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# The impact of using an intraoperative goal directed fluid therapy protocol on clinical outcomes in patients undergoing total pancreatectomy and islet cell autotransplantation

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## ABSTRACT

*Background:* Patients undergoing total pancreatectomy and islet cell autotransplant (TPIAT) for treatment of pancreatitis are at risk for complications of over and under resuscitation. We hypothesized that using a goal directed fluid therapy (GDFT) protocol might impact clinical outcomes.

*Materials and methods:* A consecutive series of adult patients undergoing TPIAT were managed intraoperatively using either standard fluid therapy (SFT, n = 44) or GDFT (n = 23) as part of a pilot study between January 2013 and May 2015. Patient characteristics, intraoperative, and postoperative data were recorded prospectively, then retrospectively analyzed for differences between the groups.

*Results:* The GDFT group had lower total fluid resuscitation (3,240 cc vs 5,173 cc, p < 0.0001) and transfusion requirements (1.0 cc/kg vs 3.3 cc/kg, p = 0.050) compared to the SFT group. The pre to postop nadir hemoglobin change was significantly less for GDFT (4.2 vs 5.1 gm/dl, p = 0.021) despite less transfusion.

*Conclusions:* Compared to SFT, using an intraoperative GDFT protocol in TPIAT patients was associated with significantly decreased intraoperative fluid resuscitation, blood transfusion and less postoperative dilutional anemia, without any difference in complications of underresuscitation. This pilot study suggests that GDFT is likely safe and further investigation is warranted. © 2017 IAP and EPC. Published by Elsevier B.V. All rights reserved.

## Introduction

Chronic pancreatitis and acute relapsing pancreatitis are progressive conditions associated with significant morbidity and mortality that can be attenuated with medical and endoscopic management [1,2]. Total pancreatectomy and islet cell auto transplant (TPIAT) is an established treatment option for painful pancreatitis that significantly impacts daily functioning when medical management fails, and provides an opportunity for pain relief and improved quality of life while simultaneously

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ameliorating the endocrine effects of total pancreatectomy [3-6].

TPIAT patients are a unique surgical patient population with a high complication rate. Specifically, the long case duration, chronic narcotic use, inflammatory stimuli of pancreatitis, infusion of an unpurified pancreatic cell preparation and potential for major blood loss are factors that may drive excessive intraoperative resuscitation. Conversely, under-resuscitation may exacerbate thrombotic risks due to decreased portal venous flow and the instant blood mediated inflammatory reaction stimulated by islet cell transplant [7,8].

Standard perioperative fluid therapy (SFT) utilizes clinical parameters such as blood pressure, central venous pressure, and heart rate, and is varied by provider preference and experience which can increase the risk of fluid overload during long operations. Overresuscitation may be associated with dilutional anemia and need

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for transfusion, hypoxia (pulmonary edema, supplemental  $O_2$  requirements), bowel edema (ileus, anastomotic leak), wound complications (seroma, infection), decreased mobility (pain, swelling, urinary tract infection), and increased resource utilization [9].

Compared to SFT, the use of goal directed fluid therapy (GDFT) in major abdominal surgery has yielded mixed results [10,11], Some randomized clinical trials of patients receiving GDFT compared to SFT have been associated with decreased morbidity, earlier return of bowel function and decreased length of stay, while other trials have failed to demonstrate a significant difference in clinical outcomes [10–16]. Nonetheless, GDFT has been increasingly incorporated into the routine practice of anesthesiology for patients ungoing major elective surgery and has even been studied in emergency surgery [17,18]. It is unclear if GDFT might lead to underresuscitation and exacerbate complications in patients undergoing pancreatectomy with islet cell autotransplant, a unique surgical population known to be at risk of portal vein thrombosis, islet cell transplant failure, and end organ injury such as acute kidney injury, hepatorenal syndrome, and respiratory failure.

The potential for GDFT to mitigate postoperative complications and improve clinical outcomes in patients undergoing TPIAT has not been previously investigated. The aim of this pilot study was to determine if the adoption of an intraoperative GDFT protocol was associated with any difference in clinical outcomes. Herein we compare the intra- and postoperative outcomes and resource utilization of patients undergoing TPIAT using a SFT vs. GDFT protocol.

### Materials and methods

### Patient population

Intraoperative GDFT was introduced in 2014 as a pilot study in adult patients undergoing pancreatectomy with islet cell transplant at the University of Minnesota. A consecutive series of these patients undergoing surgery over the course of one year were compared in a 1:2 ratio with patients receiving SFT in the period immediately preceeding the pilot study. All patients underwent surgery between January 2013 and May 2015. Patient characteristics, intra- and post-operative details and outcomes data were recorded prospectively in the medical record and retrieved by chart review at a minimum of 6 months postoperatively. Detailed patient characteristics are shown in Table 1. All patients were managed by

## Table 1

Patient characteristics.

enhanced recovery after surgery (ERAS) protocol elements including aggressive early enteral feeding, early ambulation, and advanced intra and postoperative use of multimodal non-narcotic analgesia regimens. Institutional Review Board approval was obtained (IRB# 1507M76665).

## Intraoperative fluid management and monitoring

Patients assigned to GDFT were monitored using the Vigileo monitor (Edwards Lifesciences, Irvine, CA) which monitors stroke volume variation (SVV) through a single arterial catheter. Stroke volume variation is a natural occurring phenomenon that results from changes in intra-thoracic pressure secondary to positive pressure ventilation. While SVV is not an indicator of actual preload, it is an indicator of relative preload responsiveness and when used in conjunction with a fluid replacement protocol, SVV can help guide intra-operative fluid therapy. For this study our goal was to maintain an SVV between 8 and 12%. Respiratory tidal volume was set at 6-8 cc/kg ideal body weight. Maintenance fluid (Lactated Ringers) was administered at a rate of 6 mL/kg/hour, and downadjusted to 3.5 mL/kg/hour during any laparoscopic assisted portion of the operation. Fluids were then administered based on the protocol shown in Fig. 1. The decision to administer intraoperative packed red blood cells (pRBC) was made by the anesthesiologist triggered by a combination of active intraoperative blood loss and/or hemoglobin <8.0 mg/dL. Surgeries were performed by three surgeons all with significant experience with the procedure and who follow similar postoperative care pathways incorporating other aspects of ERAS, without change during the study period.

## Data analysis

Since our goal was to study the effect of an *intraoperative* GDFT intervention (vs SFT) in this pilot study, we compared the rates of transfusion and other outcome variables potentially affected by over- or under-resuscitation such intraoperative vasopressor use, portal vein thrombotic complications, return of bowel function, length of stay, and surgical complications. Postoperative complications were graded using a Clavien scale developed for pancreatic surgery [19]. Islet cell transplant graft function was assessed at 3, 6 and 12 months postoperatively by measuring insulin use (units/kg/

	SFT ( <i>n</i> = 44)	GDFT (n = 23)	p-value
Age, years, median (range)	41 (22–67)	41 (21–59)	0.480
Gender (% Female)	33 (75%)	15 (65%)	0.409
Etiology:			
Idiopathic	15 (29%)	9 (33%)	0.797
Hereditary	9 (17%)	4 (15%)	1.000
Mechanical	23 (44%)	11 (41%)	0.993
Other (alcoholic, trauma, biliary)	5 (10%)	3 (11%)	0.998
Pancreatitis type:			0.708
Chronic	37 (84%)	21 (91%)	
Acute relapsing	7 (16%)	2 (9%)	
Years of disease, median (range)	5 (1-35)	7 (1-35)	0.686
Preoperative PERT	28 (64%)	17 (74%)	0.428
Preoperative diabetes	2 (5%)	2 (9%)	0.603
Preoperative gastroparesis	3 (7%)	0 (0%)	0.546
Preoperative IBD	10 (23%)	12 (52%)	0.027
Preoperative constipation	3 (7%)	1 (4%)	1.000
Preoperative hemoglobin g/dL, median (range)	12.2 (8.9–15.8)	12 (8.2–14.5)	0.152
Prior pancreatic surgery	7 (16%)	6 (26%)	0.344
Laparoscopic assisted vs. Open surgery	11 (25%)	8 (35%)	0.409
Weight, kg, median (range)	70.5 (42–118)	68 (50-117)	0.977
Preoperative morphine equivalents, median (range)	60 (0-570)	80 (0-382)	0.654

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