

Human Acellular Dermis versus Submuscular Tissue Expander Breast Reconstruction: A Multivariate Analysis of Short-Term Complications

Armando A. Davila¹, Akhil K. Seth¹, Edward Wang^{2,3}, Philip Hanwright¹, Karl Bilimoria², Neil Fine¹, John YS Kim¹

¹Division of Plastic and Reconstructive Surgery, ²Department of Surgery, ³Biostatistics Core, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA

Background Acellular dermal matrix (ADM) allografts and their putative benefits have been increasingly described in prosthesis based breast reconstruction. There have been a myriad of analyses outlining ADM complication profiles, but few large-scale, multi-institutional studies exploring these outcomes. In this study, complication rates of acellular dermis-assisted tissue expander breast reconstruction were compared with traditional submuscular methods by evaluation of the American College of Surgeon's National Surgical Quality Improvement Program (NSQIP) registry.

Methods Patients who underwent immediate tissue expander breast reconstruction from 2006–2010 were identified using surgical procedure codes. Two hundred forty tracked variables from over 250 participating sites were extracted for patients undergoing acellular dermis-assisted versus submuscular tissue expander reconstruction. Thirty-day postoperative outcomes and captured risk factors for complications were compared between the two groups.

Results A total of 9,159 patients underwent tissue expander breast reconstruction; 1,717 using acellular dermis and 7,442 with submuscular expander placement. Total complications and reconstruction related complications were similar in both cohorts (5.5% vs. 5.3%, $P=0.68$ and 4.7% vs. 4.3%, $P=0.39$, respectively). Multivariate logistic regression revealed body mass index and smoking as independent risk factors for reconstructive complications in both cohorts ($P<0.01$).

Conclusions The NSQIP database provides large-scale, multi-institutional, independent outcomes for acellular dermis and submuscular breast reconstruction. Both thirty-day complication profiles and risk factors for post operative morbidity are similar between these two reconstructive approaches.

Keywords Alloderm / Mammoplasty / Breast implantation / Tissue expansion devices / Complications

Correspondence: John YS Kim
Division of Plastic and Reconstructive Surgery, Northwestern University, Feinberg School of Medicine, 675 North St. Clair Street, Galter Suite 19-250, Chicago, IL 60611, USA
Tel: +1-312-695-6022
Fax: +1-312-695-5672
E-mail: jokim@nmh.org

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INTRODUCTION

Acellular dermal matrix (ADM) have been used in soft tissue reconstruction since 1995, and have continued to be used in an array of surgical procedures [1-3]. Since 2005, these allografts have been specifically described in prosthesis-based breast reconstruction, offering putative benefits of improved cosmesis, faster expansion curves, and amelioration of contracture [4-10]. Proponents of the technology argue that by cutting the pectoralis muscle, one can use ADM to more precisely align the submuscular position of the expander without the anatomic restrictions of the pectoralis muscle. This allows the expander to be placed inline with the natural contours of the breast, which theoretically provides gains with respect to aesthetic outcomes [5,7,8,10]

There have been a myriad of analyses outlining the complication profile of ADM within the literature, including several comparative, retrospective studies [11-15]. These studies have sought to address concerns over surgical complications potentially associated with ADM, including seromas, infections, and mastectomy flap loss. There continues to be debate about the true incidence of complications as cohort studies have shown a wide range of complication profiles. Moreover, demographic risk factors for complications have been difficult to discern, since multivariate analyses have been limited by insufficiently powered, single institution studies [12,13]. A recent meta analysis suggests that the use of ADM connotes a higher complication profile than submuscular reconstruction, however this sentiment has not been unanimous [16,17].

The American College of Surgeon's (ACS) National Surgical Quality Improvement Program (NSQIP) was instituted by the ACS in 2004 to track multi-institutional outcomes of surgical procedures [18]. The comprehensive nature of the database allows researchers to evaluate outcomes from large numbers of patients, increasing the statistical power of any NSQIP-based studies. In contrast to many previously reported single-surgeon or single-institution experiences in the plastic surgery literature, (including those surrounding ADM-assisted breast reconstruction) the data obtained from this 1.3 million patient, multi-institution, validated database provides the potential for a unique analysis of patient outcomes. As such we endeavored to utilize this powerful database to provide additional insight on short-term outcomes and compare patient risk factors in the current practice of acellular dermis assisted versus submuscular breast reconstruction.

METHODS

Selection criteria

A retrospective analysis of the NSQIP participant use files from

2006 to 2010 was performed for all patients who underwent tissue expander breast reconstruction following mastectomy from over 250 participating sites. The details of data collection and utility of the database have been previously described and validated [19]. Specifically, the makeup of the NSQIP clinical registry includes 240 recorded variables that are abstracted from patient charts by trained nurse reviewers, including patient demographics, comorbidities, intraoperative details, and laboratory values [20]. In addition, postoperative outcomes for thirty days following the primary operation are also recorded.

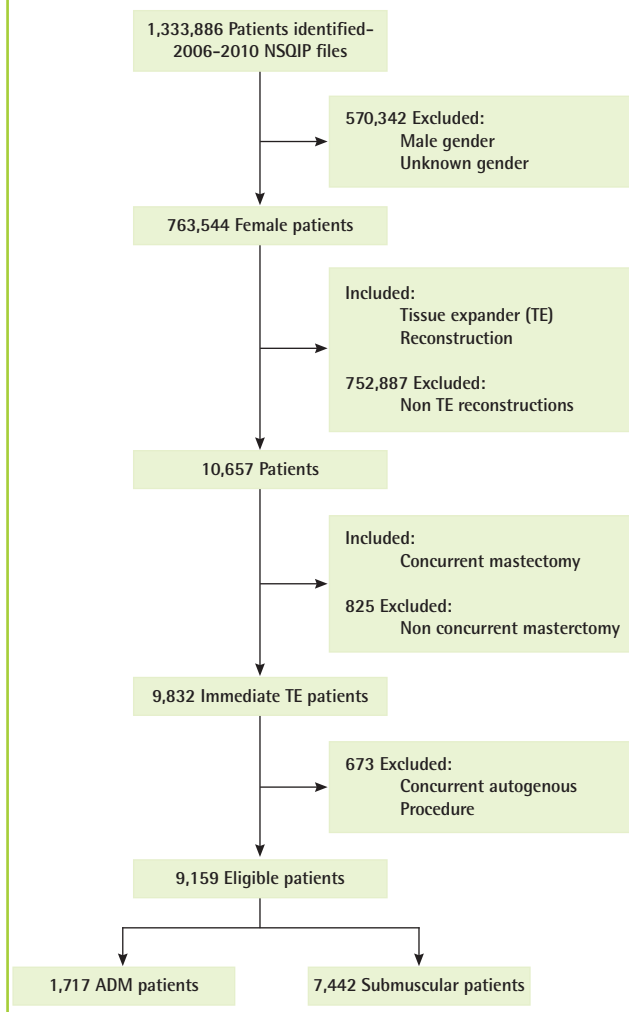
Patients who underwent tissue expander breast reconstruction were selected using concurrent surgical procedure codes. Patients who did not simultaneously undergo mastectomy were excluded from this analysis. These patients represent total mastectomy for females only, and do not include lumpectomy/partial mastectomy, or male mastectomy codes. Additionally, patients who had concurrent autogenous reconstruction were excluded. Patients were then stratified based on concurrent ADM use. Patients who did not use ADM were classified as submuscular, which was defined as any case using either partial or total pectoralis and/or serratus muscular coverage. A summary of the inclusion and exclusion criteria process can be found in Fig. 1.

Following stratification, demographics and complication profiles of both groups were extracted and analyzed. Standard definitions were used for all data collected as defined in the NSQIP User Guide. The patient demographics included for analysis consisted of age, race, ethnicity, body mass index (BMI), smoking (< 1 year prior to surgery), radiotherapy (< 90 days prior to surgery), chemotherapy (< 30 days prior to surgery), chronic use of steroids for medical disease, and previous operation (< 30 days prior to surgery). In addition, patient comorbidities were also included for analysis, specifically, diabetes mellitus, hypertension, previous percutaneous/surgical cardiac intervention, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), previous stroke/transient ischemic attack (TIA), and bleeding disorders.

Postoperative outcomes were categorized as being complications related to reconstruction or other major medical complications. Reconstruction-related complications included superficial surgical site infection (SSI), deep SSI, organ/space SSI, wound disruption, and flap/prosthesis failure. Major complications included pneumonia, unplanned re-intubation, deep vein thrombosis, pulmonary embolism, ventilator dependence greater than 48-hours, progressive renal insufficiency, acute renal failure, stroke, urinary tract infection, coma, cardiac arrest, myocardial infarction, transfusion requirement, sepsis, and septic shock. Need for re-operation within 30-days was tracked separately.

Fig. 1. Study attrition diagram

The study attrition diagram depicts a summary of the inclusion and exclusion criteria process. NSQIP, National Surgical Quality Improvement Program; ADM, acellular dermal matrix.



Data collection and analysis

Bivariate comparison of demographics and complications between the acellular dermis assisted and submuscular reconstruction groups were performed with a chi-squared test and Fisher's exact test (for small cell counts) for categorical variables, and independent t-tests for continuous variables. An alpha value of 0.05 was considered significant. To account for potential confounders, multivariate analysis was performed calculating the adjusted probabilities for complications and odds ratio. A bivariate screen was used to identify variables that demonstrated significance at P-value less than 0.20 to be entered into the multivariate regression model. If a variable contained missing values, those cases were excluded from that analysis. Additionally, variables that did not have greater than 5 events were excluded from further analysis [21]. Bivariate and multivariate analyses were also used

to identify risk factors for complications in each cohort using identical methodology. Risk factors common to both groups were compared based on odds ratios and confidence intervals. Secondary reconstructive complication outcomes (any operative site infection, wound disruption, and prosthesis failure) were assessed for only the acellular dermis cohort to further stratify individual complications using the similar methodology. Hosmer-Lemeshow and c-statistics were computed to assess model calibration and discrimination. All data manipulation and statistical calculations were performed using SPSS ver. 20.0 (IBM, Armonk, NY, USA).

RESULTS

Study population

During the study period, a total of 9,159 patients underwent immediate, tissue expander breast reconstruction. Of those, 1,717 were reconstructed using an ADM adjunct, with 7,442 undergoing submuscular tissue expander placement. Patient demographics are summarized in Table 1.

The mean age of the ADM cohort and submuscular cohort were 50.6 ± 10.5 and 51.0 ± 10.5 , respectively ($P=0.21$). The mean BMI of the ADM cohort was comparable to the submuscular cohort (27.0 ± 6.2 vs. 26.9 ± 6.3 , $P=0.55$), however there were significantly more patients without BMI data in the acellular dermis group (1.3% vs. 0.6%, $P=0.01$). All other BMI categories were similar between cohorts. The submuscular group yielded a higher portion of Hispanic (5.1% vs. 3.6%, $P<0.01$) and hypertensive (23.6% vs. 21.1%, $P=0.03$) patients and was less likely to receive preoperative chemotherapy (3.9% vs. 5.6%, $P<0.01$) compared to the ADM group. All other demographic variables were well-matched. In terms of clinical characteristics and comorbidities, there were no significant differences in smoking, preoperative radiation, diabetes, COPD, bleeding disorders, PVD, CHF, previous cardiac surgery, or previous stroke/TIA between the two study groups.

Complication profiles

The likelihood of patients experiencing one or more complications following tissue expander reconstruction were similar between the ADM and submuscular cohorts (5.5% vs. 5.3%, $P=0.68$). There were also no differences in reconstruction-related complications (4.7% vs. 4.3%, $P=0.39$) or major complications (1.6% vs. 1.5%, $P=0.84$) between both cohorts. More specifically, superficial wound infections, deep wound infections, organ/space infections, wound disruption, and prosthesis failure were similar across all reconstructions (Table 2). Thirty-day reoperation rates were also similar between both groups ($P=1.00$).

Table 1. Patient demographic data and clinical characteristics

Characteristic	Reconstruction technique		P-value
	Acellular dermis (n = 1,717)	Submuscular (n = 7,442)	
Age (mean ±SD, yr)	50.6 ±10.5	51.0 ±10.5	0.21
< 40	221 (12.9)	962 (12.9)	0.13
40-49	619 (36.1)	2,555 (34.3)	
50-59	549 (32.0)	2,316 (31.1)	
>60	328 (19.1)	1,609 (21.6)	
Race (%)			
White	1,413 (82.3)	6,007 (80.7)	0.19
Black/African American	91 (5.3)	475 (6.4)	
Asian	39 (2.3)	139 (1.9)	
Hawaiian/Pacific Islander	8 (0.5)	64 (0.9)	
American Indian	3 (0.2)	12 (0.2)	
Unknown	163 (9.5)	745 (10.0)	
Ethnicity (%)			
Hispanic	61 (3.6)	381 (5.1)	<0.01 ^{a)}
BMI (mean ± SD)	27.0 ±6.2	26.9 ±6.3	0.55
Underweight	38 (2.2)	158 (2.1)	0.02 ^{a)}
Normal	737 (42.9)	3,334 (44.8)	
Overweight	469 (27.3)	2,011 (27.0)	
Obese	450 (26.2)	1,895 (25.5)	
Unknown	23 (1.3)	44 (0.6)	
Clinical characteristics (%)			
Smokers	240 (14.0)	1,052 (14.1)	0.88
Steroid use	10 (0.6)	74 (1.0)	0.12
Radiotherapy <90 days	5 (0.3)	23 (0.3)	1.00
Chemotherapy <30 days	97 (5.6)	287 (3.9)	<0.01 ^{a)}
Previous OP <30 days	36 (2.1)	185 (2.5)	0.38
Comorbidities (%)			
Diabetes	81 (4.7)	363 (4.9)	0.85
Hypertension	362 (21.1)	1,755 (23.6)	0.03 ^{a)}
COPD	12 (0.7)	61 (0.8)	0.76
Congestive heart failure	2 (0.1)	2 (0.0)	0.16
Peripheral vascular disease	0 (0.0)	11 (0.1)	0.24
Bleeding disorders	11 (0.6)	52 (0.7)	0.87
Previous PCI/cardiac surgery	18 (1.0)	91 (1.2)	0.62
Previous stroke/TIA	18 (1.0)	81 (1.1)	1.00

BMI, body mass index; OP, operation; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.
^{a)}Denotes statistical significance.

Bivariate screen ($P < 0.20$) revealed age, BMI, smoking, diabetes, hypertension, COPD, previous cardiac intervention, and history of stroke/TIA as potential confounders for overall complications. After risk adjustment both groups illustrated similar probabilities of occurrence, with no significant difference in odds of complications; confirming the aforementioned results (Table 3, Fig. 2).

Comparative analysis of risk factors for complications

Bivariate screen for risk factors in the acellular dermis cohort revealed age, BMI, smoking, diabetes, and hypertension as risk factors eligible for multivariate analysis. Similar screen on the submuscular cohort revealed age, BMI, smoking, diabetes, hypertension, COPD, previous cardiac intervention, bleeding disorders, and history of stroke/TIA to be factors eligible for multivariate analysis. Common risk factors of age, BMI, smoking,

Table 2. Tissue expander reconstruction complication rates

Complication	Reconstruction technique		P-value
	Acellular dermis (n = 1,717)	Submuscular (n = 7,442)	
Total complications ^{a)} (%)	95 (5.5)	394 (5.3)	0.68
Reconstruction complications ^{a)} (%)	81 (4.7)	317 (4.3)	0.39
Any operative infection	66 (3.8)	246 (3.3)	0.27
Superficial wound infection	29 (1.7)	114 (1.5)	0.67
Deep wound infection	21 (1.2)	81 (1.1)	0.61
Organ space infection	17 (1.0)	55 (0.7)	0.29
Wound disruption	6 (0.3)	34 (0.5)	0.69
Prosthesis failure	18 (1.0)	59 (0.8)	0.30
Major medical complications ^{a)} (%)	27 (1.6)	115 (1.5)	0.84
Pneumonia	1 (0.1)	5 (0.1)	1.00
Unplanned intubation	0 (0.0)	4 (0.1)	1.00
Pulmonary embolus	1 (0.1)	15 (0.2)	0.34
Ventilator requirement >48 hours	0 (0.0)	1 (0.0)	1.00
Progressive renal insufficiency	0 (0.0)	0 (0.0)	-
Acute renal failure	0 (0.0)	2 (0.0)	1.00
Urinary tract infection	5 (0.3)	12 (0.2)	0.35
Peripheral nerve injury	0 (0.0)	4 (0.1)	1.00
Stroke	1 (0.1)	1 (0.0)	0.34
Coma	0 (0.0)	0 (0.0)	-
Cardiac arrest	0 (0.0)	0 (0.0)	-
Myocardial infarction	0 (0.0)	1 (0.0)	1.00
Transfusion requirement	3 (0.2)	24 (0.3)	0.46
Deep venous thromboembolism	6 (0.3)	21 (0.3)	0.62
Sepsis	11 (0.6)	34 (0.5)	0.34
Septic shock	0 (0.0)	4 (0.1)	1.00
Reoperation within 30 days (%)	119 (6.9)	515 (6.9)	1.00

^{a)}A single patient may experience more than one complication.

diabetes, and hypertension were compared between ADM and submuscular groups (Table 4). BMI and smoking were found to be significant independent risk factors for the development of reconstruction-related complications following both ADM-assisted and submuscular reconstruction. The adverse effects of BMI and smoking on reconstructive complications were slightly larger in the ADM cohort compared to the submuscular cohort, however the difference was not statistically significant (Fig. 3).

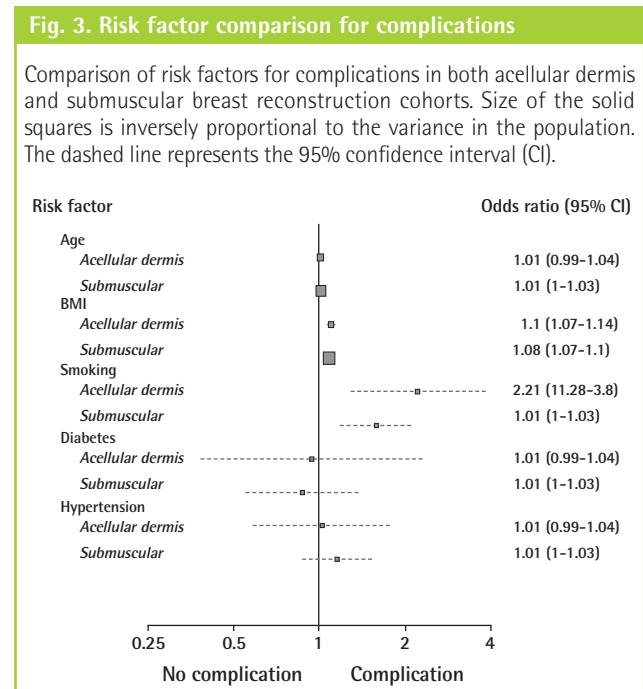
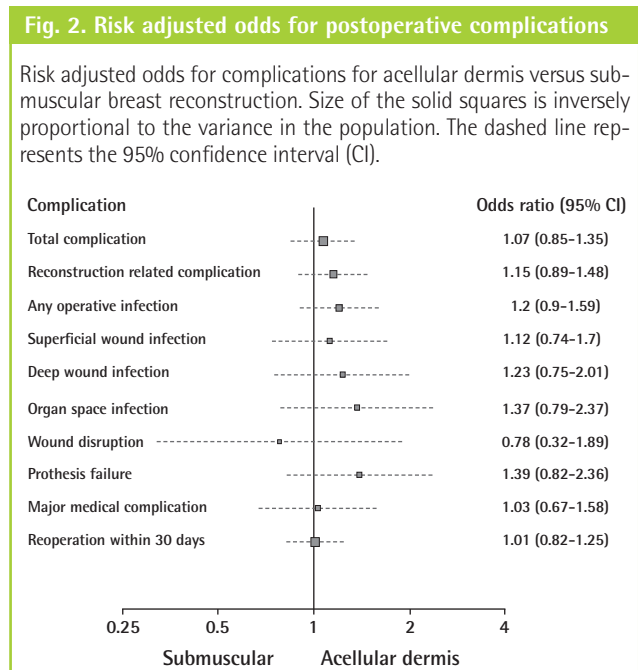
Secondary outcomes for the acellular dermis cohort

Multivariate analyses were carried out for the secondary outcomes of operative site infections (defined as all superficial wound infections, deep wound infections, and organ/space infections), wound disruption, and prosthesis failure in the acellular dermis cohort using previously identified risk factors. Increased BMI connoted a higher complication rate in all secondary outcomes ($P < 0.01$), with 1-unit BMI increase associated with a 10%, 13%, and 12% increased odds of any operative site infection, wound disruption, and prosthesis failure, respectively (Table 5). Smoking increased the odds of operative site infections (odds ratio [OR], 2.13; 95% confidence interval [CI], 1.18 to 3.86) but did not increase the odds of wound disruption or prosthesis

Table 3. Multivariate analysis of postoperative complications: acellular dermis versus submuscular reconstruction

Complication outcomes	Adjusted probabilities (%)		Odds ratio (95% CI)	P-value	HL	C-statistic
	Acellular dermis	Submuscular				
Total complications	5.6 ± 3.4	5.3 ± 3.5	1.07 (0.85-1.35)	0.57	0.68	0.65
Reconstruction related complications	4.8 ± 3.3	4.3 ± 3.4	1.15 (0.89-1.48)	0.29	0.74	0.67
Any operative infection	3.9 ± 2.9	3.3 ± 2.9	1.20 (0.91-1.60)	0.20	0.32	0.69
Superficial wound infection	1.7 ± 1.4	1.5 ± 1.4	1.12 (0.74-1.70)	0.60	0.66	0.68
Deep wound infection	1.3 ± 1.0	1.1 ± 1.1	1.23 (0.75-2.00)	0.41	0.49	0.71
Organ space infection	1.0 ± 0.7	0.7 ± 0.7	1.37 (0.79-2.37)	0.26	0.05	0.68
Wound disruption	0.4 ± 0.6	0.5 ± 0.7	0.78 (0.32-1.86)	0.57	0.94	0.76
Prosthesis failure	1.1 ± 1.0	0.8 ± 0.8	1.39 (0.82-2.37)	0.23	0.28	0.73
Major medical complications	1.6 ± 0.6	1.6 ± 0.6	1.03 (0.67-1.57)	0.91	0.75	0.61
Reoperation within 30 days	7.0 ± 2.2	6.9 ± 2.2	1.01 (0.82-1.25)	0.91	0.11	0.58

CI, confidence interval; HL, Hosmer-Lemeshow test. Model adjusted based on bivariate screen for specified outcome.



failure ($P=0.41$ and $P=0.28$, respectively). Although not a significant predictor of overall reconstructive complications, age was significant for a 5% increased odds of prosthesis failure ($P=0.05$) for every 1-year increase.

DISCUSSION

With a relatively new technology such as ADM, individual, sub-optimal studies are often the first and only data by which surgeons can make clinical (and economical) decisions. Despite a continued increase in the volume of ADM-assisted reconstruction, the conclusions of studies evaluating the risks and benefits of ADM remain conflicted, making it difficult to provide patients with a definitive understanding of its outcomes.

In response to this question, surgeons have published increasingly larger retrospective comparative cohorts to increase the power of their statistical analyses [11-15]. Additionally, several meta-analyses have been published in the hopes that pooling the current disparate studies will generate an approximation that is truer than the individual haphazard inputs [16,17]. Nevertheless, these retrospective cohorts are limited by their single institution/population basis, and the published systematic reviews are limited by the quality of the inputs. Multivariate analyses have also been undertaken by Antony et al. [12], Chun et al. [13], and Liu et al. [15], with sample sizes of 96, 283, and 343 patients respectively. Although statistically sound and providing valuable insight into risk factors for acellular dermis use, these studies may be insufficiently powered when compared to the nine thou-

Table 4. Comparison of multivariate logistic regression risk models for reconstructive complications

Patient characteristic	Acellular dermis		Submuscular ^{a)}	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Age	1.01 (0.99-1.04)	0.25	1.01 (0.99-1.02)	0.43
BMI	1.10 (1.07-1.14)	<0.01 ^{a)}	1.08 (1.06-1.09)	<0.01 ^{a)}
Smokers	2.21 (1.28-3.79)	<0.01 ^{a)}	1.58 (1.18-2.12)	<0.01 ^{a)}
Diabetes	0.94 (0.38-2.32)	0.90	0.87 (0.55-1.38)	0.57
Hypertension	1.02 (0.58-1.78)	0.96	1.15 (0.87-1.53)	0.33
COPD	NA	-	3.18 (1.54-6.45)	<0.01 ^{a)}
Bleeding disorders	NA	-	2.82 (1.16-6.85)	0.02 ^{a)}
Previous PCI/Cardiac surgery	NA	-	2.09 (1.05-4.16)	0.04 ^{a)}
Previous stroke/TIA	NA	-	1.40 (0.62-3.19)	0.42
Hosmer-Lemeshow test		0.85		0.67
C-statistic		0.69		0.68

CI, confidence interval; BMI, body mass index; COPD, chronic obstructive pulmonary disease; NA, not applicable; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.
^{a)}Denotes statistical significance.

Table 5. Multivariate analysis of secondary outcomes for the acellular dermis cohort

Patient characteristic	Any operative infection ^{a)}		Wound disruption		Prosthesis failure	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Age	1.01 (0.99-1.04)	0.43	0.98 (0.90-1.08)	0.72	1.05 (1.00-1.10)	0.05 ^{b)}
BMI	1.10 (1.06-1.14)	<0.01 ^{b)}	1.13 (1.03-1.24)	0.01 ^{b)}	1.12 (1.05-1.19)	<0.01 ^{b)}
Smokers	2.13 (1.18-3.86)	0.01 ^{b)}	2.18 (0.35-13.77)	0.41	1.88 (0.59-5.96)	0.28
Diabetes	0.60 (0.19-1.84)	0.37	6.80 (0.78-59.11)	0.08	0.98 (0.19-5.12)	0.98
Hypertension	1.14 (0.62-2.10)	0.67	0.28 (0.02-3.47)	0.32	0.65 (0.21-2.03)	0.45
Hosmer-Lemeshow Test		0.49		0.83		0.03 ^{b)}
C-Statistic		0.69		0.86		0.71

CI, confidence interval; BMI, body mass index.
^{a)}Defined as all superficial wound infections, deep wound infections, and organ space infections; ^{b)}Denotes statistical significance.

sand patients captured in this study. Additionally, although these studies have explored risk factors that pertain to morbidity with acellular dermal matrices, there have to been no comparisons between these purported risk factors and those that are inherent to submuscular reconstruction. This statistical vacuum has made it difficult to ascertain when it is most appropriate to use acellular dermis in high-risk populations. The NSQIP database is truly the first large-scale, multi-institutional database that can effectively evaluate the 30-day postoperative morbidity associated with ADM-assisted breast reconstruction and have sufficient statistical power to compare risk factors from both cohorts.

In this series, ADM did not connote an increased complication risk profile than traditional, submuscular tissue expander reconstruction. Specifically, the rates of general reconstructive complication variables were evaluated, including surgical site infection, wound disruption, and prosthesis failure, all of which showed no statistical differences between cohorts. In order to better quantify these complications and compare risk factors for developing complications in each cohort, bivariate and multi-

variate logistic regression were used.

In previous cohort studies and systematic reviews, there has been a question of increased infection rates associated with ADM use [13-15,17]. These studies have linked infections to flap necrosis and seroma formation, as physiological states that compromise the patient's ability to vascularize and incorporate ADM may increase infection risk. However, the similarities in overall infection rates in this study may reflect the multi-institutional evolution of surgical technique captured by the NSQIP database over 6 years, potentially averaging risk over time as surgeons adapt to the learning curve of a new technique. When assessing risk factors for infection, smokers, who are known to have severely compromised vasculature were more likely to develop operative site infections in the ADM cohort (OR, 2.13; 95% CI, 1.18 to 3.86); potentially supportive of the aforementioned compromised incorporation hypothesis. Previous studies have also explored smoking as a risk factor for complications [12,15]. Liu et al. [15] evaluated both the acellular dermis and submuscular cohorts as a whole, demonstrating that smoking

increased the odds of overall complications by 2.59 (95% CI, 1.22 to 5.49) but not the odds of infection ($P=0.45$) [15]. Antony et al. [12] evaluated the ADM cohort independently, with results that trended towards, but were not statistically significant for increased odds of complications in smokers (OR, 3.36; 95% CI, 0.98 to 11.55). The results of these studies were comparable to our analysis, which demonstrated that both the ADM and submuscular cohorts had statistically similar increased odds of overall complications in smokers (OR, 2.21; 95% CI, 1.28 to 3.79 vs. OR, 1.58; 95% CI, 1.18 to 2.12), while discrepancies with regards to infection were possibly related to an insufficiently powered analysis in Liu et al.'s study [15]. Smoking however, did not increase the odds of wound disruption or prosthesis failure in this study, albeit being linked to infection rates. Previous studies have also shown an association between ADM and flap necrosis, however the incidence of wound disruption and prosthesis failure in this study were similar between both cohorts [13-15]. Perhaps this is due to selection bias in that acellular dermis was not be used when mastectomy flaps were found to be significantly compromised during intraoperative assessment.

BMI was also an independent risk factor for the development of complications in both cohorts. Higher BMI is a known risk factor for complications in other methods of breast reconstruction, and has been increasingly described as a risk factor during both traditional tissue expander-based and ADM-assisted reconstructions [12,13,15]. In the NSQIP database, higher BMI increased the odds of developing all reconstruction-related complications in the acellular dermis cohort ($P < 0.01$). This effect was independent of the effects of diabetes and hypertension, which were adjusted for in the multivariate analysis. Antony et al. demonstrated an odds of any reconstructive complication to be 1.09 (95% CI, 1.01 to 1.17) per unit of BMI comparable to our results of 1.10 (95% CI, 1.07 to 1.14) per unit of BMI [12]. Additionally, Chun [13] found BMI to increase the odds of infection, demonstrating odds of 1.1 (95% CI, 1.00 to 1.22) per unit of BMI, similar to our findings. This association between obesity and reconstructive complications is likely related to several factors. Larger breast sizes generally require larger expander volumes to prevent dead space formation, and with the use of acellular dermis, there is a larger subpectoral pocket available for aggressive expansion. However, this expansion may cause perfusion defects, and with an already compromised vascular supply, the distal ends of these large mastectomy flaps are prone to necrosis and infection. Conversely, under-filling of the expander can lead to seroma formation causing poor incorporation of the dermal graft and increasing risk of infection. However, BMI was a risk factor for complications independent of ADM use, as the odds of reconstructive complications was not statistically different between the acellular

dermis and submuscular cohorts (OR, 1.10; 95% CI, 1.07 to 1.14 vs. OR, 1.08; 95% CI, 1.06 to 1.09). As such, obesity should not be considered a contraindication to acellular dermis use. Instead, a careful preoperative and intraoperative assessment is essential when choosing to use acellular dermis in obese patients, knowing that these patients are prone to a similar set of complications that afflict all expander based reconstructions.

Various studies have examined age as an independent risk factor for complications in breast reconstruction [12,22,23]. McCarthy et al. [22] explored the relationship between age and complications with the submuscular technique and found that age over 65 led to a greater risk of complications. In ADM-based reconstructions, Antony et al. [12] described an odds ratio of 1.57 for every decade increase in age (1.05 per year). Bivariate analysis indicated increasing age was a significant predictor of complications in submuscular reconstruction, and trended towards significance in ADM-assisted reconstructions, similar to Antony's results [12]. However when adjusting for other confounders in multivariate regression, age was not a statistically significant predictor of complications in the either cohort, implying some confounding effect as patients with increasing age are more likely to be diabetic, hypertensive, or smokers.

Despite our rigorous analysis, we must acknowledge the limitations of our study, which can be primarily attributed to the limitations of the NSQIP database itself. Although the NSQIP database provides a robust, unbiased, and statistically powerful database, there are nuances that limit its pertinence to plastic and reconstructive surgery. Although our study's complication rates following ADM and submuscular reconstruction were nearly equivalent at 5.5% and 5.3%, respectively, these rates may be conservative relative to the total complication rates reported in the current ADM literature, ranging from 2.4% to 59.6% [16]. A recent study summarized this literature in a meta-analysis of about 15,000 patients, where pooled overall complications in the acellular dermis cohort were 15.4%; three fold the NSQIP database outcomes [16]. This is likely due to several factors, including that the NSQIP database does not individually track a number of specific reconstructive outcomes such as seromas. The 30-day cutoff of complication tracking also limits the reporting of long-term complications such as capsular contracture. And a more subtle nuance, NSQIP variable tracking is done per patient versus per breast; frequently used to capture the bilateral incidence of complication rates. Although this simplifies demographic based risk calculations, it may lead to overall under-reporting of complications. We have attempted to circumvent these limitations by making inferences that link NSQIP reported outcomes to more commonly recognized reconstructive surgical variables, however it is impossible to have absolute certainty re-

garding the accuracy of these inferences. Also clinical and demographic variables are somewhat limited, such tracking postoperative radiation therapy. Due to the capture algorithm of NSQIP, only radiotherapy incurred prior to the operative procedure was available for analysis. Although postoperative radiotherapy and its effects on tissue expander/implant reconstruction have been well documented, studies exploring the effects of radiation prior to reconstruction are limited, particularly regarding ADM based reconstructions [24,25]. However, given these aforementioned restrictions, the indirect effect of radiation could not be properly evaluated in this study. This limitation is also true for patients who underwent chemotherapy, where only a 30 day preoperative window was available for analysis. Finally, our analysis did not factor in the institution clustering effect on patient outcomes, though we did anticipate this will change our results given the large numbers of centers included in the NSQIP data.

In spite of the limitations surrounding the NSQIP database, the large-scale (>9,000 patient), multi-institutional (>240 center) nature of the database avoids the pitfalls of inter-institution variance of procedure found in isolated retrospective cohorts, while also providing sufficient statistical power for multivariate analyses that is not always feasible by single institutions. This study is the first comparative analysis of ADM-assisted tissue expander breast reconstruction utilizing the NSQIP registry. In summary, complication profiles of ADM and traditional submuscular reconstruction appear to be similar. This study lends credence to increasing evidence that obesity and smoking are major factors in the development of postoperative complications following acellular dermis assisted tissue expander breast reconstruction. However, these, high-risk patients were no more likely to develop reconstruction related complication with the use of ADM than without.

REFERENCES

1. Wainwright DJ. Use of an acellular allograft dermal matrix (AlloDerm) in the management of full-thickness burns. *Burns* 1995;21:243-8.
2. Kim JY, Bullocks JM, Basu CB, et al. Dermal composite flaps reconstructed from acellular dermis: a novel method of neourethral reconstruction. *Plast Reconstr Surg* 2005;115:96e-100e.
3. Buinewicz B, Rosen B. Acellular cadaveric dermis (AlloDerm): a new alternative for abdominal hernia repair. *Ann Plast Surg* 2004;52:188-94.
4. Nahabedian MY. AlloDerm performance in the setting of prosthetic breast surgery, infection, and irradiation. *Plast Reconstr Surg* 2009;124:1743-53.
5. Buck DW 2nd, Heyer K, DiBardino D, et al. Acellular dermis-assisted breast reconstruction with the use of crescentic tissue expansion: a functional cosmetic analysis of 40 consecutive patients. *Aesthet Surg J* 2010;30:194-200.
6. Salzberg CA, Ashikari AY, Koch RM, et al. An 8-year experience of direct-to-implant immediate breast reconstruction using human acellular dermal matrix (AlloDerm). *Plast Reconstr Surg* 2011;127:514-24.
7. Breuing KH, Colwell AS. Inferolateral AlloDerm hammock for implant coverage in breast reconstruction. *Ann Plast Surg* 2007;59:250-5.
8. Spear SL, Parikh PM, Reisin E, et al. Acellular dermis-assisted breast reconstruction. *Aesthetic Plast Surg* 2008;32:418-25.
9. Losken A. Early results using sterilized acellular human dermis (NeoForm) in post-mastectomy tissue expander breast reconstruction. *Plast Reconstr Surg* 2009;123:1654-8.
10. Rawlani V, Buck DW 2nd, Johnson SA, et al. Tissue expander breast reconstruction using prehydrated human acellular dermis. *Ann Plast Surg* 2011;66:593-7.
11. Sbitany H, Sandeen SN, Amalfi AN, et al. Acellular dermis-assisted prosthetic breast reconstruction versus complete submuscular coverage: a head-to-head comparison of outcomes. *Plast Reconstr Surg* 2009;124:1735-40.
12. Antony AK, McCarthy CM, Cordeiro PG, et al. Acellular human dermis implantation in 153 immediate two-stage tissue expander breast reconstructions: determining the incidence and significant predictors of complications. *Plast Reconstr Surg* 2010;125:1606-14.
13. Chun YS, Verma K, Rosen H, et al. Implant-based breast reconstruction using acellular dermal matrix and the risk of postoperative complications. *Plast Reconstr Surg* 2010;125:429-36.
14. Lanier ST, Wang ED, Chen JJ, et al. The effect of acellular dermal matrix use on complication rates in tissue expander/implant breast reconstruction. *Ann Plast Surg* 2010;64:674-8.
15. Liu AS, Kao HK, Reish RG, et al. Postoperative complications in prosthesis-based breast reconstruction using acellular dermal matrix. *Plast Reconstr Surg* 2011;127:1755-62.
16. Kim JY, Davila AA, Persing S, et al. A meta-analysis of human acellular dermis and submuscular tissue expander breast reconstruction. *Plast Reconstr Surg* 2012;129:28-41.
17. Sbitany H, Serletti JM. Acellular dermis-assisted prosthetic breast reconstruction: a systematic and critical review of efficacy and associated morbidity. *Plast Reconstr Surg* 2011;128:1162-9.
18. ACS NSQIP data: participant use data file. American College of Surgeons National Surgical Quality Improvement Program [Internet]. Chicago, IL: American College of Sur-

- geons; c2002-2012 [cited 2012 Feb 15]. Available from: <http://acsnsqip.org/puf/PufRequestHomepage.aspx>.
19. Khuri SF, Daley J, Henderson W, et al. The Department of Veterans Affairs' NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA Surgical Quality Improvement Program. *Ann Surg* 1998;228:491-507.
 20. User guide for the 2010 participant use data file. American College of Surgeons National Surgical Quality Improvement Program [Internet]. Chicago, IL: American College of Surgeons; [cited 2012 Jun 21]. Available from: http://site.acsnsqip.org/wp-content/uploads/2012/03/2010-User-Guide_FINAL.pdf.
 21. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. *Am J Epidemiol* 2007;165:710-8.
 22. McCarthy CM, Mehrara BJ, Riedel E, et al. Predicting complications following expander/implant breast reconstruction: an outcomes analysis based on preoperative clinical risk. *Plast Reconstr Surg* 2008;121:1886-92.
 23. Alderman AK, Wilkins EG, Kim HM, et al. Complications in postmastectomy breast reconstruction: two-year results of the Michigan Breast Reconstruction Outcome Study. *Plast Reconstr Surg* 2002;109:2265-74.
 24. Kronowitz SJ, Robb GL. Radiation therapy and breast reconstruction: a critical review of the literature. *Plast Reconstr Surg* 2009;124:395-408.
 25. Hirsch EM, Seth AK, Dumanian GA, et al. Outcomes of tissue expander/implant breast reconstruction in the setting of prereconstruction radiation. *Plast Reconstr Surg* 2012;129:354-61.