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Retrospective Evaluation of the Perioperative Management of Patients Undergoing Total Pancreatectomy With Islet Autotransplantation:

Single Institution Review

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Abstract

Objective: The aim of this retrospective descriptive study was to examine associations with the perioperative management of patients undergoing total pancreatectomy with islet autotransplantation, which may impact complication rate and hospital length of stay.

Methods: We retrospectively collected data on 165 patients, and 161 patients were included in the final analysis. Data collected included preoperative, intraoperative, and postoperative patient and procedural characteristics.

Results: Approximately 46.6% of patients experienced 1 or more complications. The occurrence of complications was associated with postoperative day 1 hemoglobin levels, use of intraoperative goal-directed therapy, estimated intraoperative blood loss, and total amount of intraoperative insulin given. Hospital length of stay was significantly associated with number of complications, use of goal-directed therapy, procedure duration, and postoperative day 1 hemoglobin levels.

Conclusions: Overall, our retrospective descriptive study adds to the emerging body of literature determining optimal perioperative management of patients undergoing total pancreatectomy with islet autotransplantation.

Keywords

total pancreatectomy with islet autotransplantation; perioperative management; perioperative complications; goal-directed therapy

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Total pancreatectomy with islet autotransplantation (TPIAT) was first introduced into practice in 1977.[1] Since then, this procedure has improved with time and gained appeal for

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patients who experience poor quality of life related to chronic pancreatitis.[2,3] Undoubtedly, patients with chronic pancreatitis or inherited pancreatic disorders presenting for TPIAT have complicated medical milieus, but the combination of patient characteristics, postoperative complications, and overall logistics of interdisciplinary coordination of care is notably difficult. Thus, intuitively, programs that excel at TPIAT do so by examining their surgical care continuum.

Preoperative patient evaluation and selection have been well studied in TPIAT with a focus on postoperative outcomes to determine who benefits from surgical intervention.[4,5] However, intraoperative and postoperative care lacks robust attention in the literature. In addition, data on modifiable factors to potentially target best perioperative patient care strategies are relatively sparse as well.

We retrospectively identified all patients older than 18 years who underwent a TPIATat our institution between 2009 and 2016 with the intent to fill some previously mentioned gaps in the literature and contribute to emerging best practices in TPIAT. Perioperative, intraoperative, and postoperative patient and procedural characteristics are described along with complication rate, mortality, intensive care unit (ICU) length of stay, and hospital length of stay (HLOS). In addition, subsequent associations between complications and HLOS are enumerated.

MATERIALS AND METHODS

After institutional review board approval (Pro00053712), we retrospectively collected data on all 165 patients who underwent a TPIAT at the Medical University of South Carolina between March 2009 and March 4, 2016. Of the 165 patients, 4 were excluded either because of age of less than 18 years or missing intraoperative records, resulting in 161 patients in the final analysis. A new REDcap database was created by our research team, and data collected included the following: preoperative medical comorbidities, reason for surgery, preoperative medications used, demographic data, preoperative vital signs and measurements, preoperative laboratory data, surgical time, medications used intraoperatively, intraoperative laboratory data, intraoperative vital signs, total intraoperative fluid input and output, time from surgical closure to islet cell transplant, time to extubation in ICU, postoperative complications, postoperative laboratory data, postoperative medication use, postoperative vital signs, and time to discharge from ICU and hospital. Our institution transitioned from paper records to 2 different electronic record systems between 2009 and July 2014, making it more challenging to collect certain postoperative retrospective data points within the old electronic charting system, thus resulting in multiple missing data points for certain postoperative characteristics.

Statistical Analysis

Descriptive statistics were estimated for all patient, intraoperative, and postoperative characteristics. Specifically, categorical variables are reported as number of occurrences and percent and continuous variables are reported as mean and standard deviation (SD) or median and range. Median and range are reported only for those continuous variables that were highly skewed.

It was also of interest to examine potential procedural characteristics that were associated with patient outcomes. Outcomes of interest included occurrence of complications, defined as the occurrence of any complication, and ICU and HLOS. Univariate associations between the occurrences of complications with all variables were examined using a series of logistic regression models. Model assumptions for all models were checked graphically and transformations were considered when necessary. Univariate associations between patient and intraoperative characteristics with ICU and HLOS with categorical variables were examined using a Wilcoxon rank sum approach and associations with continuous variables were evaluated using Spearman rank correlation. For categorical variables associated with length of stay outcomes, the median differences between categories with 95% confidence interval (CI) were estimated using the Hodges-Lehman approach. Given the retrospective study design and exploratory nature of these analyses, only univariate models for these outcomes were considered. All analyses were conducted in SAS v. 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

Of the 161 patients, approximately 74% of the participants were female and the mean (SD) age in the population was 41.0 (12.4) years. Most patients underwent TPIAT for chronic pancreatitis (85.7%). The mean preoperative hemoglobin was 12.5 g/dL, and the mean preoperative glucose was 126 g/dL. The average duration of surgical procedure was 260 minutes (4.3 hours). Approximately 97% of patients received fentanyl, 69% received ketamine, and 52% received hydromorphone intraoperatively. Close to 85% of patients received a preoperative epidural for perioperative pain management. Ropivicaine and bupivacaine were the most commonly used intraoperative local anesthetics in the epidural.

Estimated median blood loss was 400 mL. The median crystalloid administration was 3.475 L. Approximately 39% of patients received intraoperative colloids, which included red blood cells, Voluven, albumin, platelets, cryoprecipitate, and fresh frozen plasma. Finally, 23 patients received goal-directed fluid therapy.

The mean postoperative hemoglobin (measured on the morning of postoperative day 1) was 9.7 g/dL. Approximately 67% of patients received some form of postoperative heparin administration, with 21% placed on a low-dose intravenous heparin infusion for portal vein thrombosis prevention. Approximately 27.3% of patients received a postoperative blood transfusion. Furthermore, patient, procedural, and postoperative characteristics divided by presence or absence of complication are shown in Table 1.

Occurrence of Postoperative Complications

Approximately 46.6% of patients experienced 1 or more complications. The median duration of ICU stay was 74 hours and the median HLOS was 9.8 days (Table 2).

The occurrence of postoperative complications was associated with postoperative hemoglobin levels (recorded as hemoglobin on the morning of postoperative day 1), use of goal-directed therapy, estimated blood loss, and total insulin given intraoperatively. Patients with lower postoperative hemoglobin levels had higher odds of experiencing a complication (odds ratio [OR] (1 unit decrease), 1.36; 95% CI, 1.12–1.73; $P = 0.004$). In addition, patients who did not receive goal-directed therapy had a 3.7-fold increase in the odds of having at least 1 complication (OR, 3.71; 95% CI, 1.30–10.5; $P = 0.014$). Both estimated intraoperative blood loss and total intraoperative insulin given were log transformed to meet model assumptions. A 25% increase in estimated blood loss was associated with an 11% increase in the odds of complication (OR, 1.11; 95% CI, 1.01–1.23; $P = 0.029$). Similarly, a 25% increase in the total amount of insulin given was associated with an 11% increase in the odds of complication (OR, 1.11; 95% CI, 1.01–1.22; $P = 0.030$). There was also a marginal association with procedure duration with patients who had longer total procedure duration having greater odds of experiencing a complication ($P = 0.054$). Odds ratios for all univariate models of experiencing a complication are reported in Table 3.

Intensive Care Unit and HLOS

Intensive care unit length of stay was significantly negatively correlated with postoperative hemoglobin levels ($r = -0.19$; 95% CI, −0.36 to −0.01; $P = 0.041$), suggesting that patients with lower postoperative hemoglobin had longer ICU length of stay. Intensive care unit length of stay was not significantly associated with and other patient or procedural characteristics. However, there was a significant amount of missing data (44/161 patients) most likely because of the switch in electronic record platforms, making it difficult to draw a meaningful association.

Duration of HLOS was significantly associated with the number of complications (defined here as 0, 1, or >2), use of goal-directed therapy, procedure duration, and postoperative hemoglobin levels. Patients with increasing number of complications had significantly longer HLOS ($P < 0.001$). Specifically, patients with 1 complication stayed a median of 2.5 days longer than those with no complications, and patients with 2 or more complications had a median increase in HLOS of 9 days compared with those with no complications. In addition, patients who did not have goal-directed fluid therapy had a median increase in HLOS of 1.7 days compared with those who received goal-directed therapy (GDT) ($P = 0.034$). Hospital length of stay was positively correlated with procedure duration ($P = 0.002$) indicating that subjects with longer procedure duration also had longer HLOS. Hospital length of stay was negatively correlated with postoperative hemoglobin (Hgb) ($P = 0.006$), indicating that subjects with lower postoperative Hgb levels had longer HLOS. The median differences in HLOS by number of complications and use of GDT and the estimated correlations between procedure duration and postoperative Hgb are presented in Table 4.

DISCUSSION

First performed in 1977, total pancreatectomy with islet autotransplantation (TPIAT) has been performed as a treatment of last resort for patients with intractable pain related to chronic or acute recurrent pancreatitis as well as for patients with hereditary pancreatitis syndromes who have a genetic predisposition to progress to pancreatic cancer.[1,2,6–8] The goals of the procedure are to improve the patient's quality of life by both alleviating pain and preserving exocrine and endocrine function of the pancreas. This procedure has undergone resurgence in popularity because of advances in islet cell isolation and preservation. However, the procedure is not without serious potential risks to the patient. Several studies that have evaluated outcomes after TPIAT in terms of quality of life, opioid use, and postoperative insulin requirement.[6,8–11] However, there is a paucity of evidence regarding perioperative management of patients undergoing TPIAT. Thus, it is unclear whether there are any specific modifiable factors related to perioperative management that can improve the patient's immediate postoperative course. The goals of this study were to examine the perioperative management of patients undergoing TPIAT and to examine any associations between management and overall postoperative complication rate and HLOS.

Approximately 46.6% of our patients experienced a postoperative complication during the initial admission. Approximate 10.6% needed reoperation during their inpatient stay, with 9 of the 17 patients receiving a reoperation due to bleeding complications. This is similar to the data reported by Sutherland et al[2] where 15.9% of their 409 patients required relaparotomy during initial admission with bleeding being the most common complication. Three of our patients died during initial admission, resulting in an in-hospital mortality rate of 1.86%. This is similar to Sutherland et al's[2] reported in-hospital mortality rate of 1.2% as well as Wu et al's[3] meta-analysis that reported 30-day mortality rate of 2.1%.

Patients who had larger estimated intraoperative blood loss (and thus lower post-operative day 1 hemoglobin score) had higher odds of experiencing a complication (Table 3). This may suggest that patients who had a more challenging surgical dissection and thus lost more blood intraoperatively were more at risk for postoperative complication. In addition, those patients who received more intraoperative insulin had higher odds of experiencing a complication, suggesting that those patients who had less intraoperative glucose fluctuations were less likely to develop a postoperative complication. Finally, the use of GDTwas associated lower complication rate. Goal-directed therapy at our institution was achieved by the use of arterial pressure waveform monitoring (FloTrac System; Edwards Lifesciences Corp, Irvine, Calif). We instituted goal-directed therapy for fluid administration as part of an Enhanced Recovery After Surgery protocol in 2014; thus, it is likely that it was not just GDT but the entire Enhanced Recovery After Surgery protocol itself that decreased complication rate.[12] Although anesthesiologists do not have much control over limiting surgical blood loss due to difficult dissection, these data do suggest that anesthesiologists as well as perioperative physicians have an opportunity to affect outcome by achieving optimal perioperative glucose control and maintain intraoperative euvolemia. Interestingly, the intraoperative use of neither an epidural catheter nor the amount of pain medication given intraoperatively was not significantly associated with complication rate.

Those patients with a lower post-operative day 1 hemoglobin score had a significantly increased HLOS (Table 4). Approximately 18 patients (11%) received packed red blood cells intraoperatively, and 44 patients required blood transfusion postoperatively (27.3%). Yoshimatsu et al[13] reported a 34.9% transfusion rate in the perioperative period, which is much higher than ours. They also demonstrated that allogenic blood transfusion in this surgical population led to an elevation in proinflammatory cytokines, but overall graft function was not compromised, thus suggesting that blood transfusion did not suppress the immune system to a degree that affected islet cell engraftment.[13] Again, it stands to reason that patients who lost more blood during surgery at our institution potentially had a more difficult surgical dissection leading to longer procedure duration, thus putting them at higher risk for postoperative complications and increased HLOS. However, these data in addition to Yoshimatsu et al's findings[13] might suggest that a restrictive transfusion threshold may not be warranted for this particular procedure. Finally, HLOS was not significantly associated with total morphine equivalents used intraoperatively, which suggests that amount of parental opioid given intraoperatively did not negatively or positively impact the patient's hospital course.

Limitations of this study include the retrospective accumulation of data. Much of the postoperative data originally collected had multiple missing data points, most likely because of the change in medical record platforms, making it difficult to draw any associations between postoperative characteristics and ICU and HLOS. Thus, given the sample size of the patient population, all postoperative data for which more than 15% of subjects were missing information were excluded from consideration in the analysis presented in this article. However, future directions may include prospective collection of postoperative in-hospital data, which may result in a more robust data set to evaluate modifiable factors.

In 2014, Bellin et al[4] outlined potential research gaps and opportunities for improvement in the care of patients undergoing TPIAT, including outlining the best perioperative patient care strategies. In our retrospective review, patients with 1 complication stayed a median of 2.5 days longer than patients with no complications and patients with 2 or more complications had a median increase in HLOS of 9 days compared with patients with no complications. Given the complex nature of this procedure, examining potential modifiable factors in the perioperative management of these patients to decrease complication rate can potentially have an impact both on patient outcome and on HLOS. Overall, our retrospective study can add to the body of literature in determining optimal perioperative management of these patients.

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TABLE 1.

Patient, Procedural, and Postoperative Characteristics by Occurrence of Complications

	No Complication (n = 86)	Any Complication (n = 75)	*P*
Patient characteristics			
Sex, male, n (%)*	27 (31.8)	14 (19.2)	0.072
Age, mean (SD), y*	40.8 (12.4)	41.3 (12.5)	0.791
BMI, mean (SD), kg/m^2*	26.6 (6.75)	25.5 (6.12)	0.295
Type of pancreatitis, n (%)			0.214
Hereditary	11 (12.8)	4 (5.33)	
Chronic	70 (81.4)	68 (90.7)	
Acute	5 (5.81)	3 (4.00)	
Preoperative information			
Preoperative insulin, yes, n (%)*	11 (13.3)	14 (19.2)	0.314
Preoperative sedation, yes, n (%)†	71 (89.9)	59 (93.7)	0.421
Preoperative glucose, median (IQR), mg/dL*	127.0 (60.5)	125.5 (53.9)	0.631
Preoperative hemoglobin, mean (SD), mg/dL*	12.5 (1.76)	12.5(1.92)	0.958
Intraoperative information			
Procedure duration, mean (SD), min*	250.3 (69.1)	272.1 (70.5)	0.051
Any ME, yes, n (%)	75 (100.0)	85 (98.8)	1.00
If yes, amount opiate, median (IQR), ME	25 (23.3)	25.8 (21.8)	0.262
Intraop fentanyl, yes, n (%)	86 (100.0)	70 (93.3)	0.020
If yes, amount fentanyl, median (IQR), µg	375 (250)	350 (250)	0.910
Intraop hydromorphone, yes, n (%)	43 (50.0)	41 (54.7)	0.554
If yes, amount hydromorphone, median (IQR), mg	2.0 (0.8)	2.0 (1.6)	
Intraop morphine, yes, n (%)	3 (3.49)	1 (1.33)	0.624
If yes, amount morphine, median (IQR), mg	10 (7)	40§	
Intraop dexmedetomidine, yes, n (%)	1 (1.16)	1 (1.33)	1.00
If yes, amount dexmedetomidine, µg		34	
Intraop ketamine, yes, n (%)	59 (68.6)	52 (69.3)	0.921
If yes, amount ketamine, median (IQR), mg	108 (81.85)	97 (97.7)	

	No Complication (n = 86)	Any Complication (n = 75)	*P*
Epidural, yes, n (%)	76 (88.4)	60 (80.0)	0.143
Type of epidural medications, n (%)			0.458
Bupivicaine, yes	53 (61.6)	39 (52.0)	
Ropivicaine, yes	22 (25.6)	20 (47.6)	
Lidocaine, yes	1 (1.16)	1 (1.33)	
Intraop epidural duration, mean (SD), min *	176.5 (79.5)	172.0 (87.6)	0.764
Intraop glucose management, yes, n (%) *	73 (85.9)	65 (87.8)	0.716
Colloids, yes, n (%)	30 (34.9)	33 (44.0)	0.237
RBC, yes, n (%)	6 (6.98)	12 (16.0)	0.070
Voluven, yes, n (%)	17 (19.8)	16 (21.3)	0.806
Albumin, yes, n (%)	5(5.81)	8 (10.7)	0.385
Platelets, yes, n (%)	0 (0.00)	2 (2.67)	0.216
Cryo, yes, n (%)			
FFP, yes, n (%)			
Total insulin given, mean (SD), U †	6.37 (6.0)	9.3 (9.0)	0.015
Estimated blood loss, median (IQR), mL *	350 (350)	450 (450)	0.053
Total fluid loss, median (IQR), mL ‡	790 (627.5)	830 (680)	0.454
Crystalloid, median (IQR), mL *	3500 (1600)	3375 (1650)	0.768
Urine output, median (IQR), mL *	317.5 (407.5)	375 (395)	0.503
Goal-directed therapy, yes, n (%) *	18 (20.9)	5 (6.67)	0.012
Postoperative characteristics			
Hemoglobin, mean (SD), g/dL *	10.1 (1.56)	9.28 (1.65)	0.003
Heparin use, yes, n (%)	53 (61.6)	55 (73.3)	0.115
Blood transfusion, yes, n (%)	15 (17.4)	29 (38.7)	0.003
ICU LOS, median (IQR), h †	72.0 (64.2)	75.6 (78.0)	0.164
HLOS, median (IQR), d *	8.2 (3.2)	12.0 (9.1)	<0.001

*0.5%–4.9% of subjects missing data.

†≥10% of subjects missing data; maximum missing was ICU LOS with 27% of subjects missing data.

[‡]5.0%–9.9% of subjects missing data.

[§]Only one subject who experienced a complication received intraoperative morphine and thus IQR is not calculable, thus we report only the amount of morphine this subject received.

BMI indicates body mass index; IQR, interquartile range; ME, morphine equivalents; Intraop, intraoperative; RBC, red blood cells; Cryo, cryoprecipitate; FFP, fresh frozen plasma.

TABLE 2.

Frequency and Types of Complications

No. complications	
0	86 (53.4)
1	50 (31.1)
2	14 (8.70)
>2	11 (6.83)
Glucose management, yes	6 (3.73)
Delayed gastric emptying, yes	8 (4.97)
Infection, yes	34 (21.1)
Reoperation needed, yes	17 (10.6)
Thrombosis, yes	8 (4.97)
In-hospital death, yes	3 (1.86)
Other complications, yes	38 (23.6)
Surgery for bleeding complication, yes	9 (2.29)

Data expressed as n (%).

TABLE 3.

Univariate Logistic Regression Models of Postsurgical Complications

Variable	OR (95% CI)	*P*
Postoperative hemoglobin, 1 mg/dL decrease	1.36 (1.12–1.73)	0.004
Use goal-directed therapy, no vs yes	3.71 (1.30–10.5)	0.014
Estimated blood loss, 25% increase, mL	1.11 (1.01 −1.23)	0.029
Total insulin, 25% increase, U	1.11 (1.01 −1.22)	0.03
Procedure duration, 10-min increase	1.05 (1.00–1.10)	0.054

TABLE 4.

Univariate Associations With HLOS

Variable	Median Difference or Correlation (95% CI)	*P*
No. complications*		<0.001†
0 vs 1	2.5 (1.0–3.9)	<0.001
0 vs ≥2	9.0 (4.9–15.3)	<0.001
1 vs ≥2	6.5 (1.9–12.2)	0.005
Use goal-directed therapy, no vs yes*	1.7 (0.1–3.6)	0.034
Procedure duration‡	0.25 (0.10–0.40)§	0.002
Postoperative hemoglobin‡	−0.22 (−0.37 to −0.07)§	0.006

*Median difference.

†*P* value for the global Kruskal-Wallace test of any difference by number of complications.

‡Correlation.

§Values presented are the Spearman correlation (95% CI).