



Increased risk of 30-day postoperative complications for diabetic patients following open reduction-internal fixation of proximal humerus fractures: an analysis of 1391 patients from the American College of Surgeons National Surgical Quality Improvement Program database

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ARTICLE INFO

Keywords:

Proximal humerus fractures
Diabetes
Postoperative complications
NSQIP
Open reduction-internal fixation
Insulin-dependent diabetes

Level of evidence: Level III, Retrospective Cohort Design Using Large Database, Treatment Study

Background: Prior database studies have shown that complication rates following surgical treatment of proximal humerus fractures are low. However, diabetes has been shown across orthopedics to have significantly increased risks of postoperative complications. The purpose of our study was to identify complications for which diabetic patients are at increased risk following operative treatment of proximal humerus fractures.

Methods: The National Surgical Quality Improvement Program database from 2005 to 2014 identified patients >18 years undergoing open reduction-internal fixation for proximal humerus fractures. Patients with incomplete perioperative data were excluded. Patients with non-insulin-dependent diabetes mellitus (NIDDM) and insulin-dependent diabetes mellitus (IDDM) were compared with nondiabetic patients using multivariate logistic regression analysis. Odds ratio (OR) was calculated with a 95% confidence interval, and the significance level was held at $P < .05$.

Results: There were 1391 patients identified; 1147 (82%) were not diabetic, 91 (7%) had IDDM, and 153 (11%) had NIDDM. Of these, 39.68% (550) were obese (body mass index >30.0). Hypertension, dyspnea, and chronic obstructive pulmonary disease were the most frequent concurrent patient factors in diabetic patients. Postoperatively, patients with diabetes had a statistically significant higher risk of pneumonia (OR, 2.17.80; $P = .002$) and length of stay >4 days (OR, 2.05; $P = .010$). Among diabetics, non-insulin-dependent diabetics had a greater risk of sepsis (OR, 25.84; $P = .022$) and pneumonia (OR, 12.19; $P = .013$) than insulin-dependent diabetics.

Conclusion: Both NIDDM and IDDM were associated with a number of adverse postoperative events. Importantly, NIDDM was found to be an independent risk factor for postoperative sepsis and pneumonia, whereas IDDM was identified as an independent risk factor for pneumonia and prolonged length of stay (≥ 4 days).

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The incidence of proximal humerus fracture has significantly increased in both the United States and Europe during the last 40 years, and it is now the third most common fracture overall referred to orthopedic surgeons.^{26,39,41} Proximal humerus fractures make up at least 10% of all fractures in patients older than 65 years,² and recent

epidemiologic studies show that their occurrence is most significantly increasing in women aged >80 years.^{10,24} Risk factors for proximal humerus fractures include advanced age, female gender, history of fractures, low bone mass, loss of height in the preceding 20 years, history of falls, poor vision, certain medical comorbidities (such as insulin-dependent diabetes), and low physical activity.^{9,10,30,46}

Treatment options include nonoperative treatment, open reduction-internal fixation (ORIF), hemiarthroplasty, and total joint arthroplasty, and it has been shown that operative treatments may be associated with significantly increased short-term medical risks as well as with long-term mortality.^{33,35} Hence, it is critical to thoroughly assess patient-related variables before initiating operative

This study was exempt from Institutional Review Board approval as it uses a deidentified publicly available data set.

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<http://dx.doi.org/10.1016/j.jses.2017.03.006>

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treatment to prevent or to minimize surgical complications. Decision-making principles include the type of fracture, the degree of displacement and stability of the fragments,³⁴ and the patient's comorbid conditions. Minimally displaced fractures may be treated nonoperatively, but the options for more complex patterns remain controversial.^{4,14} Young patients have had good outcomes after surgical intervention, but elderly individuals have shown varying results and higher complication rates.⁴¹ There is evidence both for and against surgical treatment of 3- and 4-part fractures in the elderly.^{16,36,42}

Regarding the patient's pre-existing medical conditions, prior national database studies in multiple orthopedic operations have elucidated comorbid conditions that are independent risk factors for postoperative complications and poorer surgical outcomes. Identified factors included obesity, need for perioperative blood transfusion, timing of surgery, and diabetes mellitus, the awareness of which has been increasing recently because of its prevalence of 9.3% in the United States.^{29,33,48,49} To our knowledge, however, only a few studies have assessed the association between diabetes and surgical outcomes of ORIF of proximal humerus fractures, and no study has stratified diabetes status into insulin dependent and non-insulin dependent. In this study, we sought to assess the impact of diabetes, stratified by insulin dependency, on the 30-day postoperative outcomes in patients with proximal humerus fracture undergoing ORIF using a large national database.

Methods

The study conforms to the Reporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement.³

Data source

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database was used for this study. The database prospectively collects approximately 150 patient variables from patient interviews, medical records, and operative reports to obtain comorbid conditions and 30-day postoperative mortality and morbidity outcomes. The NSQIP initiative began in 1994 as a quality improvement effort within the Veterans Administration health system,¹⁵ and its successful implementation subsequently led to a parallel program for hospitals in the private sector in 1998.¹⁵ For 2014, the most recent database year included in the study, the NSQIP database contained >750,000 cases from approximately 500 hospitals.³⁷ The database quality is ensured by on-site surgical clinical reviewers and the NSQIP's internal auditing process, which maintains accuracy of data collection and controls inter-rater reliability.³⁷

Study population

The NSQIP databases from 2005 to 2014 were queried. Inclusion criteria were postoperative diagnosis of proximal humerus fractures (identified with *International Classification of Diseases, Ninth Revision, Clinical Modification* codes 812.0, 812.00, 812.01, 812.02, 812.03, and 812.09) and the receipt of surgical treatment with ORIF for proximal humerus fractures (identified with *Current Procedural Terminology* codes 23615, 23630, 23660, 23670, and 23680). To study typical adult surgical candidates, we excluded patients ≤18 years of age, underweight patients (body mass index [BMI] < 18.5 kg/m²), patients who received a concomitant shoulder operation, those with non-clean wound class or preoperative sepsis, and emergency cases.

Patients meeting the inclusion and the exclusion criteria were divided into 3 cohorts: patients with non-insulin-dependent diabetes mellitus (NIDDM), patients with insulin-dependent diabetes

mellitus (IDDM), and nondiabetics. NIDDM was defined as a diagnosis of diabetes mellitus (DM) requiring management with noninsulin antidiabetic agents and excluded diet-controlled DM. IDDM was defined as DM requiring daily insulin therapy. Patients treated with both noninsulin and insulin agents were classified as IDDM. Of note, the NSQIP database tracks DM cases with insulin resistance only.³⁷

Patient factors and outcome variables

Patient variables assessed in the study were age, sex, race, BMI, and preoperative functional status (partially or totally dependent functional status requires partial or total assistance for activities of daily living; independent functional status does not require assistance for any activity of daily living). Comorbid conditions investigated included history of congestive heart failure, current hypertension requiring medication, chronic obstructive pulmonary disease (COPD), and bleeding disorder. Other patient-related factors assessed were current dialysis, corticosteroid use for chronic conditions, smoking status, dyspnea (difficult, painful, or labored breathing), and unintentional weight loss (unintentional weight loss of >10% of weight during the past 6 months). Perioperative variables assessed were American Society of Anesthesiologists (ASA) score (divided into ASA scores of 1-2 and 3-5), mean operation duration, and mean anesthesia duration.

Postoperative complications investigated were mortality, myocardial infarction, unplanned reintubation, pneumonia, progressive renal insufficiency, sepsis/septic shock, intraoperative/postoperative transfusion, deep venous thrombosis, pulmonary embolism, wound infection (superficial surgical site infection [SSI], deep incisional SSI, organ/space SSI), and urinary tract infection. Other outcomes variables assessed were prolonged length of stay (postoperative hospital stay ≥4 days), unplanned return to the operating room, and unplanned readmission, which was added to the NSQIP from year 2011. All postoperative complication variables, including unplanned readmission, are collected within 30 days of operation.

Data analysis

The SAS software (version 9.3; SAS Institute, Cary, NC, USA) was used for all statistical analyses. For continuous and categorical variables, Student *t*-test and χ^2 test were used, respectively, to assess for statistically significant differences in frequencies or means. Bivariate analyses were performed to assess associations between DM status (NIDDM or IDDM) and patient demographic factors, comorbid conditions, and postoperative complications. Multivariate analyses were performed to assess whether DM status (NIDDM or IDDM) was an independent risk factor for adverse postoperative outcomes tracked in the NSQIP database. To control for possible confounding variables, we have included in our multivariate analyses preoperative patient variables (demographics, comorbid conditions) that were found to be associated with NIDDM or IDDM with *P* value < .2 in the bivariate analyses. Statistical significance was maintained at *P* value of .05.

Results

There were 1391 patients who underwent surgical treatment of a proximal humerus fracture from 2005 to 2014 identified (M:F, 391:1000); 1147 (82%) did not have diabetes, 91 (7%) had IDDM, and 153 (11%) had NIDDM. Of these, 60.46% (841) were nonobese (BMI <29.9), 18.55% (256) were obese (BMI 30.0-34.9), 11.57% (161) were severely obese (BMI 35.0-39.9), and 9.56% (133) were morbidly obese (BMI >40). Those with either IDDM or NIDDM were associated with higher obesity class compared with those without DM (Table I). Diabetic patients had higher rates of multiple comorbid

Table I

Demographic information of patients identified in the NSQIP as having undergone ORIF for a proximal humerus fracture between 2005 and 2014

Demographic variables	Non-DM	IDDM	NIDDM	Comparisons	
				Non-DM vs. IDDM <i>P</i> value	Non-DM vs. NIDDM <i>P</i> value
N	1147	91	153		
Age group (%)				.006	<.001
18–39	8.9	2.2	0.0		
40–64	44.9	41.8	40.5		
65–74	24.1	38.5	34.0		
≥75	22.1	17.6	25.5		
Sex (%)				.615	.201
Female	72.3	74.7	67.3		
Male	27.7	25.3	32.7		
Race (%)				.294	.217
White	77.8	78.0	79.7		
Black	2.4	5.5	5.2		
Hispanic	5.4	6.6	6.5		
Asians	1.7	1.1	0.7		
Other	0.3	1.1	0.0		
Unknown	12.6	7.7	7.8		
Body mass index (%)				<.001	<.001
Nonobese (18.5–29.9 kg/m ²)	66.0	34.1	34.0		
Obese I (30.0–34.9 kg/m ²)	17.0	29.7	23.5		
Obese II (35.0–39.9 kg/m ²)	10.1	14.3	20.9		
Obese III (≥40 kg/m ²)	6.9	22.0	21.6		
Functional status before surgery (%)				.015	.123
Independent in ADLs	93.6	86.8	90.2		
Partially or totally dependent in ADLs	6.5	13.2	9.8		

NSQIP, National Surgical Quality Improvement Program; ORIF, open reduction and internal fixation; DM, diabetes mellitus; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; ADLs, activities of daily living.

Boldface values indicate statistically significant associations.

conditions. Patients with IDDM had significantly increased rates of hypertension, dyspnea, and COPD and higher ASA score, whereas patients with NIDDM had significantly increased rates of hypertension and higher ASA score. The duration of operation and anesthesia did not differ significantly among diabetic and nondiabetic patients (Table II). Postoperatively, patients with IDDM had significantly higher rates of mortality, sepsis, myocardial infarction, pneumonia, renal insufficiency, blood transfusion, and prolonged length of stay compared with nondiabetic patients. Those with NIDDM had significantly higher rates of postoperative sepsis, pneumonia, and prolonged length of stay (Table III).

In the multivariate analysis assessing IDDM as an independent predictor for postoperative complications, we controlled for age, BMI, functional status, hypertension, dyspnea, COPD, and ASA score, which are patient factors found to be associated with IDDM with $P < .2$ in

our bivariate analyses (Tables I and II). IDDM was found to be a significant independent predictor for pneumonia (odds ratio [OR], 217.80; confidence interval [CI], 7.60–999.99) and prolonged length of stay (OR, 2.05; CI, 1.19–3.54). Similarly, in the multivariate analysis assessing NIDDM as an independent predictor for postoperative complications, we included age, BMI, hypertension, and ASA score to control for potential confounding factors. NIDDM was found to be a significant independent predictor for sepsis (OR, 25.84; CI, 1.61–414.96) and pneumonia (OR, 12.19; CI, 1.69–87.91) (Table IV).

Discussion

The goal of our study was to use a large sample of patients from a national database to investigate the complications for which underlying diabetes provides significantly increased risk after operative

Table II

Prevalence and comparison of comorbidities and perioperative variables in insulin-dependent diabetic, non-insulin-dependent diabetic, and nondiabetic patients undergoing ORIF for proximal humerus fractures

Comorbidity and related patient conditions (%)	Non-DM	IDDM	NIDDM	Comparisons	
				Non-DM vs. IDDM <i>P</i> value	Non-DM vs. NIDDM <i>P</i> value
Congestive heart failure	0.9	3.3	0.7	.029	.782
Hypertension	42.2	87.9	81.7	<.001	<.001
Current smoker	20.3	15.4	16.3	.257	.247
Dyspnea	4.3	15.4	7.2	<.001	.106
COPD	4.6	12.1	5.9	.002	.492
Currently on dialysis	0.4	0.0	0.7	.573	.567
Weight loss, unintentional	0.4	1.1	0.0	.381	.413
Bleeding disorder	4.7	8.8	6.5	.086	.326
Chronic corticosteroid use	3.5	4.4	2.6	.652	.575
Perioperative variables					
ASA classification (%)				<.001	<.001
1–2	61.0	14.3	24.8		
3–5	39.0	85.7	75.2		
Operation duration, min (mean)	108.8	114.4	106.4	.361	.663
Anesthesia duration, min (mean)	170.9	197.0	159.2	.079	.304

ORIF, open reduction and internal fixation; DM, diabetes mellitus; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists.

Boldface values indicate statistically significant associations.

Table III
Postoperative complications in patients undergoing ORIF for proximal humerus fracture by diabetes status

Postoperative outcomes (%)	Non-DM	IDDM	NIDDM	Comparisons	
				Non-DM vs. IDDM <i>P</i> value	Non-DM vs. NIDDM <i>P</i> value
Any complications	9.5	16.5	11.1	.033	.528
Mortality	0.4	2.2	0.7	.015	.567
Sepsis/septic shock	0.1	1.1	2.0	.021	<.001
Myocardial infarction	0.1	1.1	0.0	.021	.715
Unplanned reintubation	0.3	1.1	1.3	.176	.050
Pneumonia	0.2	4.4	2.0	<.001	.001
Progressive renal insufficiency	0.0	1.1	0.0	<.001	—
Wound-related infection	0.6	0.0	0.0	.455	.333
Urinary tract infection	0.7	0.0	0.7	.424	.951
Deep venous thrombosis	0.5	0.0	0.0	.489	.370
Pulmonary embolism	0.5	0.0	0.0	.489	.370
Transfusion	5.8	11.0	7.2	.050	.510
Outcomes variables					
Extended length of stay (≥4 d)	16.2	35.2	25.5	<.001	.004
Return to the operating room	1.7	1.1	0.0	.685	.109
Readmission	2.6	3.3	3.3	.698	.640

ORIF, open reduction and internal fixation; DM, diabetes mellitus; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus. **Boldface values** indicate statistically significant associations.

treatment of proximal humerus fractures. Surgical treatment of proximal humerus fractures can have significant short-term medical risks as well as long-term mortality increases.^{33,35,37} Obesity, need for perioperative blood transfusion, and timing of surgery have all been shown to portend an increased risk of inpatient adverse events.^{29,33,49} The increased risks of patients with DM, known to carry a higher risk of complications across many surgical fields, were less well studied. As the prevalence of people—and therefore patients—with diabetes continues to increase, knowledge of the specific complications for which these patients may be at increased risk is important to appropriate decision-making and counseling of patients.^{13,36}

Our study confirmed that patients with diabetes have a higher risk of complications than with other comorbidities. Diabetic patients who underwent operative treatment of proximal humerus fractures were at increased risk of mortality, development of pneumonia, need for blood transfusion, and length of stay >4 days; the most statistically significant of these results was the development of pneumonia. Stratifying by insulin dependence, non-insulin-dependent diabetics had a higher risk of postoperative sepsis,

Table IV
Adjusted odds ratios for selected outcomes for the influence of diabetic status

IDDM vs. non-DM	OR	Lower 95% CI	Upper 95% CI	<i>P</i> value
Any complications	1.28	0.66	2.48	.461
Mortality	6.40	0.67	61.46	.108
Pneumonia*	217.80	7.60	>999.99	.002
Transfusion	1.42	0.65	3.13	.382
Prolonged length of stay (≥4 d)*	2.05	1.19	3.54	.010
NIDDM vs. non-DM	OR	Lower 95% CI	Upper 95% CI	<i>P</i> value
Sepsis*	25.84	1.61	414.96	.022
Pneumonia*	12.19	1.69	87.91	.013
Extended length of stay (≥4 d)	1.27	0.81	1.98	.295

DM, diabetes mellitus; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; OR, odds ratio; CI, confidence interval. In the multivariate analysis assessing IDDM as an independent predictor for postoperative complications, we controlled for age, body mass index, functional status, hypertension, dyspnea, chronic obstructive pulmonary disease, and American Society of Anesthesiologists score. In the multivariate analysis assessing NIDDM as an independent predictor for postoperative complications, we controlled for age, body mass index, hypertension, and American Society of Anesthesiologists score.

* Postoperative variables for which diabetes is a significant independent predictor.

development of pneumonia, and prolonged length of stay than insulin-dependent diabetics did.

Patients with IDDM have previously been shown to be at increased risk for the development of proximal humerus fractures.^{25,30,38,46} Risk factors for proximal humerus fractures include a history of fractures, low bone mass, loss of height in the preceding 20 years, history of falls, poor vision, certain medical comorbidities, and low physical activity.^{9,25,30} Low BMI has been associated with increased fracture risk in some studies, but others have not shown similar correlation.^{9,25,30} Diabetics are thought to be at greater risk of these fractures because of poorer performance than their nondiabetic counterparts on measures of balance and gait, peripheral neuropathy, and vision.⁴⁶ In fact, women with diabetes have a greater risk of proximal humerus fracture despite having a higher bone mineral density than women without diabetes.⁴⁶ These trends are consistent with our study population, with a greater percentage of patients in all diabetic categories being female, including 68 of 91 patients with IDDM and 103 of 153 patients with NIDDM.

Obesity is frequently cited as a risk factor both for occurrence of fractures and for poor outcomes after fracture. Prieto-Alhambra et al showed that obesity was actually protective against hip and pelvis fractures but associated with a 30% increase in risk for proximal humerus fractures compared with normal weight and underweight women.⁴⁰ In our study, 18.5% of patients were obese, 11.57% were severely obese to morbidly obese (BMI 35.0–39.9), and 9.56% were morbidly obese (BMI >40), which is near 40% of the total number of patients. Obesity is associated with increased rates of DM.^{17,19,22} In our study, 66% of nondiabetic patients were also nonobese, whereas only 34% of non-insulin-dependent and insulin-dependent diabetics were nonobese. Postoperatively, Werner et al showed that obese patients undergoing ORIF, hemiarthroplasty, or arthroplasty of the proximal humerus had an increase in 90-day local and systemic complications; in particular, ORIF and hemiarthroplasty had higher rates of postoperative venous thromboembolism and infection, but there was only an increased risk of infection after arthroplasty.

In other literature regarding proximal humerus fractures, need for perioperative blood transfusion was independently associated with occurrence of inpatient adverse events, need for prolonged hospitalization, and nonroutine discharge.²⁹ In a similar study, delaying surgery for >3 days after admission was independently associated with occurrence of inpatient adverse events and nonroutine discharge, but it was not associated with increased mortality.³³ However, neither of these studies addressed diabetes.

There is little or no literature about the association of diabetes and its complications with proximal humerus operative fixation. In one large database study, diabetes was shown to confer a small or moderate increased risk of adverse events after surgery and was a strong predictor of discharge to a long-term care facility, but it was not found to be a significant predictor of postoperative death.^{35,37} In the spine surgery literature, diabetes has been shown to be the most common comorbidity and to be one of the most significant risk factors for mortality or immediate postoperative complications.^{44,45} In hand surgery, diabetic patients have been shown to have significantly increased complication rates after distal radius fracture volar plating, and similar results were shown in treatments of ankle fractures.^{6,28}

A study by Harris et al assessing the impact of diabetes in patients undergoing total hip or knee arthroplasty is worth mentioning.¹⁸ Although the current study stratifies diabetes status on the basis of insulin dependence because of the structure of the database, Harris et al used hemoglobin A_{1c} level to quantitatively stratify diabetic patients, thus providing more granular details. The study revealed that the risk of postoperative complication increased linearly through the threshold value of 7%. It is unclear whether the results found in the total joint arthroplasty study may be extrapolated to the patients of interest in the current study, given that the majority of total joint arthroplasty cases are elective, whereas operations for proximal humerus fractures are not. Regardless, the results from the study suggest that the quantitative value of serum hemoglobin A_{1c} may be a useful tool in further stratifying risks in diabetic patients receiving ORIF for proximal humerus fracture and that the topic should be investigated further.¹⁸

Several studies have also shown that NIDDM is associated with an increased risk for development of sepsis and that patients with type 2 diabetes are at nearly twice the risk for mortality due to infections as nondiabetic patients are.⁴⁷ A study from Brazil has shown a 6 times increased risk of infection-related mortality in those with NIDDM compared with the general population.⁵ During a 4-year period in Spain, there was an increased incidence of any-stage sepsis in patients with NIDDM, greater than in the general population, and a significant association of higher increased mortality when septic shock was present.¹¹ In addition, type 2 diabetic patients with sepsis admitted to an intensive care unit for the first time had a higher risk for development of acute kidney injury and were more likely to be undergoing hemodialysis but had a lower risk of acute respiratory, hematologic, and hepatic dysfunction.⁸

However, the underlying pathologic process for this increased rate of sepsis among diabetic patients is not fully established and is likely to be multifactorial. Short- and long-term hyperglycemia has been shown to disturb neutrophil bactericidal function, cellular immunity, and complement activation and to impair chemotaxis.^{12,21,31,32} Microvascular and macrovascular insufficiency has also been implicated.²³ Cells from patients with type 2 diabetes have shown attenuated cytokine response to lipopolysaccharide (LPS) stimulation compared with cells from nondiabetics.^{7,20} In an experimental study, Andreasen et al showed that patients with NIDDM injected with LPS exhibited an attenuated increase in plasma levels of tumor necrosis factor and interleukin 1 receptor antagonist as well as an attenuated upregulation of vascular cell adhesion molecule 1 and intercellular adhesion molecule 1 to LPS *in vivo*.¹ It is theorized that these findings may provide a mechanistic explanation for the increased risk of and adverse outcomes during infectious processes in type 2 diabetic patients.

There were several limitations to our study. First, we were limited to the variables reported to the NSQIP by participating medical centers. As a result, there was no avenue to determine whether cases were revision procedures, to obtain detailed patient medical or surgical history, or to determine if data were missing overall. In addition, the observation period for perioperative morbidity is restricted to

the first 30 days after surgery, which could lead to misreporting of complications or mortality. These issues become more important as there is no means to confirm the accuracy of reporting to the NSQIP, and errors in coding may exist for certain complications.^{27,43,45} Although the NSQIP has been validated to contain more accurate data regarding complications than administrative data, concordance between the NSQIP and a protective institutional registry has still been shown to be only moderately good.²⁷

Furthermore, potential limitations include that academic medical centers are over-represented in the civilian NSQIP.^{43,45} As academic medical centers become the sites of choice for patients with severe preoperative comorbidities who are more likely to experience medical complications after, this could lead to complication rates becoming over-reported in the NSQIP database.

Conclusion

ORIF of proximal humerus fractures is a commonly performed orthopedic surgery. In the nondiabetic population, it has a low postoperative complication rate. In contrast, diabetic patients, particularly non-insulin-dependent diabetics, have a significantly higher rate of serious complications. Patients and families should be counseled preoperatively and observed closely after surgery to avoid missing the development of a life-threatening condition.

Disclaimer

The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

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