similar observations have been reported in many retrospective, single-institution studies [14–20]. However, we found in the current study that obese patients who received autologous reconstruction had higher risks of perfusion complications compared to wound complications or infection. Notably, a recent study found that preoperative weight loss helped to reduce the number of perfusion complications among patients who underwent autologous reconstruction [18,35]. Future studies should explore effective weight-loss interventions in obese women undergoing autologous reconstruction to lower their risk of perfusion complication.

Among obese patients who had undergone TE/implant-based reconstruction, seroma was the most common noninfectious complication, and the higher risk of seroma in these patients compared with non-obese patients was consistent with findings published by others [14–17]. A recent study by Ganske et al. had provided a strategy to prevent seroma complications: the use of postoperative soft compression dressings, surgical bras, and drainage of both the submastectomy flap and the sub-ADM pocket with a removal threshold of less than 20 mL/24 h reduced the rate of seroma from 18.6% to 4.7% [36]. Whether this modified postoperative management of implant-based reconstruction has the same effects on obese and non-obese patients was not addressed in that study and should be explored in future research.

Breast reconstruction-related costs are not well documented in the literature [15,21–23] two studies from the Hospital of the University of Pennsylvania reported that the reconstruction-related costs ranged from \$21,391 to \$24,370. These costs included reconstruction-related hospital stays but not professional service fees incurred during these hospitalizations [15,22]. A study using Nationwide Inpatient Sample data found that the charges for patients with complications after immediate autologous reconstruction were \$21,895 higher than that for patients with no complications [37]. It is important to note that all of these cost studies varied in methodology in costing, and none of them reported cost differences based on obesity. Our study revealed that the cost of complications within one year of breast reconstruction was higher for patients who received autologous reconstruction. However, the cost advantage of TE/implant-based reconstruction will likely diminish over time since costly procedures for TE/implant replacement or revision are common among patients treated with this type of breast reconstruction surgery. Additionally, our finding of comparable out-of-pocket costs between autologous and TE/implant-based reconstruction indicate that economic consideration is unlikely to be a pivotal factor affecting patients' decision on the type of reconstruction surgery.

Given the escalating global epidemic of obesity and increasing incidence of breast cancer world-wide [38,39], our US-based investigation of the impact of obesity on health outcomes and healthcare resources use after reconstruction also provides important insights to policy makers in other healthcare systems who are making reimbursement decision regarding breast cancer treatments. For instance, a recent UK study by Robertson and colleagues found that the actual costs of autologous reconstruction were far exceeding the reimbursement rate set by UK National Health Service [40]. If plastic surgeons in Europe are under-compensated for performing autologous reconstruction [41], we would expect a temporal trend toward more implant-based reconstruction as reported in the United States. For obese patients, our study documented that complications for implant-based reconstruction were significantly higher in this group. Therefore, if insurance payment in European countries create a disincentive to

perform autologous reconstruction, such reimbursement environment could place obese patients at greater risk of complications.

This study had several limitations. First, given that our BMI data were self-reported in a private insurance claims dataset, the proportion of obese patients could be higher as people tend to underestimate their weight. Therefore, rate differences of complications and associated costs after surgery between obese and non-obese patients would have been underestimated. Furthermore, the findings from our study may not be generalizable to the elderly population since patients in our study were women younger than 65 years. Also, in order to maintain a sufficient sample size for our study, the follow-up window was not expanded beyond one year after mastectomy. Higher rates of complications might have been detected using a longer observation window. Moreover, although the existing body of literature suggests that individual characteristics and patients' preferences have a strong impact on the short-term and long-term benefits of breast reconstruction [6], information on patient preference regarding the selection of various breast reconstruction techniques was not available from in commercial claims databases. Finally, while cosmetic satisfaction is an important outcome measure for reconstruction, it cannot be quantified using insurance claims data. To evaluate this patient-centered outcome prospective studies with sufficient long-term follow-up are needed in future research.

In conclusion, our study compared clinical and economic outcomes between obese and non-obese patients who had undergone breast reconstruction after mastectomy for the treatment of breast cancer. We found the significant higher risk of complications for obese patient underwent TE/implant-based reconstruction and comparable total health care and out-of-pocket costs between autologous and TE/implant-based reconstruction. These findings have important implications for making informed shared medical decisions among plastic surgeons, oncologists, and patients, and for advancing the ongoing initiative to achieve the highest patient satisfaction and quality of life after breast reconstruction among obese patients.

Ethical statement

An ethical approval was not required since this is an observational study using de-identified health care claims data.

Conflicts of interest

All authors declare no conflicts of interest.

Acknowledgements

This work was supported in part by the Duncan Family Institute, the fellowship from University of Texas MD Anderson Cancer Center's Halliburton Employees Foundation (Dr. Huo), Agency for Healthcare Research and Quality (Dr. Shih; R01 HS020263); Dr. Giordano is supported by CPRIT RP140020 and Komen SAC150061. Dr. Smith receives research funding from Varian Medical Systems; also, we acknowledge Tamara Locke, scientific editor from the Department of Scientific Publications and Dr. Gary Deyter, technical writer from the Department of Health Services Research, at The University of Texas MD Anderson Cancer Center for reviewing and editing the manuscript.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.breast.2016.09.004>.

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