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EPIDEMIOLOGY

Differential impact of non-insulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus on breast reconstruction outcomes

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Abstract While the comparative safety of breast reconstruction in diabetic patients has been previously studied, we examine the differential effects of insulin and non-insulin-dependence on surgical/medical outcomes. Patients undergoing implant/expander or autologous breast reconstruction were extracted from the National Surgical Quality Improvement Program 2005–2012 database. Preoperative and postoperative variables were analyzed using chi-square and Student's *t* test as appropriate. Multivariate regression modeling was used to evaluate whether non-insulin-dependent diabetes mellitus (NIDDM) or insulin-dependent diabetes mellitus (IDDM) is independently associated with adverse 30-day events following breast reconstruction. Of 29,736 patients meeting inclusion criteria, 23,042 (77.5 %) underwent implant/expander reconstructions, of which 815 had NIDDM and 283 had IDDM. Of the 6,694 (22.5 %) patients who underwent autologous reconstructions, 286 had NIDDM and 94 had IDDM. Rates of overall and surgical complications significantly differed among non-diabetic, NIDDM and IDDM patients in both the implant/expander and autologous cohorts on univariate analysis. After multivariate analysis, NIDDM was significantly associated with surgical complications (OR 1.511); IDDM was significantly associated with medical (OR 1.815) and overall complications (OR 1.852); and any type of diabetes was significantly associated with surgical (OR 1.58) and overall (OR 1.361) complications after autologous reconstruction. Diabetes of any type was not associated with any type of complication after implant/expander reconstruction. In this large, multi-institutional study, diabetes mellitus was significantly associated with adverse outcomes after autologous, but not implant-based breast reconstruction. The multivariate analysis in this study adds granularity to the differential effects of NIDDM and IDDM on complication risk.

The NSQIP and the hospitals participating in the NSQIP are the source of the data used herein; they have not been verified and are not responsible for the statistical validity of the data analysis, or the conclusions derived by the authors of this study.

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Introduction

Recent studies have demonstrated an upward trend in mastectomy [1–5] and immediate breast reconstruction in the last decade, particularly of the prosthetic modality [6, 7]. Hematological and wound healing abnormalities, which have been previously documented in diabetic patients [8, 9], suggest a higher risk of postsurgical morbidity in this group. Studies on the relationship between other preoperative variables, such as obesity or BMI, and post-reconstructive complications are exhaustive [10–14]. In contrast, much less has been examined regarding AE profiles in diabetic patients. Studies are limited by single-institution sample size, failure to categorize the diabetic cohort, and/or reconstructive procedure [5, 15, 16]. Diabetes mellitus (DM) itself is the end result of a number of different metabolic processes, the majority of which fall into two distinct disease processes: Type 1 DM or insulin-dependent DM (IDDM); and Type 2 DM or non-insulin-dependent DM (NIDDM). Both processes have distinct etiologies, treatment strategies, duration of onset, and long-term sequelae.

Without adequate statistical power, no study has been able to evaluate whether NIDDM and/or IDDM independently predict a greater risk of complications following prosthetic or autologous breast reconstruction. Fischer et al. [5] recently reported an increase in the incidence of surgical and wound complications in diabetics undergoing breast reconstruction compared to non-diabetics. Because there is a lack of context by which to evaluate this and similar studies, we performed the first multi-institutional regression analysis via the National Surgical Quality Improvement Program (NSQIP) database to assess the variable influence of NIDDM and IDDM on breast reconstruction. Knowledge of specific risk factors for surgical and medical complications following a high-volume surgery such as breast reconstruction will steer strategies for quality improvement, patient informed consent, and risk stratification, improving outcomes and reducing complications.

Methods

Population

We performed a retrospective analysis of patients in the NSQIP database. The NSQIP was instituted by the American College of Surgeons in 2004 and provides comprehensive information for major surgical procedures at more than 240 institutions across the USA [17]. Since then, it has played a crucial role in the mission for continued quality improvement in the surgical field [18]. Data files from 2005 to 2012 were reviewed to collect data on all female patients undergoing breast reconstruction during that period. Patients were identified using primary or concurrent Current Procedural Terminology (CPT) codes 19340 and 19357 for implant/expander reconstructions, and 19361, 19364, 19367, 19368, and 19369 for autologous reconstructions. Reconstructions that had the concurrent presence of an autologous and a prosthetic CPT code, with the exception of latissimus/tissue-expander combinations were excluded from the analysis ($n = 258$, 0.8 % of all reconstructions). The process by which patients were extracted from the database is detailed in the attrition chart in Fig. 1. Patients were initially stratified into prosthetic ($n = 23{,}042$) and autologous ($n = 6{,}694$) cohorts. Within each cohort, patients were grouped according to diabetic status: not diabetic, NIDDM, and IDDM for comparison of perioperative variables and covariate screening.

Variables

National Surgical Quality Improvement Program-defined preoperative variables were compared among the respective diabetic groups for each reconstruction type (autologous or prosthetic). They included demographic variables (e.g., age, BMI class); lifestyle variables (e.g., smoking), and medical comorbidities (e.g., diabetes, dyspnea, hypertension, COPD, congestive heart failure, bleeding disorders, prior angioplasty or cardiac surgery, previous stroke or transient ischemic attack, radiotherapy within 90 days of operation, chemotherapy within thirty days of operation, previous operations within 30 days of operation). Additionally, the sum of relative units for additional procedures was computed and included in the analysis given the inherent complexity differences between concurrent procedures [19]. Tracked outcomes were categorized as surgical complications, medical complications, and overall complications. Surgical complications included superficial, deep, or organ–space surgical site infection (SSI); wound disruption; graft/prosthesis/flap failure. Medical complications included deep venous thrombosis (DVT), pulmonary embolism (PE), unplanned re-intubation, ventilator dependence >48 h, progressive renal insufficiency, acute renal failure, coma, stroke, cardiac arrest, myocardial infarction (MI), peripheral nerve injury, pneumonia, urinary tract infection (UTI), blood transfusions, and sepsis/septic shock. All morbidities were used as defined in the NSQIP user guide. Overall complications included all surgical and medical complications.

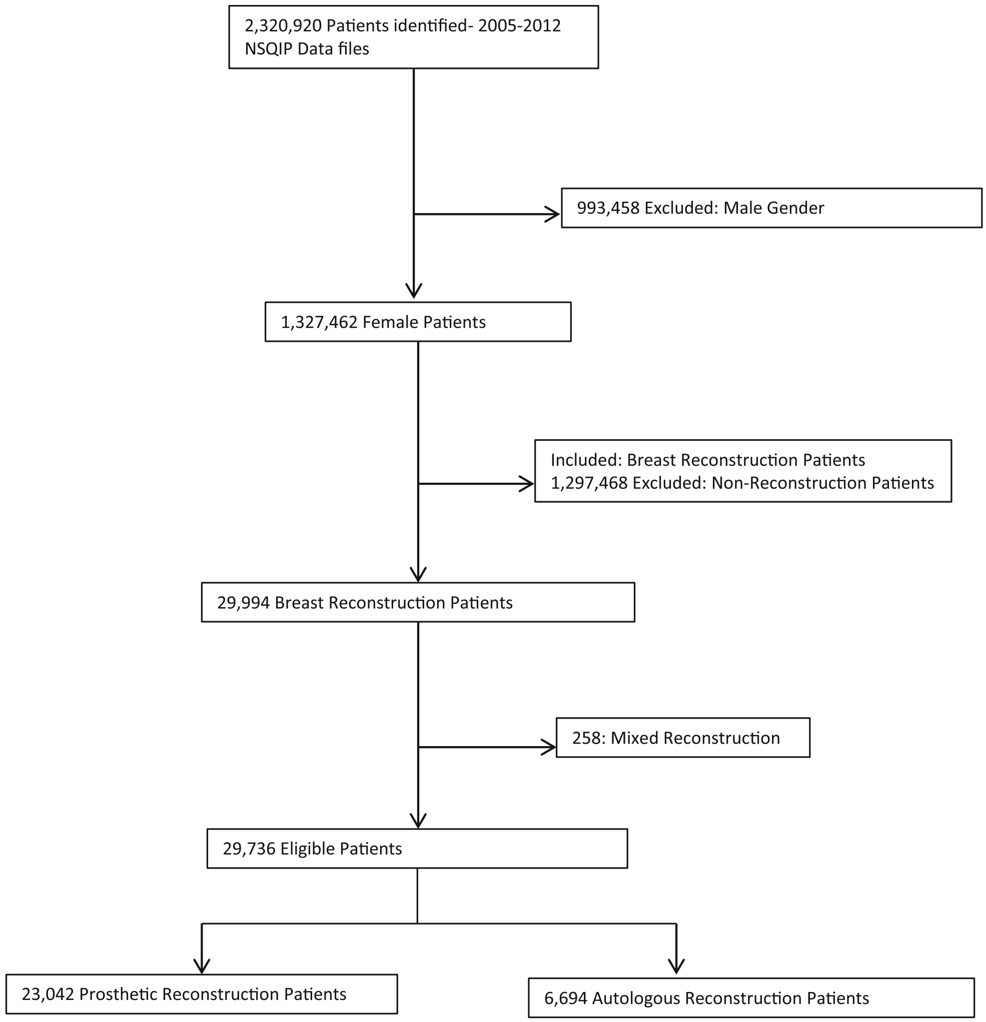

Fig. 1 Attrition diagram

Statistical analysis

Chi-square tests, for categorical variables, and Student's *t* test, for continuous variables, were used to identify differences in perioperative variables among the non-diabetic, NIDDM, and IDDM cohorts. Significance was defined as $P < 0.05$. This method was then used within the prosthetic and autologous cohort to identify differences in overall, medical, and surgical complications. Perioperative variables with $n \geq 10$ and $P < 0.2$ were identified as possible predictors and included in a binary logistic regression. These predictors associated with diabetic status were assessed for overall, medical, and surgical complications. Again, $P < 0.05$ was considered significant. Hosmer–Lemeshow (H–L) and c-statistics were calculated to assess model calibration and discriminatory capability, respectively [20, 21]. All analysis was performed using SPSS version 20 (IBM Corp Armonk, NY, USA).

Results

Population demographics

The identification and inclusion criteria are detailed in Fig. 1. A total of 29,736 patients met the inclusion criteria of which 23,042 (77 %) received a prosthetic reconstruction and 6,694 (23 %) received an autologous reconstruction. Within the prosthetic cohort, 21,944 (95 %) patients were not diabetic, 815 (4 %) were NIDDM, and 283 (1 %) were IDDM. Within the autologous cohort, 6,314 (94 %) patients were not diabetic, 286 (4 %) were NIDDM, and 94 (2 %) were IDDM. Tables 1 and 2 display the distribution of demographics and comorbidities among the three cohorts within the prosthetic and autologous cohorts, respectively. In the prosthetic cohort, significant differences existed among not diabetic, NIDDM, and IDDM patients in smoking (13.30 vs. 8.96 vs. 14.13 %), chemotherapy

Table 1 Prosthetic patient demographics and comorbidities

Preoperative variable	Non-diabetic (21,944)	% total	Non-insulin-dependent (815)	% total	Insulin-dependent (283)	% total	P
Age (year)	50.9 (10.7)		59.5 (9.4)		55.9 (10.2)		<0.001
Total operation time (year)	190.6 (90.4)		184.1 (86.6)		182.7 (85.7)		0.351
Total operation time (z score)[a]	3,226	14.70	97	11.90	37	13.07	0.063
Length of hospital stay (days)	1.6 (4.2)		2.07 (12.9)		1.7 (1.4)		0.002
BMI class*							<0.001
Less than 30	16,687	76.04	330	40.49	117	41.34	
Between 30 and 40	4,426	20.17	364	44.66	129	45.58	
40 and over	706	3.22	118	14.48	37	13.07	
Race							<0.001
White	17,540	79.93	604	74.11	207	73.14	
Black	1,328	6.05	100	12.27	46	16.25	
Asian	663	3.02	30	3.68	7	2.47	
Other	2,413	11.00	81	9.94	23	8.13	
Active smoker*	2,919	13.30	73	8.96	40	14.13	0.001
Steroid use	231	1.05	11	1.35	6	2.12	0.167
Radiotherapy (<90 days)	68	0.31	3	0.37	0	0.00	0.615
Chemotherapy (<30 days)*	844	3.85	16	1.96	10	3.53	0.021
Previous OP <30 days	350	1.59	15	1.84	5	1.77	0.841
Dyspnea*	624	2.84	58	7.12	27	9.54	<0.001
Hypertension*	4,683	21.34	576	70.67	188	66.43	<0.001
COPD*	152	0.69	16	1.96	9	3.18	<0.001
Congestive heart failure*	6	0.03	0	0.00	1	0.35	0.007
Bleeding disorders*	125	0.57	8	0.98	5	1.77	0.012
Previous PCI/cardiac surgery*	148	0.67	17	2.09	16	5.65	<0.001
ASA class 3 or 4	3,855	17.57	412	50.55	189	66.78	<0.001
Stroke*	162	0.74	18	2.21	9	3.18	<0.001

Continuous variables expressed as mean (SD)

* Denotes significant value $P < 0.05$

[a] Represents number of patients with operation times 1 standard deviation or greater from the mean

30 days prior to the operation (3.85 vs. 1.96 vs. 3.53 %), dyspnea (2.84 vs. 7.12 vs. 9.54 %), hypertension (21.34 vs. 70.67 vs. 66.43 %), COPD (0.69 vs. 1.96 vs. 3.53 %), congestive heart failure (0.03 vs. 0 vs. 0.35 %), bleeding disorders (0.57 vs. 0.98 vs. 1.77 %), previous PCI/cardiac surgery (0.67 vs. 2.09 vs. 5.65 %), and previous stroke (0.74 vs. 2.21 vs. 3.18 %). In the autologous cohort, significant differences were noted with respect to steroid use (1 vs. 2.8 vs. 2.13 %), dyspnea (3.14 vs. 6.99 vs. 8.51 %), hypertension (24.82 vs. 69.93 vs. 65.96 %), and previous PCI/cardiac surgery (0.51 vs. 2.45 vs. 4.26 %).

Outcomes comparison

Endpoint distributions among the three diabetic classes within prosthetic and autologous cohorts are displayed in Tables 3 and 4, respectively. In the prosthetic cohort, rates of overall complications (5.45 vs. 8.34 vs. 9.54 %; $P < 0.001$) and surgical complications (4.33 vs. 7.73 vs. 8.48 %; $P < 0.001$) significantly differed across the three diabetic classes. In the autologous cohort, rates of overall complications (14.68 vs. 22.03 vs. 29.79 %; $P < 0.001$), surgical complications (7.65 vs. 14.34 vs. 14.89 %; $P < 0.001$), and medical complications (8.92 vs. 11.19 vs. 18.09 %; $P = 0.004$) were significantly different among the three diabetic classes.

Regression analysis of overall, surgical, and medical complications within cohorts

The results of the multivariate regression analysis are displayed in Tables 5 and 6. H–L and c-statistics are included under each table. NIDDM was an independent predictor for surgical complications after autologous reconstruction (OR 1.511) IDDM was an independent predictor for medical (OR 1.815) and overall complications (OR 1.852).

Table 2 Autologous patient demographics and comorbidities

Preoperative variable	Non-diabetic (6,314)	% total	Non-insulin-dependent (286)	% total	Insulin-dependent (94)	% total	P
Age (year)	51.5 (9.7)		57.2 (8.6)		56.8 (9.8)		<0.001
Total operation time (min)	381.0 (196.5)		380.9 (187.3)		322.0 (171.1)		0.115
Total operation time (z score)[a]	924	14.63	50	17.48	9	9.57	0.152
Length of total hospital stay (days)	4.0 (7.9)		3.9 (2.6)		4.8 (7.8)		0.582
BMI class*							<0.001
30 and less	4,155	65.81	92	32.17	35	37.23	
30–40	1,893	29.98	155	54.20	41	43.62	
40 and over	241	3.82	37	12.94	17	18.09	
Race							<0.001
White	4,654	73.71	187	65.38	64	68.09	
Black	689	10.91	64	22.38	21	22.34	
Asian	190	3.01	7	2.45	1	1.06	
Other	781	12.37	28	9.79	8	8.51	
Active smoker	688	10.90	23	8.04	12	12.77	0.26
Steroid use*	63	1.00	8	2.80	2	2.13	0.01
Radiotherapy (<90 days)	42	0.67	2	0.70	0	0.00	0.728
Chemotherapy (<30 days)	246	3.90	5	1.75	2	2.13	0.123
Previous OP <30 days	165	2.61	8	2.80	5	5.32	0.267
Dyspnea*	198	3.14	20	6.99	8	8.51	<0.001
Hypertension*	1,567	24.82	200	69.93	62	65.96	<0.001
COPD	48	0.76	5	1.75	2	2.13	0.072
Congestive heart failure	1	0.02	0	0.00	0	0.00	0.97
Bleeding disorders	47	0.74	2	0.70	0	0.00	0.701
Previous PCI/cardiac surgery*	32	0.51	7	2.45	4	4.26	<0.001
ASA class 3 or 4	1,525	24.15	157	54.90	62	65.96	<0.001
Stroke	41	0.65	1	0.35	2	2.13	0.18

Continuous variables expressed as mean (SD)

* Denotes significant value $P < 0.05$

[a] Represents number of patients with operation times 1 standard deviation or greater from the mean

Diabetes was not shown to independently predict either overall, surgical, or medical complications after prosthetic reconstruction. When examining all DM patients (i.e., both IDDM and NIDDM combined), DM was associated with overall and surgical complications on multivariate analysis in the autologous cohort, but was not associated with any category of complications in the prosthetic cohort.

Discussion

Given the increasing utilization of breast reconstruction, and a concurrent focus on surgical outcomes to guide reimbursement, renewed interest has been paid to risk factors in breast reconstruction. While a great deal has been written on tobacco and obesity, there is relatively little characterizing diabetes mellitus as an independent predictor of complications following breast reconstruction surgery. DM itself is the end result of a number of different metabolic processes, the majority of which fall into two distinct disease processes: Type 1 DM or IDDM; and Type 2 DM or NIDDM. This study is one of the first to separately examine insulin-dependent and non-insulin-dependent diabetes mellitus using a robust population of autologous and prosthetic reconstructions from the NSQIP 2005-2012 datasets. Almost exclusively, the previous literature has grouped the two forms of DM together, in spite of different etiologies and disease progression. Large database populations such as NSQIP are powerful enough to detect differences in these populations.

There is a growing literature reporting differences in surgical outcomes between patients with NIDDM versus IDDM. The onset of IDDM is earlier in the majority of cases and treatment centers on insulin replacement or

Table 3 Unadjusted postoperative outcomes prosthetic

Complication category	Specific complication	Non-diabetic (21,944)	% total	Non-insulin-dependent (815)	% total	Insulin-dependent (283)	% total	P
Overall complications*		1,196	5.45	68	8.34	27	9.54	<0.001
Surgical complications*		950	4.33	63	7.73	24	8.48	<0.001
	Superficial infection	390	1.78	20	2.45	6	2.12	0.335
	Deep infection*	202	0.92	19	2.33	6	2.12	<0.001
	Organ–space infection*	169	0.77	15	1.84	3	1.06	0.003
	Wound disruption*	118	0.54	13	1.60	4	1.41	<0.001
	Flap/prosthesis failure*	146	0.67	4	0.49	7	2.47	0.001
Medical complications		344	1.57	10	1.23	4	1.41	0.729
	DVT	51	0.23	1	0.12	0	0.00	0.586
	Pulmonary embolism	34	0.15	1	0.12	0	0.00	0.783
	Unplanned reintubation	6	0.03	0	0.00	0	0.00	0.861
	Ventilator (>48 h)*	2	0.01	1	0.12	0	0.00	0.02
	Renal insufficiency	3	0.01	0	0.00	0	0.00	0.928
	Acute renal failure*	2	0.01	1	0.12	0	0.00	0.02
	Coma	0	0.00	0	0.00	0	0.00	
	Stroke*	4	0.02	0	0.00	1	0.35	0.001
	Cardiac arrest	0	0.00	0	0.00	0	0.00	
	Myocardial infarction	1	0.00	0	0.00	0	0.00	0.975
	Peripheral nerve injury	6	0.03	0	0.00	0	0.00	0.861
	Pneumonia	15	0.07	1	0.12	0	0.00	0.766
	UTI	45	0.21	3	0.37	0	0.00	0.449
	Transfusion	111	0.51	1	0.12	3	1.06	0.126
	Sepsis/septic shock	91	0.41	4	0.49	0	0.00	0.513
Death		1	0.00	0	0.00	0	0.00	0.975
Reoperation		1,442	6.57	64	7.85	26	9.19	0.08

* Denotes significant value $P < 0.05$

pancreatic transplantation. NIDDM is associated with obesity and insulin resistance and is managed in many cases with surgical and non-surgical weight loss [22]. Particular studies have linked IDDM, but NIDDM with increased serious AE's, including death and myocardial infarction [23, 24]. However, none of these reports have the patient numbers and detail of the NSQIP datasets.

The historical literature has implicated DM as a risk factor for AE's in breast esthetic surgery, breast reconstruction, abdominal surgery, and abdominoplasty. Hensel et al. [25] found that DM was significantly associated with minor wound healing complications after abdominoplasty. However, this was a single-center study, and no multivariable analysis was performed. Hanamann et al. [26] examined 13,475 consecutive cosmetic breast cases between 2003 and 2009 utilizing the CosmetAssure database. They found a statistically insignificant increased risk of AE's in DM patients (3.8 vs. 1.7 %, $P = 0.055$). This risk was further increased in mastopexy patients (over augmentation patients). However, given the self-reported nature of the database, reporting error is a significant concern for data validity.

More recently, analysis of large datasets has presented a mixed evaluation of the role of DM as a predisposing factor for AE's. The breast reconstruction risk assessment (BRA) score risk calculator calculates a 2.81 % relative risk of medical complications and 2.44 % risk of surgical site infection for DM patients undergoing autologous reconstruction compared to a 2.81 % risk of medical complications and 1.97 % risk of surgical site infections for non-DM patients. The American College of Surgeons Risk Calculator computes the relative risk for any AE after implant-based breast reconstruction (CPT code 19357) as 5 % for IDDM, 5 % for NIDDM, and 5 % for non-DM; conversely, for pedicled transverse rectus abdominis breast (TRAM) breast reconstruction (CPT code 19367) relative risks were 9 % for NIDDM, 10 % for IDDM, and 9 % for non-DM (referenced March 28 2014). Fisher et al. [5] analyzed 16,063 patients in the 2005–2010 NSQIP datasets undergoing breast reconstruction. They made a number of

Table 4 Unadjusted postoperative outcomes autologous

Complication category	Specific complication	Non-diabetic (6,314)	% total	Non-insulin-dependent (286)	% total	Insulin-dependent (94)	% total	*P*
Overall complications*		927	14.68	63	22.03	28	29.79	<0.001
Surgical complications*		483	7.65	41	14.34	14	14.89	<0.001
	Superficial infection*	195	3.09	16	5.59	5	5.32	0.033
	Deep infection*	101	1.60	11	3.85	5	5.32	0.001
	Organ–space infection	34	0.54	3	1.05	0	0.00	0.401
	Wound disruption*	71	1.12	10	3.50	5	5.32	<0.001
	Flap/prosthesis failure	135	2.14	6	2.10	1	1.06	0.773
Medical complications*		563	8.92	32	11.19	17	18.09	0.004
	DVT	39	0.62	1	0.35	0	0.00	0.636
	Pulmonary embolism	33	0.52	1	0.35	1	1.06	0.707
	Unplanned reintubation	10	0.16	2	0.70	0	0.00	0.098
	Ventilator (>48 h)	8	0.13	1	0.35	0	0.00	0.565
	Renal insufficiency*	0	0.00	2	0.70	0	0.00	<0.001
	Acute renal failure*	1	0.02	0	0.00	1	1.06	<0.001
	Coma	0	0.00	0	0.00	0	0.00	
	Stroke*	1	0.02	0	0.00	1	1.06	<0.001
	Cardiac arrest	3	0.05	0	0.00	0	0.00	0.914
	Myocardial infarction*	3	0.05	0	0.00	1	1.06	<0.001
	Peripheral nerve injury*	4	0.06	0	0.00	1	1.06	0.002
	Pneumonia	22	0.35	0	0.00	1	1.06	0.299
	UTI	48	0.76	2	0.70	1	1.06	0.938
	Transfusion	399	6.32	20	6.99	9	9.57	0.403
	Sepsis/septic shock*	49	0.78	8	2.80	3	3.19	<0.001
Death		3	0.05	0	0.00	0	0.00	0.914
Reoperation		597	9.46	36	12.59	11	11.70	0.168

* Denotes significant value $P < 0.05$

Table 5 Risk-adjusted regression analysis: *prosthetics in the 2005–2012 ACS-NSQIP dataset*

Preoperative variable	Overall complications				Surgical complications				Medical complications			
	P	OR	95 % CI		*P*	OR	95 % CI		*P*	OR	95 % CI	
NIDDM	0.548	1.093	0.818	1.458	0.183	1.227	0.908	1.657	0.212	0.645	0.324	1.284
IDDM	0.767	0.93	0.573	1.508	0.892	0.965	0.574	1.622	0.659	0.796	0.289	2.194
DM	0.631	1.065	0.824	1.377	0.242	1.175	0.897	1.538	0.204	0.685	0.382	1.228
	HL-stat, 0.747				HL-stat, 0.159				HL-stat, 0.720			
	C-stat, 0.666				C-stat, 0.679				C-stat, 0.665			

observations on univariate analysis, including increased wound complications (4.6 vs. 9.8 %, $P < 0.001$) and major postoperative complications. However, DM was not found to be a significant predictor of AE on regression analysis (OR 1.2, 95 % CI 0.9–1.7, $P = 0.26$). Xue [27] performed a systematic review/meta-analysis of 2,745 patients in 8 case–control studies between 1998 and 2010. They reported a statistically insignificant increased rate of SSI in DM patients of 1.88 (95 % CI 1.47–2.39, $P = 0.78$). Their study was limited in that the number of studies included in the meta-analysis was relatively small (i.e., 8 studies); there were no African–American patients in the study (which is poorly representative of both NSQIP and the US population); and their statistical analysis was unadjusted for other relevant factors (e.g., smoking, BMI, chemotherapy, radiation therapy). McCarthy et al. [28] performed

Table 6 Risk-adjusted regression analysis: *autologous in the 2005–2012 ACS-NSQIP dataset*

Preoperative variable	Overall complications				Surgical complications				Medical complications			
	P	OR	95 % CI		*P*	OR	95 % CI		*P*	OR	95 % CI	
NIDDM	0.239	1.218	0.877	1.692	0.026	1.511	1.051	2.172	0.915	0.978	0.646	1.479
IDDM	0.016	1.852	1.12	3.064	0.11	1.622	0.896	2.937	0.049	1.815	1.002	3.285
DM	0.034	1.361	1.024	1.809	0.005	1.58	1.145	2.182	0.31	1.192	0.849	1.674
	HL-stat, 0.740				HL-stat, 0.427				HL-stat, 0.117			
	C-stat, 0.680				C-stat, 0.647				C-stat, 0.706			

a single-center review of 1,170 implant-based breast reconstructions in 984 patients between 2003 and 2004. An advantage of their study was that they followed patients for 6 months. They found that DM was neither a predictor of AE, or reconstructive failure (OR 1.2, 95 % CI 0.2–5.3, $P = 0.88$). Andree [16] reviewed their single-center experience of 144 abdominally based free flaps for breast reconstruction between 2004 and 2011. They found that DM had no effect on free flap loss or donor-site complications. However, they analyzed only Type I DM patients and performed ANOVA analysis of data. Miller et al. [15] studied 893 patients undergoing autologous reconstruction at a single center between 1985 and 1997. They separated patients into IDDM and NIDDM, and compared flap and donor-site complications in a prospectively maintained database. They performed a robust, multivariable analysis of relevant factors and found no association between AE's and DM. However, this was a single-center study, with relatively low numbers, an extremely experienced surgeon group and was performed 20–30 years ago. Davis et al. [29] utilized the 2005–2009 NSQIP database to examine mastectomy-specific complications in 38,739 mastectomies. On univariate analysis, DM increased the rate of SSI (3.8 vs. 2.1 %, $P < 0.001$), which was verified on multivariable analysis (OR 1.28, 95 % CI 1.06–1.54, $P = 0.008$). Both Momeni [30] and Neaman [31] reported that DM had no effect on outcomes after abdominoplasty. Our findings suggest that DM is an independent predictor of overall and surgical complications after autologous, but not prosthetic breast reconstruction. Furthermore, this effect is subtly different between IDDM versus NIDDM. IDDM versus NIDDM demonstrate different effects on the profile of AE's, with IDDM demonstrating increased overall and medical complications, and NIDDM demonstrating increased rates of surgical complications. That DM (of any type) is not associated with increased medical complications strengthens IDDM as an independent predictor of medical complications. It is possible that the increased rates of medical complications in IDDM patients are similar to those seen in other studies linking IDDM to increased medical morbidity and mortality in these patients. This phenomenon is thought to be a factor of increased multisystem organ dysfunction in IDDM patients, given their much longer duration of disease compared to NIDDM. Ultimately, these patients present with more advanced cardiac, vascular, and renal disease than their NIDDM counterparts. Conversely, it is possible that the increased rate of surgical complications in NIDDM patients is a factor of the increased utilization of autologous reconstruction in this cohort (4.2 vs. 1.4 % of all autologous reconstructions for NIDDM and IDDM, respectively).

It is unclear why DM did not appear to influence AE's in prosthetic breast reconstruction. It has been suggested that selection bias may play in a role in the greater number of diabetic patients undergoing autologous rather than prosthetic reconstruction [32], as patients and surgeons may be averse to placing prostheses in patients with multiple comorbidities. In the current study, autologous patients had significantly increased age, ASA class and BMI, and increased rates of radiotherapy <90 days prior to the surgery, operation <30 days prior to the surgery, hypertension, open/infected wound, and DM. Other surgical specialties routinely use implants in diabetic patients. Total joint replacement in orthopedic surgery is one such example, and extensive data is available on their rates of AE's in diabetic patients. Marchant [33] examined over 1 million patients undergoing total joint arthroplasty, using the Nationwide Inpatient Sample (NIS) database from 1988 to 2005. DM was associated with increased AE's after total joint arthroplasty, and patients with uncontrolled DM exhibited significantly increased odds of surgical and systemic complications, higher mortality, and increased length of stay during the index hospitalization with increased hospital charges. Belmont et al. [34] analyzed 15,321 patients between 2006 and 2010 using the NSQIP database. DM was associated with increased 30-day mortality (OR 2.99, 95 % CI 1.35–6.62), but not any other AE's. Bolognesi [35] also used the NIS database to analyze 751,340 patients between 1988 and 2003. DM was associated with specific increased medical complications, including pneumonia, stroke, and transfusion ($P < 0.001$). Although complications were not uniformly otherwise increased, diabetic patients also had fewer routine discharges and higher inflation-adjusted hospital charges for all procedures. Overall, these studies show an increased risk of specific adverse events, including mortality and some medical complications, but no higher risk of implant failure in patients with controlled DM. This is consistent with our findings and suggests that plastic and orthopedic surgeons are doing an appropriate job of addressing potential infectious implant risks in this cohort. Future studies should attempt to correlate degree of DM control with AE's, perhaps by addressing the relationship between hemoglobin A1C levels and AE's.

Limitations of outcomes tracking using NSQIP are well described [36, 37]. In particular, NSQIP does not tack specialty-specific outcomes measures; factors relevant to the current study include hematoma, seroma, donor-site morbidity, esthetic outcomes, hemorrhage, and outcomes beyond 30 days. In addition, NSQIP does not track hemoglobin A1C levels, which would be relevant for tracking the degree of diabetic control. In spite of the large NSQIP dataset size, DM patients are represented in relatively few cases (5 % of all cases). Our data show a trend toward increased complications regardless of DM type in autologous reconstruction, but surprisingly does not demonstrate any increased risk in the prosthetic cohort. As the NSQIP dataset grows, an increased number of diabetic cases will help to confirm or refute these findings.

Conclusions

Our data in the current study suggests that breast reconstruction in DM patients results in a small, but significant increase in a number of specific complication types, but that this increase is well within an acceptable range. Specifically, DM (of any type) is associated with 30-day overall and surgical complications after autologous, but not prosthetic breast reconstruction. IDDM versus NIDDM demonstrate different effects on the profile of AE's, with IDDM demonstrating increased overall and medical complications, and NIDDM demonstrating increased rates of surgical complications. It is possible that our results our confounded by additional comorbidities in autologous reconstruction cohort, although multivariate analysis refutes this argument. These data may change the attitudes of patients and surgeons alike toward prosthetic breast reconstruction in DM patients. These data are important to proper patient informed consent and for risk stratification efforts. In addition, they suggest future directions for research in these patient populations.

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Conflict of interest The authors declare that they have no conflict of interest.

Ethical standard De-identified patient information is freely available to all institutional members who comply with the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Data Use Agreement. The Data Use Agreement implements the protections afforded by the Health Insurance Portability and Accountability Act of 1996 and the ACS-NSQIP Hospital Participation Agreement, and conforms to the Declaration of Helsinki.

References

1. Habermann EB et al (2010) Are mastectomy rates really increasing in the United States. J Clin Oncol 28(21):3437–3441
2. Tracy MS et al (2013) Contralateral prophylactic mastectomy in women with breast cancer: trends, predictors, and areas for future research. Breast Cancer Res Treat 140(3):447–452
3. Tuttle TM et al (2010) The increasing use of prophylactic mastectomy in the prevention of breast cancer. Curr Oncol Rep 12(1):16–21
4. Tuttle TM et al (2007) Increasing use of contralateral prophylactic mastectomy for breast cancer patients: a trend toward more aggressive surgical treatment. J Clin Oncol 25(33):5203–5209
5. Fischer JP et al (2013) Complications and morbidity following breast reconstruction: a review of 16,063 cases from the 2005–2010 NSQIP datasets. J Plast Surg Hand Surg 48:104–114
6. Albornoz CR et al (2013) A paradigm shift in U.S. Breast reconstruction: increasing implant rates. Plast Reconstr Surg 131(1):15–23
7. Cemal Y et al (2013) A paradigm shift in U.S. breast reconstruction: part 2. The influence of changing mastectomy patterns on reconstructive rate and method. Plast Reconstr Surg 131(3):320e–326e
8. Jones RL, Peterson CM (1981) Hematologic alterations in diabetes mellitus. Am J Med 70(2):339–352
9. Simpson LO (1985) Intrinsic stiffening of red blood cells as the fundamental cause of diabetic nephropathy and microangiopathy: a new hypothesis. Nephron 39(4):344–351
10. Fischer JP et al (2013) Impact of obesity on outcomes in breast reconstruction: analysis of 15,937 patients from the ACS-NSQIP datasets. J Am Coll Surg 217(4):656–664
11. Hanwright PJ et al (2013) The differential effect of BMI on prosthetic versus autogenous breast reconstruction: a multivariate analysis of 12,986 patients. Breast 22(5):938–945
12. Fischer JP et al (2013) Peri-operative risk factors associated with early tissue expander (TE) loss following immediate breast reconstruction (IBR): a review of 9,305 patients from the 2005–2010 ACS-NSQIP datasets. J Plast Reconstr Aesthet Surg 66(11):1504–1512
13. Moran SL, Serletti JM (2001) Outcome comparison between free and pedicled TRAM flap breast reconstruction in the obese patient. Plast Reconstr Surg 108(7):1954–1960 (discussion 1961–2)
14. Chang DW et al (2000) Effect of obesity on flap and donor-site complications in free transverse rectus abdominis myocutaneous flap breast reconstruction. Plast Reconstr Surg 105(5):1640–1648
15. Miller RB et al (2007) Microvascular breast reconstruction in the diabetic patient. Plast Reconstr Surg 119(1):38–45 (discussion 46–8)
16. Andree C et al (2013) A single center prospective study of bilateral breast reconstruction with free abdominal flaps: a critical analyses of 144 patients. Med Sci Monit 19:467–474
17. Birkmeyer JD et al (2008) Blueprint for a new American College of Surgeons: National Surgical Quality Improvement Program. J Am Coll Surg 207(5):777–782
18. Ingraham AM et al (2010) Quality improvement in surgery: the American College of Surgeons National Surgical Quality Improvement Program approach. Adv Surg 44:251–267

19. Henderson WG, Daley J (2009) Design and statistical methodology of the National Surgical Quality Improvement Program: why is it what it is? Am J Surg 198(5 Suppl):S19–S27
20. Merkow RP, Bilimoria KY, Hall BL (2011) Interpretation of the C-statistic in the context of ACS-NSQIP models. Ann Surg Oncol 18(Suppl 3):S295 (author reply S296)
21. Paul P, Pennell ML, Lemeshow S (2013) Standardizing the power of the Hosmer–Lemeshow goodness of fit test in large data sets. Stat Med 32(1):67–80
22. Schauer PR et al (2014) Bariatric surgery versus intensive medical therapy for diabetes: 3-year outcomes. N Engl J Med 370:2002–2013
23. Conrotto F et al (2014) Impact of diabetes mellitus on early and midterm outcomes after transcatheter aortic valve implantation (from a multicenter registry). Am J Cardiol 113(3):529–534
24. Yeh CC et al (2013) Adverse outcomes after noncardiac surgery in patients with diabetes: a nationwide population-based retrospective cohort study. Diabetes Care 36(10):3216–3221
25. Hensel JM et al (2001) An outcomes analysis and satisfaction survey of 199 consecutive abdominoplasties. Ann Plast Surg 46(4):357–363
26. Hanemann MS Jr, Grotting JC (2010) Evaluation of preoperative risk factors and complication rates in cosmetic breast surgery. Ann Plast Surg 64(5):537–540
27. Xue DQ et al (2012) Risk factors for surgical site infections after breast surgery: a systematic review and meta-analysis. Eur J Surg Oncol 38(5):375–381
28. McCarthy CM et al (2008) Predicting complications following expander/implant breast reconstruction: an outcomes analysis based on preoperative clinical risk. Plast Reconstr Surg 121(6):1886–1892
29. Davis GB et al (2013) Identifying risk factors for surgical site infections in mastectomy patients using the National Surgical Quality Improvement Program database. Am J Surg 205(2):194–199
30. Momeni A et al (2009) Complications in abdominoplasty: a risk factor analysis. J Plast Reconstr Aesthet Surg 62(10):1250–1254
31. Neaman KC, Hansen JE (2007) Analysis of complications from abdominoplasty: a review of 206 cases at a university hospital. Ann Plast Surg 58(3):292–298
32. Pinsolle V et al (2006) Complications analysis of 266 immediate breast reconstructions. J Plast Reconstr Aesthet Surg 59(10): 1017–1024
33. Marchant MH Jr et al (2009) The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty. J Bone Joint Surg Am 91(7):1621–1629
34. Belmont PJ Jr et al (2014) Thirty-day postoperative complications and mortality following total knee arthroplasty: incidence and risk factors among a national sample of 15,321 patients. J Bone Joint Surg Am 96(1):20–26
35. Bolognesi MP et al (2008) The impact of diabetes on perioperative patient outcomes after total hip and total knee arthroplasty in the United States. J Arthroplast 23(6 Suppl 1):92–98
36. Epelboym I et al (2014) Limitations of ACS-NSQIP in reporting complications for patients undergoing pancreatectomy: underscoring the need for a pancreas-specific module. World J Surg 38:1461–1467
37. Sippel RS, Chen H (2011) Limitations of the ACS NSQIP in thyroid surgery. Ann Surg Oncol 18(13):3529–3530