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Intraoperative Fluid Administration Is Associated With Perioperative Outcomes in Pancreaticoduodenectomy: A Single Center Retrospective Analysis

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Background: Recent studies on perioperative fluid administration in patients undergoing major abdominal surgery have suggested that increased fluid loads are associated with worse perioperative outcomes. However, results of retrospective analyses of the relationship between intraoperative fluid (IOF) administration and perioperative outcomes in patients undergoing pancreaticoduodenectomy (PD) are conflicted. We sought to investigate this relationship in patients undergoing PD at our academic center.

Methods: A retrospective analysis of 124 patients undergoing PD from 2007 to 2012 was performed. IOF administration rate (ml/kg/hr) was correlated with perioperative outcomes. Outcomes were also stratified by preoperative serum albumin level.

Results: Regression analyses were performed comparing independent perioperative variables, including IOF rate, to four outcomes variables: length of stay, severity of complications, number of complications per patient, and 30-day mortality. Both univariate and multivariate regression analyses showed IOF rate correlated with one or more perioperative outcomes. Patients with an albumin $\leq$3.0 g/dl who received more than the median IOF rate experienced more severe complications, while patients with an albumin $>$3.0 g/dl did not.

Conclusion: Increased IOF administration is associated with worse perioperative outcomes in patients undergoing PD. Patients with low preoperative serum albumin levels ($\leq$3.0 g/dl) may be a group particularly sensitive to volume overload.

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INTRODUCTION

Defining the optimal strategy for perioperative fluid administration in major abdominal surgery remains a challenging clinical problem. At first glance, the problem seems rather simple: replace the fluid and electrolytes lost during surgery with a goal of maintaining normal physiologic parameters. However, there are numerous factors to consider in estimating fluid loss, including operative blood and insensible fluid losses during open laparotomy, and the loss of extravascular fluid volume through the so-called “third-space effect”. The concept that surgical trauma produces a loss of extravascular fluid volume that is proportional to the magnitude of the surgical stress and needs to be replaced with crystalloids was first introduced by Tom Shires in the 1960s, based on the work of Dr. Alfred Blalock, and has since served as a guiding principle in perioperative fluid management [1]. Nonetheless, the clinician must estimate these losses, often in the setting of disease states that affect the body’s normal fluid and electrolyte homeostasis, including congestive heart failure, cirrhosis, cancer, and malnutrition, with the latter two being particularly prevalent in patients undergoing pancreaticoduodenectomy (PD).

Based in part on Shires’s influence, guidelines for perioperative fluid management during intra-abdominal surgery have favored liberal administration of fluid to prevent intravascular hypovolemia and decreased end-organ perfusion. These guidelines include intraoperative fluid (IOF) replacement at rates ranging from 10–15 ml/kg/hr with replacement of blood volume losses with crystalloid at a 3:1 ratio or colloid at a 1:1 ratio [2–4]. This management often results in whole body fluid overload as manifested by a weight gain of 5–10 kg and edema [5,6]. This edema has negative clinical consequences on a number of organ systems, including the cardiopulmonary, renal, and gastrointestinal systems [5,7]. In particular, fluid overload causes impaired gut motility as well as mucosal edema, which can impair the healing of bowel anastomoses. These observations have led to the hypothesis that limiting perioperative fluid administration during major abdominal surgery will lead to improvements in morbidity and length of stay. This hypothesis was first tested by Lobo et al. in 2002 in a randomized trial on colon surgery, and has since been validated by several other randomized studies [7–9]. With the exception of one study, patients undergoing PD were not included.

PD is a procedure characterized by a long duration, extensive dissection, potential for large volume blood loss, high surgical morbidity, lengthy hospital stay, and is often performed in patients with a substantial burden of disease. Preoperative serum albumin level is an indicator of nutritional status as well as severity of disease, and has been demonstrated to be an independent predictor of morbidity and mortality in patients undergoing surgical procedures [10]. As serum albumin is a major determinate of plasma oncotic pressure, we hypothesized that hypoalbuminemia may exacerbate the negative effects of volume overload in our patient cohort.

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The optimal perioperative fluid management for PD has yet to be defined. In fact, the relationship of perioperative fluid administration to surgical morbidity and length of stay is controversial. Jarnagin et al. reported on a randomized trial of acute normovolemic hemodilution (ANH) in PD, which was designed to determine if ANH could decrease the need for allogeneic red blood cell transfusion. In this trial, patients in the ANH arm received an average of over two liters of fluid more than control arm patients. The investigators observed that in the ANH arm, not only the frequency, but also the severity of complications related to the pancreatic anastomosis were increased [11]. Subsequently, Melis et al. retrospectively analyzed 188 patients at a single center and did not find that intraoperative intravenous fluid administration significantly correlated with surgical morbidity or length of stay [12]. Most recently, Brennan et al. retrospectively examined 1,030 pancreatic resections (of which 679 were PD) and were not able to demonstrate a significant association between intravenous fluid administration and postoperative complications [13]. Given this uncertainty, we investigated the relationship between perioperative fluid management and outcomes in patients undergoing PD at our center.

METHODS

Fluid Administration Rate

A retrospective analysis was based on data acquired from an institutional review board-approved, retrospectively acquired database and electronic medical records at Robert Wood Johnson University Hospital (New Brunswick, NJ). A total of 124 patients who underwent PD from July 2007 to May 2012 with complete data on perioperative fluid administration were identified. Three surgeons performed all of the operations over this time period. At our institution, neither anesthetic approaches to replacement of blood or fluid losses, nor postoperative care processes were standardized. However, discussions between the anesthesiologist and surgeon regarding blood product transfusions were generally initiated when hemoglobin levels were less than 8 g/dl in patients without coronary artery disease (CAD) or less than 10 g/dl in patients with CAD. Blood was replaced with crystalloid at a 3:1 ratio and colloid at a 1:1 ratio.

Data collected included patient demographics, laboratory studies, co-morbidity index (ASA score), operative time, estimated blood loss, perioperative fluid administration volumes (crystalloid, colloid, and blood products), length of stay, and complications. Fluid administration for each patient was calculated by combining all crystalloid, colloid, and blood products administered. Blood product volumes were estimated to be 250 ml for each unit of packed red blood cells, fresh frozen plasma, or cryoprecipitate, and 50 ml for each unit of platelets. IOF data were collected from anesthesia records and analyzed by fluid rate (ml/kg/hr). Perioperative variables and outcomes compared included estimated blood loss, operative duration, length of stay, complications per patient, and severity of complications. Severity of complications was determined using the Clavien–Dindo classification system [14].

Preoperative Albumin Stratification

The mean albumin level for our cohort was 3.44 g/dl, slightly below the laboratory normal of 3.5 g/dl. To compare outcomes by perioperative fluid rate stratified by preoperative albumin, patients were separated into two groups based on their preoperative serum albumin, ≤ 3.0 versus >3.0 g/dl. The cutoff of 3.0 g/dl was chosen somewhat arbitrarily to represent a group of patients we considered relatively more hypoalbuminemic compared to the average patient in the entire cohort. Each group's outcomes were compared between patients stratified by median IOF rate. Perioperative variables and outcomes compared included estimated blood loss, operative duration, length of stay, complications per patient, and severity of complications.

Statistical Analysis

Statistical analysis included either Student's *t*-tests for continuous variables and chi-squared tests for categorical data. Wilcoxon–Mann–Whitney rank sum tests were performed for ordinal variables. Linear regression was used for analyzing length of stay and Poisson regression for complications per patient. Logistic regression was used for analyzing the mortality variable, and a proportion odds model was used for Clavien–Dindo grades. Statistical significance was accepted at a level of $P < 0.05$.

RESULTS

Fluid Administration Rate

Patient demographics are shown in Table I. The mean age was 64.5 years, and 52.4% of the cohort was female. 47.6% of patients were diagnosed with pancreatic adenocarcinoma. Perioperative outcomes are shown in Table II. Median IOF rate was 13.95 ml/kg/hr, and mean estimated blood loss was 909 ml. Median length of stay was 9 days. Mean Clavien–Dindo classification was 1.8, and the mean number of complications per patient was 1.4. Overall 30-day mortality was 6.5%. We then stratified the patient cohort into three groups based on IOF rates administered in ml/kg/hr. The cutoffs we used for these three groups were based on current anesthetic guidelines for IOF administration (10–15 ml/kg/hr) [2–4]. When we stratified 30-day mortality in the patient cohort by rates of <10, 10–15, and >15 ml/kg/hr, we found that 30-day mortality was 0%, 1.5%, and 14.3%, respectively ($P = 0.02$).

We sought to further understand the role of IOF administration in the context of variables that could possibly affect outcomes. We conducted univariate analyses of 16 perioperative variables, using as dependent variables four perioperative outcomes: length of stay, Clavien–Dindo classification, number of complications per patient, and 30-day mortality, Table III. The following variables were significant with at least one of the four outcomes variables: age, CAD, ASA score, chronic obstructive pulmonary disease (COPD)/obstructive sleep apnea (OSA)/asthma, epidural analgesia, estimated blood loss, gender, IOF rate, operative time, and preoperative serum albumin level. Of note, three variables were significant for all four outcomes variables: estimated blood loss, IOF rate, and preoperative serum albumin level, with estimated blood loss as the most significant variable. We then conducted four separate multivariate logistic regression analyses using the same four outcomes variables, Table IV. IOF rate significantly correlated with two of four outcomes variables (number of complications per patient and 30-day mortality). Estimated blood loss significantly correlated with three of four variables (length of stay, Clavien grade, and complications per patient). Several other variables were significant for at least one of the four outcomes variables, including age, ASA score, CAD, COPD/OSA/asthma, and preoperative serum albumin level.

TABLE I. Demographics of the Patient Cohort

N	124
Mean age, years (SD)	64.5 (13.3)
Number female (%)	65 (52.4)
Past medical history (%)	
Coronary artery disease	19 (15.3)
Chronic obstructive pulmonary disease, asthma, obstructive sleep apnea	21 (16.9)
Diabetes mellitus	44 (35.5)
Smoking	28 (22.6)
Diagnosis of pancreatic adenocarcinoma (%)	59 (47.6)
Mean co-morbidity index, ASA score (SD)	2.4 (0.6)
Mean preoperative weight, kg (SD)	75.8 (15.0)
Mean preoperative serum albumin, g/dL (SD)	3.44 (0.65)

TABLE II. Perioperative Outcomes of the Patient Cohort

N	124
Median intraoperative fluid rate, ml/kg/hr (range)	13.95 (7.02–38.56)
Mean operative time, min (SD)	445 (118)
Mean estimated blood loss, ml (SD)	909 (910)
Intraoperative transfusion (%)	52 (41.9)
Postoperative transfusion (%)	20 (16.1)
Median length of stay, days (range)	9 (4–68)
Clavien–Dindo classification at 90 days, N (%)	
Clavien 0	40 (32.2)
Clavien 1–2	47 (37.9)
Clavien 3–5	37 (29.8)
Mean Clavien–Dindo classification at 90 days (SD)	1.8 (1.7)
30-day mortality (%)	8 (6.5)
By intraoperative fluid rate:	
0–10 ml/kg/hr, N = 9	0 (0)
10–15 ml/kg/hr, N = 66	1 (1.5)
>15 ml/kg/hr, N = 49	7* (14.3)
Mean complications per patient (SD)	1.4 (1.8)

*$P = 0.02$ in comparison to the 0–10 and 10–15 ml/kg/hr groups.

Blood loss and IOF are intimately related, as the former is usually treated with volume administration, and this complicates the ability to discern the effects of either of these variables on outcomes. In an attempt to separate the effects of blood loss from those of IOF, we examined the relationship of IOF rate in a subgroup of patients in which the top quartile of patients who experienced the greatest blood loss was removed. We performed separate multivariate analyses in patients below the 75th percentile of blood loss ($\leq$900 ml), Table V. We found that IOF rate remained significant with one outcomes variable (30-day mortality). Blood loss, however, remained significant for the same three outcomes variables (length of stay, Clavien grade, and complications per patient).

To examine the correlation of IOF with specific complications, we examined the complication profile of this cohort stratified by median IOF rate (13.95 ml/kg/hr; Table VI). Patients in the >13.95 ml/kg/hr group experienced more pulmonary, gastrointestinal, and infectious complications. In particular, these patients experienced more instances of hypoxia/respiratory failure ($P < 0.050$), delayed gastric emptying ($P < 0.050$), and sepsis ($P < 0.050$). Interestingly, this is a complication profile that is typically associated with volume overload, including delayed gastric emptying [7–9].

Preoperative Albumin Stratification

Patients with a low preoperative serum albumin ($\leq$3.0 g/dl, N = 27) were compared to those with a preoperative serum albumin of >3.0 g/dl (N = 97). Not surprisingly, patients in the $\leq$3.0 g/dl group experienced longer median lengths of stay ($P < 0.05$) and more severe complications ($P = 0.01$). When patients with a preoperative serum albumin of $\leq$3.0 g/dl were then stratified into two subgroups by median IOF rate (median 15.12 ml/kg/hr), mean estimated blood loss and length of stay were not significantly different between groups, but complication severity score was greater in the > 15.12 ml/kg/hr group ($P < 0.05$). When patients with a preoperative serum albumin of >3.0 g/dl were stratified similarly by their median IOF rate (median 13.64 ml/kg./hr), there was a difference in mean estimated blood loss ($P < 0.05$) but not in complication severity score ($P = 0.30$; Table VII).

DISCUSSION

Perioperative fluid administration in major abdominal surgery, particularly gastrointestinal surgery, is undergoing a fundamental change, as previous dogma supporting liberal fluid administration practices has been challenged. Indeed, Level 1 evidence now exists supporting the use of "restricted" fluid administration practices to reduce perioperative morbidity. Yet, for the most part, these studies have applied to patients undergoing colorectal surgery, with patients undergoing PD only comprising a subset of one of these studies. Thus, it remains an open question as to whether these findings apply to patients undergoing PD.

The relationship of perioperative intravenous fluids to PD has been controversial. Three studies have focused specifically on PD; however, it is somewhat difficult to compare their results due to differences in study design. Jarnagin et al. found a significant association, but this study was a randomized prospective trial not designed specifically to study the relationship of IOF to perioperative outcomes, and this association was found on retrospective analysis of the data [11]. Furthermore, the use of acute normovolemic hemodilution introduced an entirely different physiology, thus also limiting the interpretation of this study in the general patient population. This is very different than the studies of both Melis and Brennan, which were retrospective analyses of the relationship of intra-operative fluids to outcomes in patients undergoing PD. Both of these studies failed to find a significant relationship of IOF to patient outcomes [12,13]. One limitation acknowledged by these authors was that IOF are determined by the length of surgery and

TABLE III. Univariate Analyses of Perioperative Variables on Outcomes; Calculated *P*-Values Are Shown

	Length of stay	Clavien–Dindo classification	Complications per patient	30-day mortality
Age	0.11	<0.01	<0.001	0.58
CAD	0.02	0.18	0.02	0.01
Cancer	0.95	0.52	0.52	0.87
Co-morbidity index (ASA)	0.10	<0.01	<0.0001	0.04
COPD/OSA/asthma	0.72	0.09	<0.01	0.11
DM	0.47	0.84	0.18	0.12
Epidural analgesia	0.49	0.54	0.02	0.24
Estimated blood loss	<0.0001	<0.0001	<0.0001	0.01
Gender	0.29	0.07	<0.001	0.13
Intraoperative fluid rate	0.03	<0.001	<0.0001	<0.01
Operative time	0.04	<0.01	<0.001	0.42
Pancreatic adenocarcinoma	0.95	0.63	0.26	0.16
Preoperative serum albumin	0.02	<0.01	<0.0001	0.02
Preoperative weight	0.75	0.51	0.77	0.71
Smoking	0.18	0.47	0.88	0.08
Vascular resection	0.53	0.12	0.37	0.91

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea; DM, diabetes mellitus.

TABLE IV. Multivariate Analyses of Perioperative Variables on Outcomes; Statistically Significant *P*-Values ($P < 0.05$) Are Shown

	Length of stay	Clavien–Dindo classification	Complications per patient	30-day mortality
Age	—	<0.01	<0.01	—
CAD	—	—	—	0.04
Co-morbidity index (ASA)	—	—	0.04	—
COPD/OSA/asthma	—	0.02	<0.01	—
Estimated blood loss	<0.01	<0.0001	0.03	—
Intraoperative fluid rate	—	—	0.04	<0.01
Preoperative serum albumin	—	<0.01	—	—

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea.

estimated blood loss; thus, these variables would need to be controlled for in a prospective randomized study to really determine if different IOF regimens can impact perioperative outcomes. We sought to minimize this limitation by comparing IOF *rates* that control for patient weight and operative time differences.

In our cohort, both operative time and blood loss were greater, which may explain why we found a significant correlation between IOF and outcomes compared to prior studies. Moreover, patients undergoing PD at our institution are not managed by the same team of anesthesiologists, and, as a result, anesthetic fluid practices are much more heterogeneous. This intimate association of IOF and blood loss was further illustrated in our univariate and multivariate analyses of IOF volume on perioperative outcomes. Both IOF and blood loss significantly correlated with all four measured perioperative outcomes on univariate analysis, and both variables remained significantly correlated with at least one perioperative outcome on multivariate analyses of both the entire cohort and in the patient group below the 75th percentile of blood loss.

Red blood cell transfusions have been associated with worse perioperative outcomes in surgery for multiple cancer types, but these have mostly been attributed to infectious complications, presumably due to the immunosuppressive effects of allogenic blood that is leukocyte rich [15–18]. Consistent with this, we found that infectious complications were more frequent in patients who received more IOF. Despite this, these patients also experienced more pulmonary and gastrointestinal complications, which is more consistent with complications related to volume overload in prior studies [8,9,19]. Nonetheless, it is likely that the worse perioperative outcomes we observed in patients receiving more intravenous fluids is in part related to the negative effects of transfusions that go beyond their contribution to total perioperative volume administered. Separating the negative effects of transfusions as a form of volume replacement from other negative effects such as immunosuppression is difficult and is one of the limitations of this retrospective study.

The contribution of transfusions to perioperative fluid volume administered is not negligible in PD and therefore needs to be included in this type of analysis. In our study, 41.1% of patients received at least one unit of blood intraoperatively. In support of this is the study by Jarnagin et al., in which the primary endpoint was a reduction in allogenic red blood cell transfusions [11]. This study was powered to detect a decrease in red blood cell transfusions from 50% to 25%. The endpoint, though, was not reached, as they reported similar transfusion rates between ANH (16.9%) and control groups (18.5%). However, the ANH group received a significantly greater crystalloid volume, and this was associated with significantly greater complications related to the pancreatic anastomosis and a trend towards more severe complications. Moreover, in our preoperative serum albumin stratification, we found that among patients with a low serum albumin (≤3.0 g/dl), blood loss was not significantly different between the two groups stratified by median IOF rate, yet the median complication severity score was significantly higher in the group receiving more IOF. In addition, in our group of patients with a serum albumin >3.0 g/dl, blood loss was significantly greater in the group that received a higher IOF rate, yet length of stay and severity of complications were not.

The optimal fluid administration regimen in PD has yet to be determined. Anesthetic guidelines recommend IOF rates of 10–15 ml/kg/hr [2–4]. Prospective randomized trials that have demonstrated improved perioperative outcomes with fluid restriction have used variable regimens of fluid restriction ranging from 0 to 4 ml/kg/hr [8,9]. Currently, prospective randomized trials of restrictive versus liberal perioperative fluid management in patients undergoing PD are underway at Memorial Sloan-Kettering Cancer Center (NCT01058746) and Thomas Jefferson University (NCT01428050). These trials will certainly provide important information on the optimal intravenous fluid rate to be administered intraoperatively.

Maintaining a state of zero fluid balance has been advocated by the studies of Lobo et al. and Brandstrup et al. rather than either fluid restriction or fluid overload [8,19,20]. More recently, the concept of providing an optimal intravenous fluid rate in ml/kg/hr has been challenged in favor of administering fluid based on hemodynamic parameters measured by intraoperative transesophageal Doppler ultrasound. The supposed advantage of such a technique is it provides an amount of intravenous fluid customized to the individual

TABLE V. Multivariate Analyses of Perioperative Variables on Outcomes in Patients Below the 75th Percentile of Blood Loss (≤900 ml); Statistically Significant *P*-Values ($P < 0.05$) Are Shown

	Length of stay	Clavien–Dindo classification	Complications per patient	30-day mortality
Age	—	—	<0.01	—
CAD	—	—	—	—
Co-morbidity index (ASA)	—	<0.01	—	—
COPD/OSA/asthma	—	—	<0.0001	—
Estimated blood loss	<0.001	0.02	0.02	—
Intraoperative fluid rate	—	—	—	0.01
Preoperative serum albumin	—	0.04	0.02	—

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea.

TABLE VI. Summary of Complications in Patient Groups Divided by Median Intraoperative Fluid Rate, ml/kg/hr

	<13.95	>13.95	*P*-value
Number of patients	62	62	
Cardiovascular (%)	8 (12.9)	13 (20.1)	0.23
Arrhythmia	3	3	
Cardiac arrest	1	3	
Deep venous thrombosis	1	—	
Disseminated intravascular coagulation	—	1	
Hepatic artery pseudoaneurysm	1	2	
Venous thrombosis (portal vein, hepatic vein)	1	1	
Heparin-induced thrombocytopenia	1	—	
Myocardial infarction	—	3	
Pulmonary (%)	3 (4.8)	18 (29.0)	<0.01
Hypoxia or respiratory failure	2	9	<0.05
Pneumonia	—	6	
Pulmonary embolism	1	3	
Gastrointestinal (%)	19 (30.6)	33 (53.2)	0.01
Anastomotic leak (gastrojejunostomy)	1	1	
Abscess	2	4	
Colocutaneous fistula	—	1	
Delayed gastric emptying	5	13	<0.05
Diarrhea	2	3	
Gastrointestinal tract bleeding	3	3	
Ileus	2	3	
Intra-abdominal fluid collection (sterile)	2	—	
Intra-abdominal hemorrhage/hematoma (not from pancreas)	2	1	
Ischemic colitis	—	1	
Mesenteric ischemia	—	1	
Small bowel obstruction	—	1	
Small bowel perforation	—	1	
Liver (%)	2 (3.2)	4 (6.5)	0.40
Bile leak	2	3	
Liver dysfunction	—	1	
Pancreas (%)	9 (14.5)	11 (17.7)	0.80
Anastomotic leak/abscess/fistula	6	8	
Hemorrhage/hematoma	3	3	
Other infections (%)	16 (25.8)	21 (33.9)	0.33
Sepsis	3	11	<0.05
From pancreatic leak	1	3	
Catheter-related infection	1	—	
Clostridium difficile colitis	2	2	
Urinary tract infection	2	5	
Wound infection/dehiscence	8	3	0.11
Miscellaneous (%)	4 (6.5)	5 (8.1)	0.73
Altered mental status	4	5	
Mortality at 30 days	—	8	<0.01
Mortality at 90 days	3	2	
Total	64	115	
Complications per patient	1.03	1.86	

TABLE VII. Patients Stratified by Preoperative Serum Albumin Level, With Subgroups Divided by Median Intraoperative Fluid Rate (ml/kg/hr) of Each Group

			P-value
Albumin ≤ 3.0 g/dl, N = 27			
Intraoperative fluid volume, ml/kg/hr	**≤15.12**	**>15.12**	
Mean estimated blood loss, ml	761	1,512	0.14
Median length of stay, days	10	12	0.47
Mean Clavien–Dindo classification at 90 days	1.8	3.6	**<0.05**
Mean preoperative serum albumin, g/dl	2.5	2.4	0.43
Albumin > 3.0 g/dl, N = 97			
Intraoperative fluid rate, ml/kg/hr	**≤13.64**	**>13.64**	
Mean estimated blood loss, ml	656	1,020	**<0.05**
Median length of stay, days	8	9	0.31
Mean Clavien–Dindo classification at 90 days	1.4	1.7	0.27
Mean preoperative serum albumin, g/dl	3.7	3.7	0.43

Note that the median intraoperative fluid rates were determined separately for each cohort and are therefore different.

patient's physiology. This technique was evaluated in a randomized trial in colorectal surgery patients, in which the control group received fluids per the anesthesiologist's discretion, while the experimental group received them according to hemodynamic measurements by Doppler ultrasound. The experimental group was associated with a decreased length of stay and fewer immediate or major complications [21]. Urine output, in the setting of normal renal function, is a useful marker of intraoperative volume status and much less expensive and complicated than using transesophageal Doppler. It would be interesting to see if future methodologies could compare the two in their ability to assess volume status and guide IOF management.

Our albumin stratification analysis provided more insight into the population of patients particularly affected by fluid overload in PD. We found that patients with a preoperative serum albumin level ≤3.0 g/dl clearly experienced more severe complications in conjunction with greater fluid rates, whereas patients with an albumin of >3.0 g/dl did not. This suggests a greater sensitivity to increased fluid administration rates in such patients. Given that patients undergoing PD are often hypoalbuminemic (41.9% of our patients had a preoperative serum albumin of <3.5 g/dl), our data suggest that particular efforts should be made to avoid fluid overload in this group of patients.

The limitations of this study include its retrospective design and small cohort of patients. Due to the nature of this study, we were unable to control for intimately related variables to IOF such as estimated blood loss. In addition, we were unable to collect reliable data regarding total perioperative fluid administration, which would provide further insight into the relationship of fluid administration and outcomes in PD.

CONCLUSION

Our findings indicate that increased IOF administration is associated with worse perioperative outcomes in PD, but we cannot conclude that it is the sole cause of these adverse outcomes. Most importantly, this study substantiates the need for further clinical investigation in randomized studies to determine if this relationship is causal and not merely a correlation that is indirectly related to the association of other more impactful variables, such as blood loss. As of now, the two prior retrospective analyses examining this relationship of IOF to outcomes in PD (Melis et al., Brennan et al.) do not support such studies. The goal of these studies should be to determine if morbidity and mortality in PD can be reduced with a perioperative fluid regimen that attempts to achieve a zero fluid balance. How that goal is achieved (either by lower perioperative fluid rates or by the administration of fluid guided by physiologic measurements) will need to be determined by future clinical investigations. Such investigations are needed, as surgical morbidity in PD remains high even in high volume centers.

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