



# Preoperative diabetes complicates postsurgical recovery but does not amplify readmission risk following pancreatic surgery

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**Background:** Diabetes is a significant and prevalent medical condition associated with increased comorbidities, longer hospital length of stay, and higher healthcare costs. We aimed to assess the association between diabetes mellitus and postoperative outcomes following pancreatic surgeries.

**Methods:** Records for patients with major elective pancreatic surgeries were retrieved retrospectively from the Nationwide Readmission Database (2010–2014). Association of diabetic status with postoperative complications, in-hospital mortality, length of stay (LOS), readmission rate, and hospital costs were investigated. Logistic regression and decision tree analyses were employed to predict adverse outcomes.

**Results:** A total of 8,401 patients who had pancreatic surgery were included. They were categorized according to their diabetic diagnosis. Results showed that diabetic patients had a higher risk of postoperative complications compared to non-diabetics (OR: 1.27, 95% CI: 1.08–1.49, P=0.003). Bleeding and renal complications were the most significant. Uncontrolled diabetes significantly required a longer hospital stay (9.17±4.28 *vs.* 8.03±4.96 days, P=0.001), and incurred higher hospital costs (\$34,171.04±\$20,846.61 *vs.* \$28,182.21±\$24,070.27, P=0.001). After multivariate regression, no association was found with in-hospital mortality or readmission rates; however, diabetic patients' length of stay during readmission was increased at 30- and 90-day readmissions (P=0.004 and 0.007, respectively).

**Conclusions:** Among patients who underwent pancreatic surgery, those with diabetes had a higher rate of postoperative complications compared to non-diabetics. Additionally, diabetic patients had higher hospital charges and costs during primary admission. Initial analysis of patients with diabetes showed they had higher rates of 30- and 90-day readmissions, though this did not maintain significance after regression analysis. Exploring the mechanisms underlying this finding would aid in preventing postoperative complications and reducing healthcare costs.

**Keywords:** Pancreatectomy; readmission; mortality; cost; national database

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## Introduction

Diabetes mellitus is growing in prevalence worldwide. In 2014–2015, approximately 420 million people worldwide had diabetes, representing a staggering 8.5–8.8% of the total adult population, and prevalence is predicted to rise to 10.4% by 2040 (1,2). Without proper control, people with diabetes often develop multiple comorbidities, including ophthalmologic, cardiovascular, and renal complications, including renal failure. In addition, patients often develop microvascular complications leading to poor circulation, infection, and peripheral neurologic deficits. In 2012, 3.7 million deaths were attributable to diabetes and diabetic complications (2).

Patients with diabetes are more likely to require surgery in their lifetimes than non-diabetic patients (3,4). Patients with uncontrolled diabetes and hyperglycemia have increased admission rates to the Intensive Care Unit (ICU), in-hospital mortality, risk of infection, re-operative intervention, and death (5,6). Additionally, diabetic patients' hospital stays are longer and more expensive than non-diabetics (7-9). In 2007, it was estimated that diabetes-related chronic medical problems in the U.S. cost a total of \$116 billion in excess medical costs (10). In 2014, total medical care costs of diabetes were estimated at \$827 billion globally (1).

This study reviewed postoperative outcomes in diabetic and non-diabetic patients undergoing partial pancreatotomy, total pancreatotomy, or radical pancreaticoduodenectomy. Our focus was on the risks of postoperative complications, length of stay, in-hospital mortality, readmission risk, and hospital costs in diabetic patients compared to non-diabetic patients. We present the following article in accordance with the STROBE reporting checklist (available at <https://ga.amegroups.com/article/view/10.21037/ga-21-648/rc>).

## Methods

### Data source

A cross-sectional analysis of the National Readmission Database (NRD) from 2010 to 2014 was performed. The NRD is sponsored by the Healthcare Cost and Utilization

Project (HCUP) State Inpatient Databases. It contains data from over 14 million discharges per year in over 2,000 hospitals in 22 states (11). International Classification of Disease, 9<sup>th</sup> revision (ICD-9), was used to define diagnoses and procedures of interest. The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013). The data are deidentified and publicly available, and thus exempt from institutional review board approval, and individual consent for this retrospective analysis was waived.

### Study population

The study population included adult ( $\geq 18$  years) inpatients who underwent major elective pancreatotomy: partial (ICD-9: 5200, 5209, 525, 5251, 5253, 5259, 522, 5221, 5222), total (ICD-9: 526), or radical (ICD-9: 527). Indications for pancreatotomy were classified as functional disorder (ICD-9: 2515, 2518, 2519, 5770, 5771, 5772, 5778, 5779), benign disease (ICD-9: 2116), or malignant disease (ICD-9: 1570, 1571, 1572, 1573, 1578, 1579). Missing data for in-hospital mortality or length of stay were excluded.

### Identification of readmission cases

Since patients cannot be traced across calendar years, patient and hospital linkage numbers were used to follow-up all discharge records that belong to the same patient throughout the year. To capture readmissions in NRD within 30- or 90-day following discharge, admission records between January to November or January to September were only captured, respectively, to allow for tracing rehospitalization in 30 or 90 days of the calendar year. Index hospitalization data was combined with the closest rehospitalization data.

### Study variables

Patient factors included age, gender, state of residence, median annual household income (categorized into four quartiles), primary insurance type (Medicare, Medicaid, private insurance, self-pay, and other), and a number of chronic diseases. The causes of primary admissions (functional, benign, or malignant conditions) and in-

hospital procedures (partial or complete resection) were identified. Cumulative comorbidities were assessed using a modified Charlson Comorbidity Index (CCI) score (12). Patients were given a score based on the number of comorbidities (0, 1,  $\geq 2$ ). Hospital characteristics examined were hospital procedure volume, hospital teaching status (metropolitan teaching, metropolitan non-teaching, and non-metropolitan), and hospital bed size (small, medium, and large).

### Study outcomes

The main study outcomes included length of stay (LOS), postoperative complications, mortality, readmission rates at 30 and 90 days, and hospital costs in diabetic and non-diabetic patients undergoing partial pancreatectomy, total pancreatectomy, or radical pancreaticoduodenectomy. Postoperative complications were defined as the dichotomized presence or absence of one or more general or specific complications based on secondary diagnoses during the hospital stay. Complications considered were bleeding/shock, infection/sepsis, technical complications, cardiovascular complications, pulmonary complications, renal complications, endocrine complications, and wound complications (Table S1). Any patient with missing data for any of our main outcomes was removed from the study. The database included hospital charges associated with each admission. Additional files specific to the cost-to-charge ratio for each hospital were supplied by the HCUP, which allows for the conversion of charge values to cost values. Based on All Patients Refined Diagnosis Related Group (DRG) defined by the HCUP, we identified the topmost common diagnosis group on readmission.

### Statistical analysis

Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and SPSS version 27.0. Data analysis was performed using weighted measurements to reflect the national estimate level. The recorded weights are available in the NRD data and were calculated based on the stratification variables used. Based on the HCUP user agreement, some variables with low number of observations were not reported to avoid patient tracking. Unbiased and a priori cut-off value of quantitative variables was set at the 75<sup>th</sup> percentile levels. Therefore, LOS, hospital charge, and hospital cost were classified at a cutoff of 9 days, \$97,775.0, and \$45,395.2, respectively. Two-tailed  $\chi^2$  and

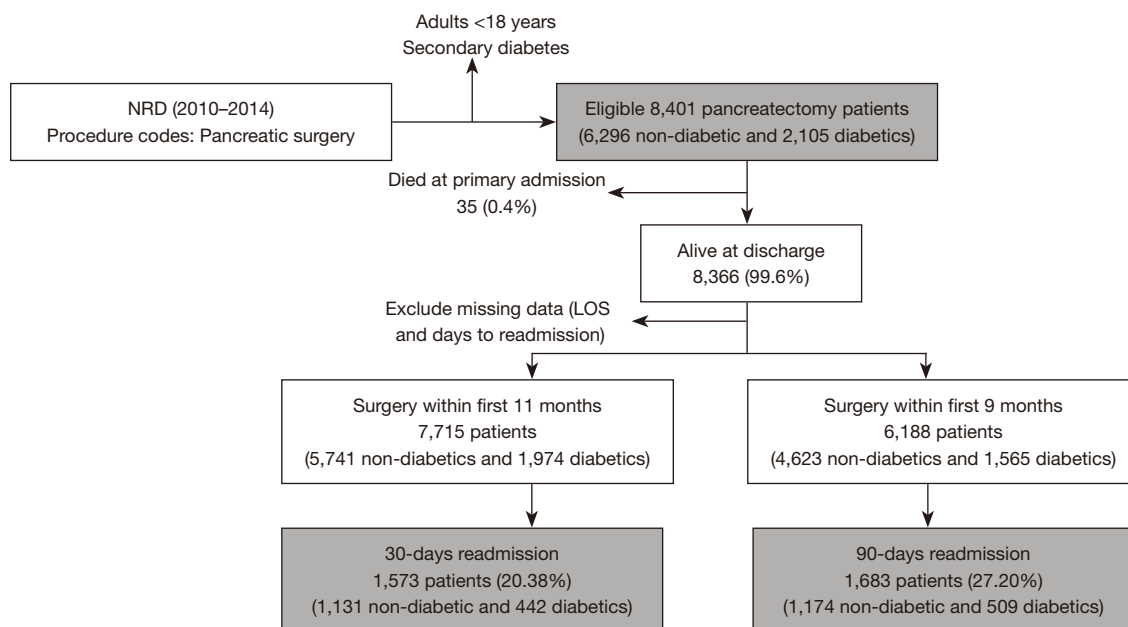
student's *t*-tests were performed regarding postoperative complications, length of stay, and hospital costs comparing non-diabetic and diabetic patients. Diabetic patients were then stratified by (I) type 1 *vs.* type 2 diabetes, (II) controlled *vs.* uncontrolled diabetes, and (III) the presence of pre-existing diabetic complications. A two-tailed  $\chi^2$  test was performed on a stratification analysis detailing the type of postoperative complication when comparing non-diabetic and diabetic patients. Next, a two-tailed  $\chi^2$  test compared readmission rates and hospital costs at 30 and 90 days between non-diabetic and diabetic patients. Multivariate logistic regression was then performed to calculate adjusted odds ratios of postoperative complications and readmission rates. Odds ratio (OR) and 95% confidence interval (CI) were estimated. Log-rank test was calculated to compare the days to readmission in non-diabetic and diabetic patients.

## Results

### Characteristics of the study population

A total of 8,401 eligible patients had undergone pancreatic surgery between 2010 and 2014, 25.05% of whom were diabetic. Of the study population, 1,573 patients (20.38%) and 1,683 patients (27.20%) were readmitted within 30 and 90 days of discharge, respectively (Figure 1). On primary admission, the mean age of pancreatic surgery patients was 58.87 $\pm$ 10.78 years, and 51.4% were female. The annual prevalence of diabetic patients who required pancreatectomy rose significantly from 17.1% to 23.8% across the five-year study period. Non-insulin-dependent diabetes was the most common type, represented in 1,937 (92.0%) of the patients. About 200 patients (9.5%) had uncontrolled diabetes, and 88 patients (4.2%) had diabetic complications (Figure 2).

A comparison between diabetic and non-diabetic cohorts is shown in Table 1. The mean age of non-diabetic patients was 58.25 $\pm$ 14.39 years, and diabetic patients were 60.74 $\pm$ 13.19 years old ( $P < 0.001$ ). Women accounted for 53.2% of non-diabetic patients and 46.3% of the diabetic group ( $P < 0.001$ ). Patients who underwent partial and total pancreatectomy represented 29.5% and 3.6% of the sample, respectively, while 66.9% had radical pancreaticoduodenectomy. Diabetic patients were less likely to have a functional disease as the primary admission diagnosis compared to non-diabetic patients (39.7% *vs.* 44.1%,  $P < 0.001$ ). Subjects with diabetes were more likely to have postoperative complications (33.2% *vs.* 27.4%,  $P < 0.001$ ) and to be associated with a higher cost (11.9% *vs.*



**Figure 1** Workflow for selection of the study population. Grey boxes indicate patients included in the study. Values in the workflow chart represent the actual frequencies without national estimation. NRD, National Readmission Database; LOS, length of stay.

9.1%,  $P < 0.001$ ).

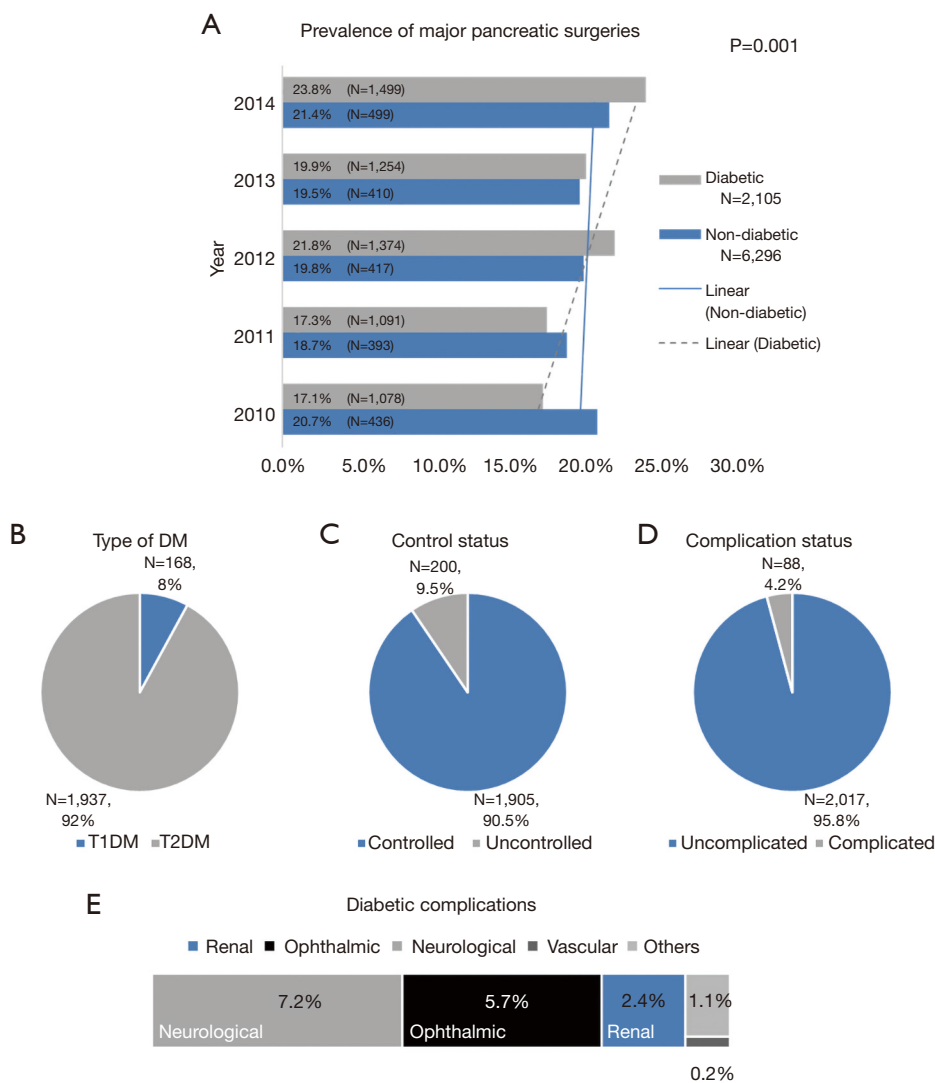
Characteristics of the diabetic patients according to the type of diabetes, presence of diabetic complications, and control status are shown in *Table 2*. Patients with type 1 diabetes were more likely to have a higher comorbidity score (48.2% *vs.* 7%,  $P < 0.001$ ) and postoperative complications (64.9% *vs.* 30.5%,  $P < 0.001$ ) than those with type 2 diabetes. Having controlled diabetes rather than uncontrolled diabetes significantly decreased the chance of postoperative complications (31.3% *vs.* 51.5%,  $P < 0.001$ ) and required a shorter hospital stay ( $8.03 \pm 4.96$  *vs.*  $9.17 \pm 4.28$  days,  $P = 0.001$ ). The presence or absence of diabetic complications was also considered. Patients with complicated diabetes were more likely to have comorbidities compared to patients with uncomplicated diabetes (25.1% *vs.* 14.3%,  $P < 0.001$ ). Complicated diabetes patients also had an increased risk of postoperative complications (49.4% *vs.* 28.8%,  $P < 0.001$ ). Controlled diabetes was associated with a significant reduction in hospital costs compared to uncontrolled ( $\$28,182.21 \pm \$24,070.27$  *vs.*  $\$34,171.04 \pm \$20,846.61$ ,  $P = 0.001$ ). In contrast, subjects with type 1 diabetes ( $\$62,592.76 \pm \$36,238.50$  *vs.*  $\$25,511.12 \pm \$20,248.92$ ,  $P < 0.001$ ) or those that had diabetic complications ( $\$47,177.01 \pm \$35,085.96$  *vs.*  $\$26,530.02 \pm \$28,834.56$ ,  $P < 0.001$ ) incurred higher hospital costs.

### ***Risk of postoperative complications, mortality, and readmission***

Higher frequencies of postoperative bleeding (12.6% *vs.* 10.4%, OR: 1.07, 95% CI: 1.25–1.45,  $P < 0.001$ ) and renal complications (6.7% *vs.* 3.7%, OR: 1.48, 95% CI: 1.84–2.28,  $P < 0.001$ ) were observed in diabetic patients compared to non-diabetic patients (*Figure 3*), but there was no significant difference in mortality rates at primary admission or within 30 or 90 days after discharge (*Figure 4A*). However, early and late readmissions were significantly more prevalent among diabetic patients ( $P = 0.014$  and  $< 0.001$ ) (*Figure 4B*). Kaplan–Meier curve showed that both cohort groups had similar readmission times at an average of 10 days ( $P = 0.96$ ). Top causes of readmission are described in *Figure 5*.

### ***Predictive factors for poor outcomes***

As depicted in *Table 3*, diabetes was associated with a higher risk of postoperative complications (OR: 1.27, 95% CI: 1.08 to 1.49,  $P = 0.003$ ), but posed no significant influence on rehospitalization risk (OR: 1.00, 95% CI: 0.85 to 1.17,  $P = 0.98$ ). Increased length of stay was associated with higher odds of both postoperative complications (OR: 2.50, 95%



**Figure 2** Prevalence of pancreatic surgeries and clinical status of diabetic patients. (A) Prevalence of major elective pancreatic surgery. All values are presented as weighted national estimates. (B) Type of diabetes. (C) Control status of patients. (D) Presence of complications. (E) Types of complications. Data are presented as a percentage. Two-tailed Chi-square was performed between different years. Statistical significance was set at  $P < 0.05$ . T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

CI: 2.14 to 2.92,  $P < 0.001$ ) and readmission risk (OR: 1.48, 95% CI: 1.27 to 1.73,  $P < 0.001$ ). Total pancreatectomy (OR: 2.24, 95% CI: 1.50 to 3.35,  $P < 0.001$ ) and admission to nonmetropolitan hospitals (OR: 2.60, 95% CI: 1.06 to 6.40,  $P = 0.037$ ) were found to have an increased risk of readmission. In contrast, having a higher median household income was associated with a lower risk of readmission.

**Healthcare burden**

Both diabetic and non-diabetic cohorts had similar lengths

of stay during primary admission ( $P = 0.38$ ); however, diabetic patients experienced prolonged hospital stays during their 30-day (7.9 days, 95% CI: 7.15–8.64 vs. 6.7 days, 95% CI: 6.35–7.18,  $P = 0.004$ ) and 90-day readmissions (7.1 days, 95% CI: 6.48–7.67 vs. 6.12 days, 95% CI: 5.75–6.5,  $P = 0.007$ ) than non-diabetics, *Figure 6A*. Conversely, diabetic patients had a higher hospital cost during primary admission than non-diabetic patients ( $P = 0.011$ ) but did not have significantly higher hospital costs during 30- or 90-day readmissions (*Figure 6B*). National estimates showed an extra 62.7 hospital days and

**Table 1** Bivariate analysis of patient and hospital characteristics present in patients following pancreatic surgery

Characteristics at primary admission	Levels	Pancreatic surgery		P value
		Non-diabetic (N=6,296)	Diabetic (N=2,105)	
Age (year)	Mean ± SD	58.25±14.39	60.74±13.19	<0.001
	>18–45	1,222 (19.4)	290 (13.8)	<0.001
	>45–65	2,912 (46.3)	943 (44.8)	
	>65	2,162 (34.3)	872 (41.4)	
Gender	Male	2,945 (46.8)	1,131 (53.7)	<0.001
	Female	3,351 (53.2)	974 (46.3)	
Median annual household income	Quartile 1 lowest	1,349 (21.9)	582 (28.4)	<0.001
	Quartile 2	1,493 (24.3)	467 (22.8)	
	Quartile 3	1,514 (24.6)	518 (25.3)	
	Quartile 4 highest	1,799 (29.2)	484 (23.6)	
Residence in hospital state	Different state	1,065 (16.9)	230 (10.9)	<0.001
	Same state	5,231 (83.1)	1876 (89.1)	
CCI score	0	5,094 (80.9)	1505 (71.5)	<0.001
	1	972 (15.4)	383 (18.2)	
	≥2	230 (3.7)	217 (10.3)	
Type of surgical procedure	Partial pancreatectomy/excision	1,612 (30.2)	464 (27.4)	0.007
	Total pancreatectomy	183 (3.4)	68 (4)	
	Radical pancreaticoduodenectomy	3,538 (66.4)	1,166 (68.6)	
Cause of surgery	Functional disorders	1,708 (44.1)	559 (39.7)	<0.001
	Benign disorders	481 (12.4)	100 (7.1)	
	Malignant disorders	1,682 (43.5)	750 (53.2)	
Postoperative complications	None	4,570 (72.6)	1,406 (66.8)	<0.001
	One or more	1,727 (27.4)	699 (33.2)	
LOS, days	Mean ± SD	8.69±11.34	8.13±4.95	0.028
	Short stay*	4,489 (71.3)	1,412 (67)	<0.001
	Long stay	1,807 (28.7)	694 (33)	
Hospital charge, \$	Mean ± SD	90,123.28±122,931.75	99,369.85±107,073.95	0.003
	Low charge*	4,621 (76.7)	1,434 (71.3)	<0.001
	High charge	1,400 (23.3)	578 (28.7)	
Hospital costs, \$	Mean ± SD	26,797.33±31,066.51	28,566.33±24,245.18	0.020
	Low cost*	5,471 (90.9)	1,772 (88.1)	<0.001
	High cost	550 (9.1)	240 (11.9)	

**Table 1** (continued)



Table 1 (continued)

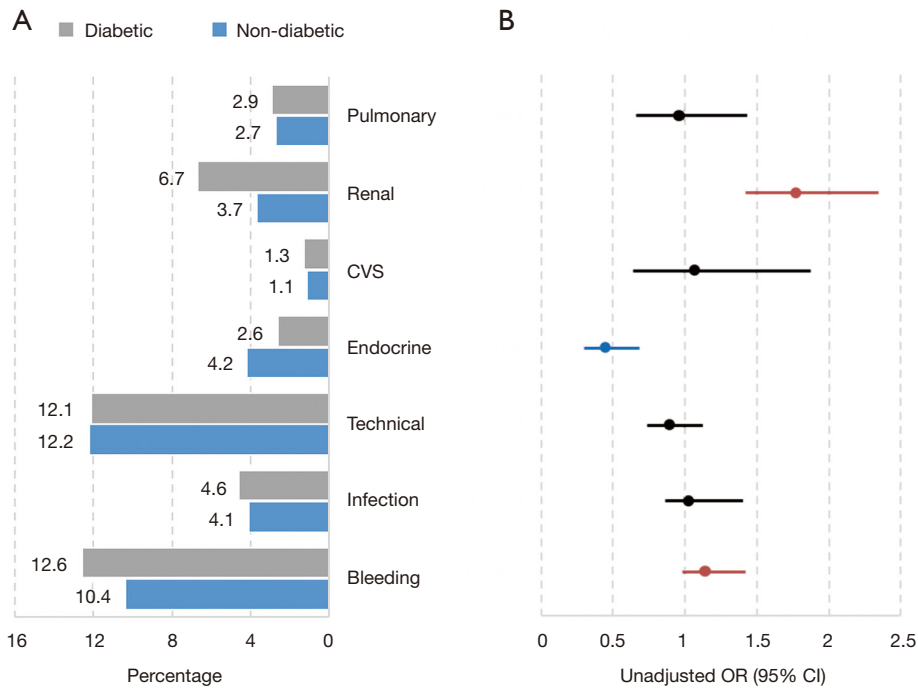
Characteristics at primary admission	Levels	Pancreatic surgery		P value
		Non-diabetic (N=6,296)	Diabetic (N=2,105)	
Hospital volume	Low	1,826 (29)	738 (35)	<0.001
	Medium	2,964 (47.1)	848 (40.3)	
	High	1,507 (23.9)	520 (24.7)	
Hospital type	Metropolitan nonteaching	537 (8.5)	200 (9.5)	0.27
	Metropolitan teaching	5,698 (90.5)	1,880 (89.3)	
	Nonmetropolitan hospital	62 (1)	25 (1.2)	
Hospital Bed Size	Small	326 (5.2)	129 (6.1)	0.048
	Medium	805 (12.8)	299 (14.2)	
	Large	5,165 (82)	1,678 (79.7)	

Data is shown as number (percentage) or mean ± standard deviation (SD). All numbers are presented as weighted national estimates. Two-sided Chi-square and Student's *t*-tests were used. Statistical significance was set at P<0.05. \*, LOS, cost, and charge were classified based on ≤75<sup>th</sup> and >75<sup>th</sup> percentile at a cutoff of 9 days, \$97,775.0, and \$45,395.2, respectively. Hospital volume (surgeries/year) was divided into ≤25<sup>th</sup>, ≤75<sup>th</sup>, and >75<sup>th</sup> percentiles. CCI, Charlson Comorbidity Index; LOS, Length of stay.

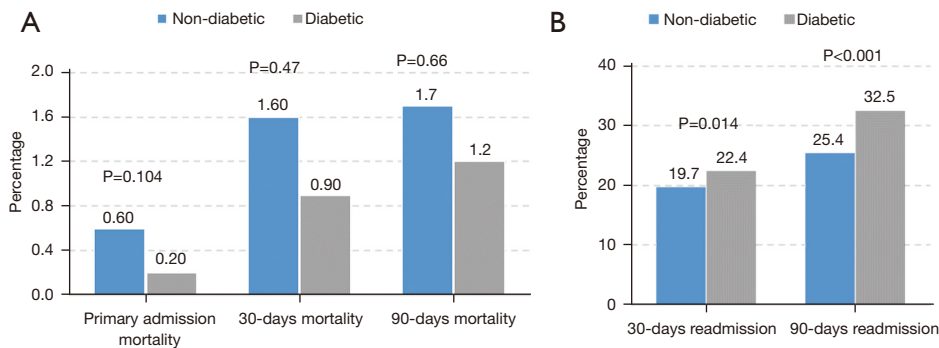
Table 2 Stratification analysis of diabetic patients according to their diabetic status

Characteristics	Levels	Type of diabetes			Diabetic control			Diabetic complications		
		T1DM (N=168)	T2DM (N=1,937)	P value	Controlled (N=1,905)	Uncontrolled (N=200)	P value	Uncomplicated (N=2,017)	Complicated (N=88)	P value
Age (year)	Mean ± SD	46.73±13.39	61.95±12.45	<0.001	60.08±13.59	61.32±12.05	0.20	58.96±14.09	54.16±15.37	<0.001
Gender	Male	101 (60.5)	1,030 (53.1)	0.040	1,027 (53.9)	99 (49.3)	0.21	1,080 (53.6)	51 (57.5)	0.41
	Female	67 (39.5)	907 (46.9)		873 (46.1)	101 (50.7)		937 (46.4)	37 (42.5)	
CCI score	0	77 (45.8)	1,428 (73.7)	<0.001	1,372 (72.5)	132 (68.9)	0.41	1,404 (69.6)	51 (57.4)	0.015
	1	10 (6)	373 (19.2)		341 (17.9)	41 (20.3)		325 (16.1)	15 (17.5)	
	≥2	81 (48.2)	136 (7)		189 (9.6)	22 (10.8)		288 (14.3)	22 (25.1)	
Postoperative complications	None	59 (35.1)	1,347 (69.5)	<0.001	1,309 (68.7)	97 (48.5)	<0.001	1,367 (71.2)	40 (50.6)	<0.001
	One or more	109 (64.9)	590 (30.5)		596 (31.3)	103 (51.5)		650 (28.8)	48 (49.4)	
LOS, days	Mean ± SD	7.96±3.36	8.14±5.07	0.64	8.03±4.96	9.17±4.28	0.001	8.56±10.25	8.10±4.08	0.39
Hospital costs, \$	Mean ± SD	62,592.76±36,238.50	25,511.12±20,248.92	<0.001	28,182.21±24,070.27	34,171.04±20,846.61	0.001	26,530.02±28,834.56	47,177.01±35,085.96	<0.001

Data is shown as number (percentage) or mean ± standard deviation (SD). All numbers are presented as weighted national estimates. Two-sided Chi-square and Mann-Whitney U tests were used. Statistical significance was set at P<0.05. LOS, number of chronic diseases and cost were classified based on ≤75<sup>th</sup> and >75<sup>th</sup> percentile. CCI, Charlson Comorbidity Index; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; LOS, length of stay.



**Figure 3** Types of postoperative complications following pancreatic surgeries. (A) Frequency of complications in diabetic and non-diabetic groups. All numbers are presented as weighted national estimates. A two-sided Chi-square test was used. (B) Unadjusted odds and 95% confidence intervals of postoperative complications in diabetic patients are shown in the right panel. Significant values are represented by red and blue bars for increased and decreased odds, respectively. CVS, cardiovascular system; OR, odds ratio.



**Figure 4** Postoperative morbidity and readmission rates in patients who underwent a pancreatic surgical procedure. (A) Frequency of mortality at index hospitalization and during readmission in diabetic and non-diabetic cohort. (B) Frequency of 30 days and 90 days readmission classified by diabetes status. A two-sided Chi-square test was used.

\$0.76 million in additional hospital costs per year in diabetic patients.

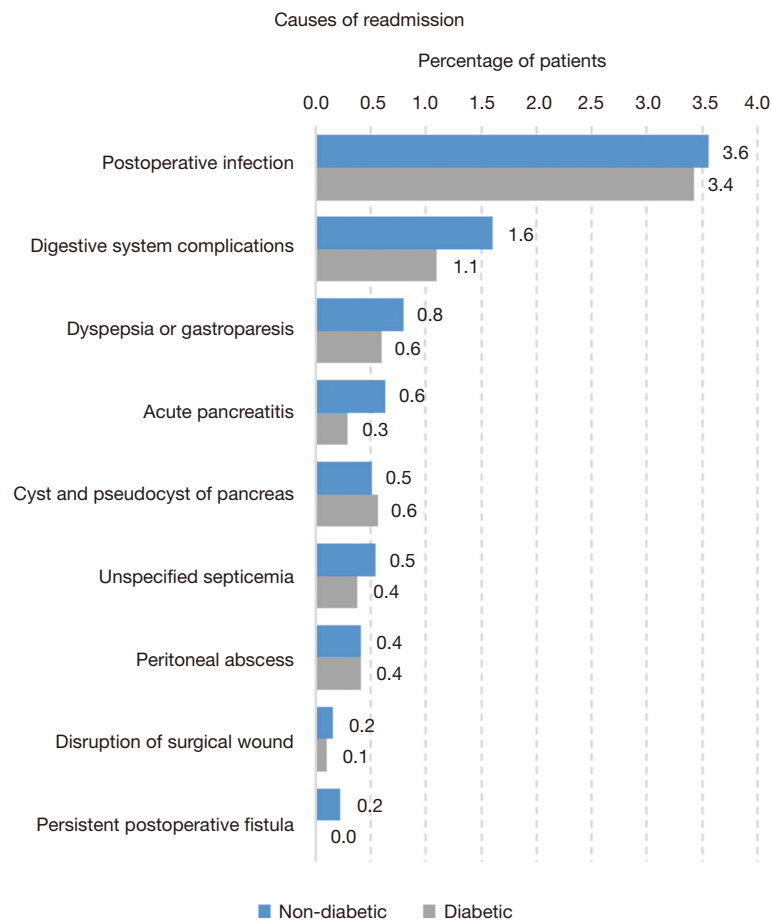
**Discussion**

The data here included 8,401 patients who underwent partial pancreatectomy, complete pancreatectomy, or radical

pancreaticoduodenectomy between 2010–2014. The study’s main objective was to investigate correlations between the presence of diabetes in patients undergoing those procedures and the risk of postoperative complications, increased hospital length of stay, increased readmission rates, and hospital cost.

We found that having diabetes, particularly type 1





**Figure 5** Causes of readmission in diabetic and non-diabetic cohorts.

diabetes that was either uncontrolled or complicated, was a risk factor for postoperative complications. These findings are similar to those of multiple previous studies across a variety of surgical procedures (4,12-16). The sample sizes of these other articles vary greatly; our study has one of the larger patient populations. Additionally, only one of the previous papers included patients that had undergone partial or total pancreatectomy or pancreaticoduodenectomy.

While we did not find an increased LOS during primary admission or risk of 30- or 90-day readmission after regression analysis, we found an increase in LOS during both readmission time points for subjects with diabetes. Furthermore, patients who experienced postoperative complications were more likely to have an increased LOS, and increased primary LOS was correlated with an increased risk of subsequent readmission. The type of surgical procedure performed did not influence the rate of postoperative complications when subjected

to multivariate regression. Additionally, those who underwent total pancreatectomy were more likely to be readmitted than partial, whereas those undergoing radical pancreaticoduodenectomy were not. In 2019, Passeri *et al.* looked at 30-day mortality, 30-day readmission, and long-term survival when comparing partial to total pancreatectomy and total pancreatectomy to pancreaticoduodenectomy. Still, they did not report significant differences between the groups (17). A study by Casadei *et al.* also showed no differences in postoperative outcomes and overall survival between patients who had undergone total pancreatectomy or pancreaticoduodenectomy (18). There was no correlation between total pancreatectomy and increased risk of postoperative complications. This discrepancy in readmission may be due to the larger sample size of our study compared to the others. Passeri *et al.* noted an increase in the rate of readmission following their 43 total

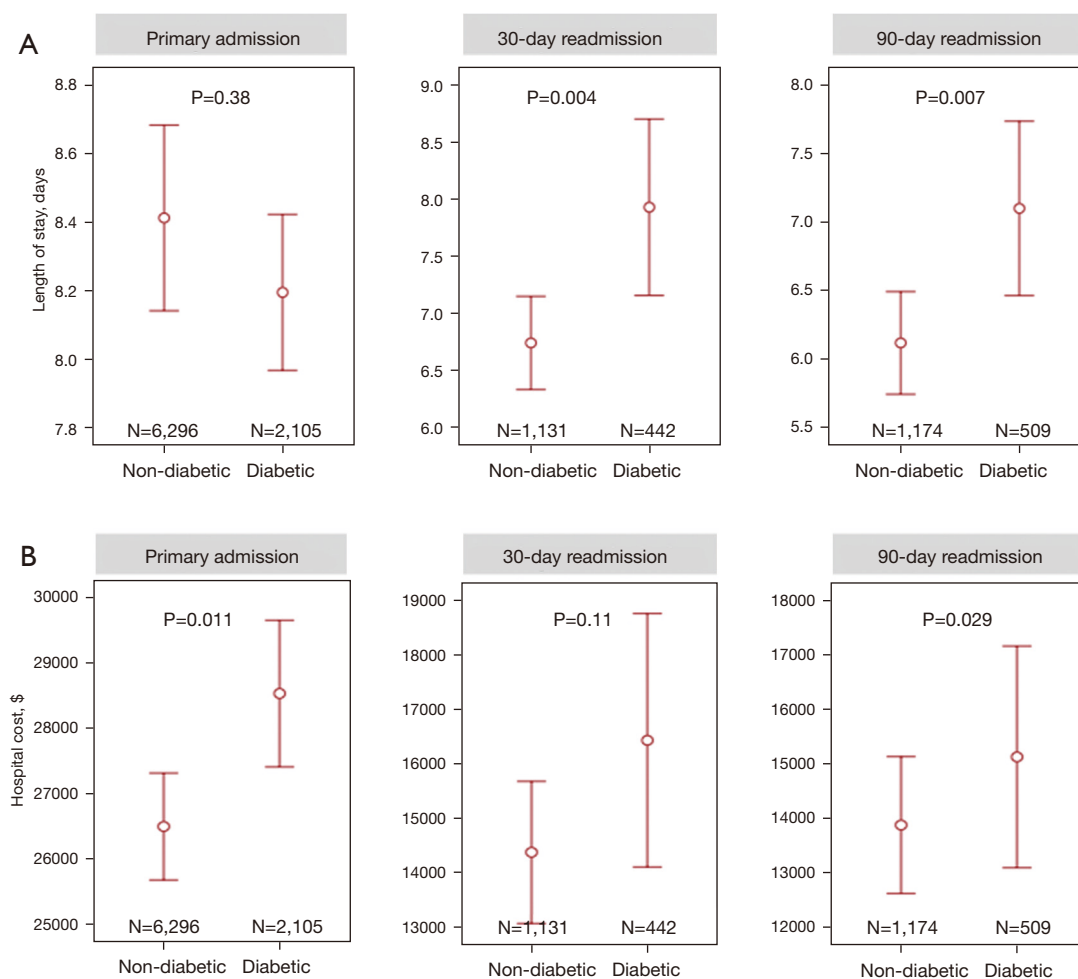
**Table 3** Multivariate logistic regression analysis depicting factors associated with post-operative outcomes in diabetic patients after pancreatic surgery

Variables	Levels	Post-operative complications			Readmission		
		aOR	95% CI	P value	aOR	95% CI	P value
Age (year)	>18–45	Reference			Reference		
	>45–65	1.27	1.02, 1.60	0.035	1.26	1.01, 1.59	0.043
	>65	1.27	1.00, 1.62	0.049	1.21	0.95, 1.54	0.11
Gender	Male	Reference			Reference		
	Female	1.00	0.86, 1.15	0.95	0.92	0.80, 1.06	0.24
Median annual household income	Quartile 1 lowest	Reference			Reference		
	Quartile 2	0.94	0.76, 1.15	0.52	0.79	0.65, 0.97	0.027
	Quartile 3	0.77	0.63, 0.94	0.012	0.77	0.63, 0.94	0.011
	Quartile 4 highest	0.70	0.58, 0.86	0.001	0.70	0.57, 0.85	<0.001
Type of surgical procedure	Partial pancreatectomy/excision	Reference			Reference		
	Total pancreatectomy	1.56	0.98, 2.48	0.05	2.24	1.50, 3.35	<0.001
	Radical pancreaticoduodenectomy	1.10	0.90, 1.33	0.35	1.15	0.95, 1.39	0.16
Cause of surgery	Non-cancer	Reference			Reference		
	Cancer	0.27	0.23, 0.32	<0.001	0.89	0.69, 1.14	0.36
CCI score	0	Reference			Reference		
	1	0.93	0.77, 1.12	0.45	1.03	0.86, 1.24	0.71
	≥2	1.09	0.76, 1.56	0.64	2.55	1.80, 3.60	<0.001
Diabetic state	Non-diabetic	Reference			Reference		
	Diabetic	1.27	1.08, 1.49	0.003	1.00	0.85, 1.17	0.98
Postoperative complications	None	NA	NA	NA	Reference		
	One or more	NA	NA		0.92	0.79, 1.08	0.33
Length of stay, days	≤9	Reference			Reference		
	>9	2.50	2.14, 2.92	<0.001	1.48	1.27, 1.73	<0.001
Hospital volume	Low	Reference			Reference		
	Medium	1.00	0.83, 1.20	0.98	1.06	0.88, 1.27	0.54
	High	1.22	0.99, 1.50	0.06	1.07	0.86, 1.34	0.53
Hospital type	Metropolitan nonteaching	Reference			Reference		
	Metropolitan teaching	1.20	0.90, 1.59	0.21	1.04	0.77, 1.39	0.80
	Nonmetropolitan hospital	0.40	0.14, 1.19	0.10	2.60	1.06, 6.40	0.037

All numbers are presented as weighted national estimates. Statistical significance was set at  $P < 0.05$ . CCI, Charlson Comorbidity Index; aOR, adjust odds ratio.

pancreatectomies (5.3% vs. 3.8%); however, it did not reach significance. Our analysis used the NRD, a multi-institutional dataset that includes different settings and volumes of hospitals, whereas the results presented in

Casadei *et al.* were from a single, high-volume, metropolitan institution. The overall rates of all readmissions were higher at non-metropolitan hospitals in our study when compared to metropolitan hospitals. Further insight into the risk



**Figure 6** Healthcare burden of diabetes following pancreatic surgery. (A) Length of hospital stay at primary admission and readmission following pancreatic surgery. (B) Hospital cost at primary admission and readmission following pancreatic surgery. Bars represent mean and 95% confidence intervals. Mann-Whitney U test was used.

factors for readmission for total pancreatectomy patients in this cohort group would be illuminating.

Multiple studies have found that complex operations in high-volume hospitals with more experienced surgeons were protective against negative postoperative outcomes (19-26) as well as readmission rates (27-29). Similarly, Mehta *et al.* (30) reported that low-volume hospitals were not associated with either complications or 30-day readmission. The data analyzed here showed no increase in the risk of postoperative complications based on hospital volume or location, in accordance with other studies. It did, however, find an increased risk of readmission in non-metropolitan hospitals. This could potentially be indicative of an expansion of the healthcare gap. We found that

patients with diabetes compared to non-diabetics, and complicated diabetes compared to uncomplicated were less likely to travel for care. Additionally, being in the lowest quartile of median household income was identified as a risk factor for diabetes. It was associated with a higher risk for postoperative complications and 30- and 90-day readmission when compared to the third and fourth quartiles. Similar findings were published by Hernandez-Meza *et al.* (27), who found that bottom quartile income was related to an 8% increase in readmission risk. These data indicate that low-income patients with diabetes currently have less access to quality healthcare and are less likely to afford the costs associated with traveling to receive care. Further regionalization and concentration of surgical

procedures into metropolitan and high-volume hospitals could inadvertently cause a worsening of the healthcare gap, as access to quality healthcare has been cited as a cause of the socioeconomic health gap (26,31,32). Further studies using the NRD database should be performed to determine the source of these discrepancies.

Additionally, we found that hospital charges and costs were significantly higher in patients with diabetes compared to non-diabetic subjects. Further, those with uncontrolled diabetes had higher expenses and costs than those with controlled diabetes. Umpierrez *et al.* (6) showed that hyperglycemia was associated with higher mortality rates, longer LOS, and increased ICU admissions. We found similar results when we stratified patients with diabetic complications against those without. It stands to reason that patients with uncontrolled and complicated diabetes (i.e., those predisposed to previously mentioned adverse outcomes) would have higher associated hospital charges and costs, a finding that has been reported in multiple studies (7-9). The complications of uncontrolled and complicated diabetes are preventable; however, national estimates show an excess of 62.7 hospital-days and excess \$0.76 million in hospital costs per year in diabetic patients. Therefore, tighter glycemic control post-operatively possibly with insulin drips might mitigate these expected complications and extra expenditure. Considering the complex postoperative medical management, improvement in glycemic control and nutritional status after pancreatotomy further reduced pancreatic exocrine and endocrine insufficiency, and were associated with better survival, and prevented early complications and tumor recurrence (33).

Limitations of this study include the limitations of the NRD patient database itself. Since it tracks in-hospital data, it is possible that several subjects had complications treated in an outpatient setting and were thus not included in the data set. To that end, it is possible that by looking only at patients deemed ill enough to readmit, the study may be predisposed to selection bias. Additionally, this dataset did not have the power to assess for differences in mortality rates between the patient populations in question, which we had initially sought to quantify, and detailed perioperative management plan during hospitalization were not available. However, strength is using the NRD patient database, as it provides a broad scope of hospital data from over 2000 hospitals in 22 states. This data is weighted to represent national averages and should provide an approximation of the impact of diabetes mellitus on pancreatotomy or pancreaticoduodenectomy.

## Conclusions

Among patients undergoing pancreatic surgery, those with diabetes were more likely to develop postoperative complications than non-diabetics. Additionally, diabetic patients had higher hospital costs during primary admission and higher rates of 30- and 90-day readmissions. A better understanding of the causes would aid in setting up protective therapeutic strategies.

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The data are deidentified and publicly available, and thus exempt from institutional review board approval, and individual consent for this retrospective analysis was waived.

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**Table S1** ICD-9-CM Diagnosis and procedure Codes for study variables

Variables	Codes
<b>Main study variables</b>	
Obesity	278, 2780, 27800–27803
Body mass index	V85, V850, V851, V852 V8521-V8525, V853 V8530-V8539, V854 V8540-V8545
Metabolic syndrome	2777, 41400–41407, 27800–27803
Diabetes	250 Diabetes mellitus 2500 DM, Uncomplicated 2501–2509 DM, Complicated
Type I: (controlled, uncontrolled)	25001, 25003, 25011, 25013, 25021, 25023, 25031, 25033, 25041, 25043, 25051, 25053, 25061, 25063, 25071, 25073, 25081, 25083, 25091, 25093
Type II or unspecified (controlled, uncontrolled)	25000, 25002, 25010, 25012, 25020, 25022, 25030, 25032, 25040, 25042, 25050, 25052, 25060, 25062, 25070, 25072, 25080, 25082, 25090, 25092
Controlled vs. Uncontrolled	24900, 24901, 24910, 24912, 24920, 24922, 24930, 24932, 24940, 24942, 24950, 24952, 24960, 24962, 24970, 24972, 24980, 24982, 24990, 24992
<b>Diagnosis</b>	
Functional disorder	2515, 2518, 2519, 5770, 5771, 5772, 5778, 5779
Benign disease	2116
Malignant disease	1570, 1571, 1572, 1573, 1578, 1579
<b>Procedures</b>	
Partial pancreatectomy	5200, 5209, 525, 5251, 5253, 5259, 522, 5221, 5222
Total pancreatectomy	526
Radical pancreaticoduodenectomy	527
<b>Complications</b>	
Bleeding/shock	2851, 9981, 99811, 99812, 99813, 9982, E8700, 3998, 9904
Infection/sepsis	0380, 0389, 78552, 6822, 9983, 99831, 99832, 9985, 99851, 99859, 99883, 8604, 543, 5491
Technical complications	9982, 9984, 9986, 9987, 55321, 5778, 4143, 415, 4195, 5061, 5069, 3932
Cardiovascular complications	41000, 41001, 41002, 41010, 41050, 41051, 41052, 41060, 41061, 41062, 41070, 41071, 41072, 41080, 41081, 41082, 41090, 41091, 41092, 41511, 99701, 99702, 9972, 99779, 78559, 4010, 40509, 4275, 99791, 9980
Renal complications	584, 5845, 5846, 5847, 5848, 5849, 5856, 586
Pulmonary complications	518, 5181, 5184, 5187, 5188, 5185, 51881, 51882, 9973, 9672
Endocrine complications	2513, 2554, 2521, 27541, 2440, 2554
Wound complications	9983, 99883