

# Comparison of intraoperative basal fluid requirements in distal pancreatectomy: Laparotomy vs. laparoscopy

## A retrospective cohort study

Ji-Won Han, MD<sup>a</sup>, Ah-Young Oh, MD, PhD<sup>a,b,\*</sup>, Kwang-Suk Seo, MD, PhD<sup>c</sup>, Hyo-Seok Na, MD, PhD<sup>a</sup>, Bon Wook Koo, MD, PhD<sup>a</sup>, Yea Ji Lee, MD<sup>a</sup>

### Abstract

There has been recent progress in intraoperative fluid therapy. However, little is known about intraoperative fluid therapy in laparoscopic surgery. The purpose of this study is to determine whether there are differences in the basal fluid requirements during surgery between laparotomy and laparoscopic distal pancreatectomy.

This retrospective cohort study analyzed the electronic medical records of 253 patients who underwent distal pancreatectomy via either laparotomy (73 patients) or laparoscopy (180 patients) between June 2006 and March 2016. The volume of intraoperative fluid administered, postoperative complications, length of hospital stay, and readmission rate were evaluated. The total volume of fluids was calculated as the sum of the volume of crystalloid plus the volume of colloid multiplied by 1.5 or 2.0.

Patients who had laparotomy were older and had higher American Society of Anesthesiologists classes. Anesthesia time was longer and estimated blood loss was larger in laparotomy. More colloid (1.8 mL/kg per h vs. 1.2 mL/kg per h,  $P < .001$ ) and more total calculated fluid (1.5 times: 11.7 mL/kg per h vs. 10.6 mL/kg per h,  $P = .002$ ; 2.0 times: 12.6 mL/kg per h vs. 11.2 mL/kg per h,  $P = .001$ ) were infused in laparotomy. Crystalloid (9.0 mL/kg per h vs. 8.9 mL/kg per h,  $P = .203$ ) did not show significant difference. Postoperative complications were more frequent (63% vs. 45%,  $P = .008$ ), the hospital stay was longer (18 days vs. 13.4 days,  $P < .001$ ), and readmission rate was higher (15% vs. 5.6%,  $P = .02$ ) in laparotomy. By logistic regression analysis, we could find that operation type (laparotomy vs. laparoscopy, odds ratio 1.900, 95% confidence interval 1.072–3.368) and operation time ( $P = .004$ ) had effect on complications.

In patients undergoing distal pancreatectomy, basal fluid requirements were larger in laparotomy compared with laparoscopy. Operation time and estimated blood loss had effects on fluid administration. Postoperative complications were more frequent in laparotomy but we could not find relationships with infused colloid or total calculated fluid volumes. Operation type (laparotomy vs. laparoscopy) and operation time were the only related factors to postoperative complications.

**Abbreviations:** ASA = American Society of Anesthesiologists, EBL = estimated blood loss, Hb = hemoglobin, HES = hydroxyethyl starch, IV = intravenous,  $r_s$  = Spearman correlation coefficient.

**Keywords:** distal pancreatectomy, fluid therapy, laparoscopic surgery

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<sup>a</sup> Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, Seongnam-si, Gyeonggi-do, <sup>b</sup> Department of Anesthesiology and Pain Medicine, Seoul National University College of Medicine, <sup>c</sup> Department of Dental Anesthesiology, Seoul National University School of Dentistry, Seoul, Republic of Korea.

\* Correspondence: Ah-Young Oh, Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, 82, Gumi-ro 173 beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do, Republic of Korea (e-mail: oay1@snuhb.org).

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## 1. Introduction

Adequate intraoperative fluid management is an essential determinant of the surgical outcome and patient prognosis. Insufficient intraoperative fluid infusion leads to tissue hypoperfusion, leading to major organ damage, such as acute kidney injury.<sup>[1]</sup> Excessive fluid infusion can lead to postoperative complications such as anastomotic leakage, wound dehiscence, wound infection, and pulmonary edema, especially in major abdominal surgery.<sup>[2]</sup> However, the fluid requirements are dynamic, with great interindividual variability, making it difficult to adjust the volumes administered with sufficient accuracy. And there has been recent progress in intraoperative fluid therapy.

The total fluid requirements include the preoperative deficit due to fasting and bowel preparation, intraoperative blood loss, urine output, redistribution due to anesthetic drugs, and inflammation and insensible loss. Conventional concepts of the insensible loss are that additional fluid administration is required at 2 to 6 mL/kg per min depending on the degree of the surgical procedure.<sup>[3,4]</sup> However, the new concept is that the insensible loss is at most 1 mL/kg per h in major abdominal surgery with

maximal bowel exposure.<sup>[5,6]</sup> The concept of context sensitivity has been introduced in fluid volume kinetics, and individualized delicate titration of fluid volume to avoid both over- and under-hydration is now recommended, instead of administering a fixed calculated volume of fluid.<sup>[7,8]</sup>

Laparoscopic surgery has become a standard form of surgery, with rapid recovery, less postoperative pain, and shorter hospital stays. Despite the increasing indications for, and the use of, laparoscopic surgery, there are no established principles for fluid management in laparoscopic surgery. The evaporative fluid loss during laparoscopic surgery is believed to be less than that during laparotomy, which has more exteriorized viscera. However, effect of insufflating dry air into the abdomen on fluid loss is not clear and the basal fluid requirements during laparoscopic surgery are unknown.<sup>[8]</sup>

This study retrospectively reviewed the volume of fluid administered during laparotomy and laparoscopic distal pancreatectomy to determine whether there are differences in the basal fluid requirements during surgery between the 2 surgical methods.

## 2. Materials and methods

This retrospective cohort study was approved by the local ethics committee on August 21, 2015 (Institutional Review Board of Seoul National University Bundang Hospital, Healthcare innovation park, 172 Dolma-ro, Bundang-gu, Seongam-si, Gyeonggi-do, Republic of Korea, Chairperson Professor Hak-Chul Jang, application number B-1508-312-102) and the need for informed consent was waived. The study protocol was registered at [clinicaltrials.gov](http://clinicaltrials.gov) (registration number: NCT03060408). The study was based on a retrospective review and analysis of the electronic medical records of patients who underwent distal pancreatectomy at Seoul National University Bundang Hospital between June 2006 and March 2016. The patients who had intraoperative transfusions, underwent another operation at the same time, did not undergo the intended operation, classified as American Society of Anesthesiologists (ASA) physical status 4 or more were excluded. Data were collected on age, sex, weight, height, ASA physical status, preoperative and postoperative hemoglobin (Hb) levels, durations of surgery and anesthesia, volumes of crystalloid and colloid infused intraoperatively, intraoperative transfusion, urine output, and estimated blood loss (EBL). Postoperative complications, length of hospital stay, and readmission within 6 months were also evaluated.

The primary outcome variable was the total volume of fluid infused intraoperatively, which was calculated as the sum of the volume of crystalloid plus the volume of colloid multiplied by 1.5 or 2.0.<sup>[9,10]</sup> This was based on the revised Starling equation and the glycocalyx model paradigm. According to the theory, 1.5 to 2.0 times volume of crystalloid is needed to obtain a similar volume effect of colloid.<sup>[7,10,11]</sup> The calculated value divided by the patient's weight and operation time was compared between the groups. Secondary outcome variables were postoperative complications, length of hospital stay, and rate of readmission. Surgical complications were graded in severity from 1 to 5 using a modified Dindo-Clavien classification: Grade 1 is minor-risk events not requiring pharmacological treatment; Grade 2 requires pharmacological treatment; Grade 3 requires a surgical, endoscopic, or radiological intervention, and is subdivided into 3A if not under general anesthesia and 3B if under general anesthesia; Grade 4 is a life-threatening complication; and Grade 5 results in death.<sup>[12]</sup>

Anesthetic management followed our routine practice. Invasive arterial pressure monitoring was used in all patients, in addition to routine monitoring with an electrocardiogram, pulse oximetry, noninvasive blood pressure, body temperature, end-tidal CO<sub>2</sub> concentration, and urine output. Anesthesia was induced with intravenous (IV) propofol, remifentanyl, and rocuronium and maintained with inhaled sevoflurane in addition to IV remifentanyl and rocuronium. Intraoperative management of fluid administration followed our institutional guidelines and decisions were made by the anesthesiologist in charge. The guidelines for intraoperative fluid management in our institution involve administering fluid based on the EBL and the patient's volume status, as comprehensively determined by the vital signs (blood pressure and heart rate), shape of the invasive arterial pressure waveform, and amount and color of urine output. Hydroxyethyl starch (HES) 6% 130/0.4 (Voluven or Volulyte, Fresenius Kabi AG, Bad Homburg, Germany) was used for colloid replacement.

## 3. Statistical analysis

SPSS was used for the statistical analyses. All data are presented as the mean (standard deviation) or number (% incidence). For continuous variables, Kolmogorov–Smirnov test and Shapiro–Wilk test were done to check the distribution condition. For variables showing normal distribution, Levene test of equality and Student *t* test were used and for those showing abnormal distribution, Mann–Whitney *U* test was used. For categorical variables, chi-squared test and Fischer exact test were used. Spearman correlation analysis was performed to identify factors associated with the volume of fluid administered. To determine the causes of complications, we divided the patients into 2 groups with and without complications and compared the possible variables using the Student *t* test, Mann–Whitney *U* test, chi-squared test, and Fischer exact test, as appropriate. To exclude the effect of confounding variables, we also performed logistic regression analysis of the factors with  $P < .1$ .

## 4. Results

The records of 301 consecutive patients who underwent distal pancreatectomy under general anesthesia between June 2006 and March 2016 were retrieved: 106 patients underwent laparotomy and 195 underwent laparoscopic surgery. The 34 patients who had intraoperative transfusions were excluded. More patients in the laparotomy group received intraoperative transfusions (23.6% vs. 4.6%,  $P < .001$ ). We also excluded 13 patients who underwent another operation at the same time and 1 patient classified as ASA physical status 4. As a result, 253 patients (73 laparotomy and 180 laparoscopic surgeries) were evaluated (Fig. 1).

Some of the patient characteristics differed significantly according to laparotomy versus laparoscopic surgery. The patients who underwent laparotomy tended to be older, included a higher proportion of males, weighed less, and had higher ASA physical status scores compared with those undergoing laparoscopic surgery (Table 1).

Table 2 summarizes the outcome variables related to intraoperative fluid therapy. Both the operating and anesthesia times were about 30 min longer in the laparotomy group (260 min vs. 228 min,  $P = .005$ ; 303 min vs. 273 min,  $P = .010$ ). Though we excluded patients who had intraoperative transfusion, EBL during surgery was larger in laparotomy group (417

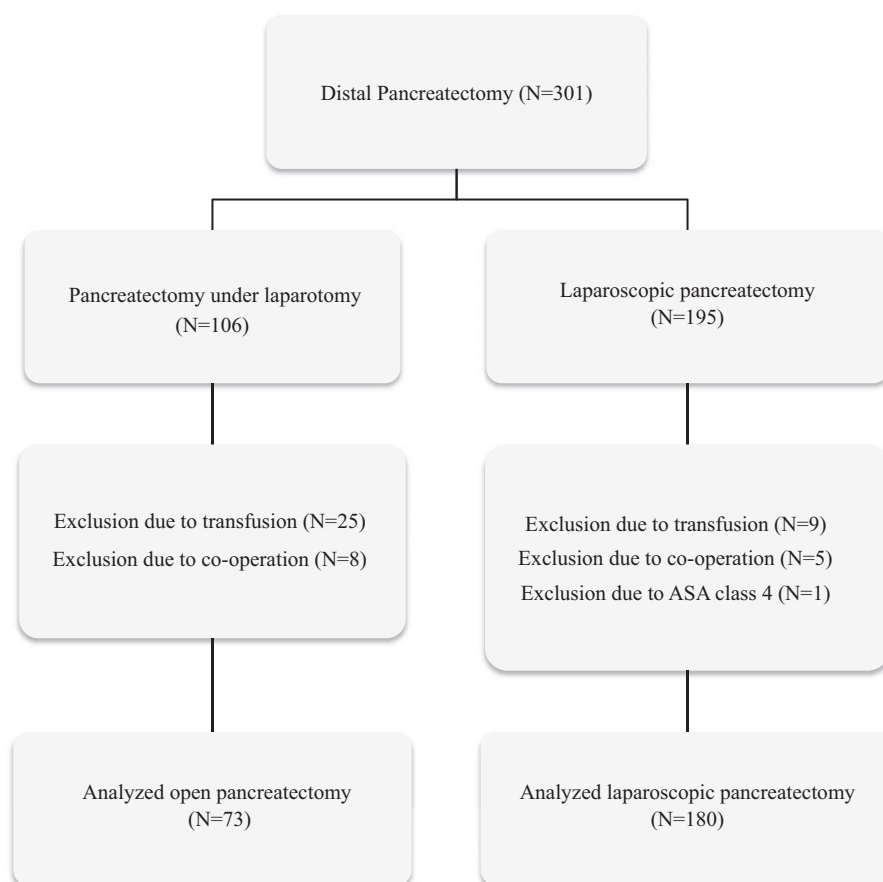


Figure 1. Patient flow diagram illustrates number of exclusion and analyzed data. ASA=American Society of Anesthesiologists.

mL vs. 320 mL,  $P < .001$ ). The infused volume of crystalloid (9.0 mL/kg per h vs. 8.9 mL/kg per h,  $P = .203$ ) did not show the difference between the groups but those of colloid (1.8 mL/kg per h vs. 1.2 mL/kg per h,  $P < .001$ ) and total calculated fluid (1.5 times: 11.7 mL/kg per h vs. 10.6 mL/kg per h,  $P = .002$ ; 2.0 times: 12.6 mL/kg per h vs. 11.2 mL/kg per h,  $P = .001$ ) were larger in laparotomy group compared with laparoscopic group.

For potential confounders for fluid administration, such as age, gender, ASA class, anesthesia time, preoperative Hb value, and

EBL, a Spearman correlation analysis ( $r_s$ , Spearman correlation coefficient) was done for the amount of crystalloid and colloid infused. Operation time ( $r_s = 0.381$ ,  $P < .001$ ) and EBL ( $r_s = 0.531$ ,  $P < .001$ ) had effects on colloid administered (Table 3).

Table 4 shows postoperative outcomes including the numbers and kinds of postoperative complications. Table 5 lists outcome variables with potential relationships to complications. To detect the variables related to complications, patients were divided into no complication and complications group. Patients with any degree of

**Table 1**  
Patients' characteristics.

	Laparotomy (N=73)	Laparoscopic (N=180)	P
Age, y	67 ± 13	58 ± 16	<.001
Gender			
Male	43 (58.9%)	68 (37.8%)	.003
Female	30 (41.1%)	112 (62.2%)	
Weight, kg	58 ± 9	62 ± 11	.017
Height, cm	161 ± 9	161 ± 8	.896
BMI, kg/m <sup>2</sup>	22.5 ± 3	23.9 ± 3	.002
ASA class			
I	16	78	<.001
II	50	98	
III	7	4	

The data are presented as mean ± standard deviation or number (%). ASA=American Society of Anesthesiologist, BMI=body mass index.

**Table 2**  
Outcome variables related to intraoperative fluid therapy.

	Laparotomy (N=73)	Laparoscopic (N=180)	P
Operation time, min	260 ± 94	228 ± 89	.005
Anesthesia time, min	303 ± 93	273 ± 89	.010
Estimated blood loss, mL	417 ± 347	320 ± 514	<.001
Urine output, mL	371 ± 283	226 ± 188	<.001
Total crystalloid, mL	2206 ± 1237	2018 ± 1665	.055
Total colloid, mL	475 ± 434	315 ± 509	.001
Crystalloid, mL/kg per h	9.0 ± 4.1	8.9 ± 5.9	.203
Colloid, mL/kg per h	1.8 ± 1.5	1.2 ± 1.7	<.001
Total fluids (1.5), mL/kg per h*	11.7 ± 4.6	10.6 ± 7.3	.002
Total fluids (2.0), mL/kg per h†	12.6 ± 4.9	11.2 ± 7.8	.001

The data are presented as mean ± standard deviation.

\* Total fluids (1.5)=[crystalloids (mL) + 1.5 × colloids (mL)]/body weight (kg)/operation time (h).

† Total fluids (2.0)=[crystalloids (mL) + 2.0 × colloids (mL)]/body weight (kg)/ operation time (h).

**Table 3****Effect of each variables on basal fluid requirements.**

	Crystalloid, mL/kg per h		Colloid, mL/kg per h	
	$r_s$	<i>P</i>	$r_s$	<i>P</i>
Age, y	0.143	.022	0.144	.022
Gender, M/F	0.040	.530	0.14	.831
ASA class (1/2/3)	0.078	.214	0.088	.165
Operation time, min	0.040	.523	0.381	<.001
Anesthesia time, min	0.137	.029	0.175	.005
Preoperative Hb, g/dL	-0.172	.044	-0.117	.063
EBL	0.476	<.001	0.531	<.001
Urine output, mL	0.106	.093	0.101	.111
Complication grade	0.045	.470	0.121	.055
Readmission	0.019	.763	0.024	.708

ASA=American Society of Anesthesiologists, EBL=estimated blood loss, Hb=hemoglobin,  $r_s$ =Spearman correlation coefficient.

postoperative complications were divided into complications group. Each variable was compared using the Student *t* test, Mann-Whitney *U* test, chi-squared test, and Fischer exact test, as appropriate (Table 5). To evaluate the effect on the postoperative complications, Backward stepwise (Wald) logistic regression analysis were done for factors showing fluid administration and with  $P < .1$ . That is, operation type (laparotomy vs. laparoscopy), age, gender, operation and anesthesia times, EBL, and colloid. No relationship was found between the volumes of infused colloid and postoperative complications. Among them, only operation type (laparotomy vs. laparoscopy, odds ratio 1.900, 95% confidence interval 1.072–3.368) and operation time ( $P = .004$ ) had effect on the postoperative complications (Table 6).

## 5. Discussion

In this retrospective cohort study of patients who underwent distal pancreatectomy, we found that the basal fluid requirements were larger in laparotomy compared with laparoscopy. However, the difference was not large and was only 1 to 2 mL/kg per h. The main difference was the colloid infused and crystalloid amount was not different.

We excluded the patients who had intraoperative transfusion because our concern was the basal fluid requirements. The transfusion rate was significantly higher in laparotomy group. Although we excluded the patients who had intraoperative

**Table 4****Postoperative outcome variables.**

	Laparotomy (N=73)	Laparoscopy (N=180)	<i>P</i>
Postoperative complications, total	46 (63%)	81 (45%)	.008
Grade 1	22 (30.1%)	49 (27.3%)	—
Grade 2	6 (8%)	7 (3.8%)	—
Grade 3A	14 (19.1%)	24 (13.3%)	—
Grade 3B	2 (2.7%)	1 (0.5%)	—
Grade 4	0	1 (0.5%)	—
Grade 5	2 (2.7%)	0	—
Admission date, d	18±9.4	13.4±7.5	<.001
Readmission	11 (15%)	10 (5.6%)	.02

Values are number of patients (%) or mean±standard deviation. Postoperative complications are classified by grade: Grade 1=minor risk events unnecessary pharmacological treatment, Grade 2=requiring pharmacological treatment, Grade 3=requiring surgical, endoscopic, and radiological intervention, Grade 3A=intervention not under general anesthesia, Grade 3B=intervention under general anesthesia, Grade 4=life-threatening complication, and Grade 5=result in death.

**Table 5****Effect of each variables on postoperative complications.**

	No complication (N=127)	Complication (N=126)	<i>P</i>
	Operation type: laparotomy/laparoscopy	27/100	46/80
Age, y	59±16	64±14	.036
Gender, male/female	47/80	64/62	.031
Weight, kg	61±11	61±10	.335
Height, cm	161±8	161±9	.831
BMI, kg/m <sup>2</sup>	23.4±3	23.6±3	.647
ASA class (1/2/3)	53/69/5	41/79/6	.336
Operation time, min	219±79	257±99	.002
Anesthesia time, min	263±80	301±98	.002
Preoperative Hb, g/dL	13.4±1.3	13.6±1.6	.555
EBL, mL	340±598	357±300	.008
Urine output, mL	256±235	277±221	.300
Crystalloid, mL/kg per h	9.1±5.3	8.7±5.6	.175
Colloid, mL/kg per h	1.2±1.8	1.5±1.5	.032
Total fluid (1.5), mL/kg per h*	11.0±6.8	10.9±6.4	.794
Total fluid (2.0), mL/kg per h†	11.5±7.4	11.6±6.8	.541
Admission date, d	11.2±3.7	18.3±10.1	<.001

Patients with any degree of postoperative complications are divided into complications group. The data are presented as the mean±standard deviation or number of patients.

ASA=American Society of Anesthesiologists, BMI=body mass index, EBL=estimated blood loss, Hb=hemoglobin.

\* Total fluids (1.5)=[crystalloids (mL) + 1.5 × colloids (mL)]/body weight (kg)/operation time (h).

† Total fluids (2.0)=[crystalloids (mL) + 2.0 × colloids (mL)]/body weight (kg)/operation time (h).

transfusion, EBL was still larger in laparotomy group and correlation analysis showed that EBL had a significant effect on the fluid requirement. The patients who underwent laparotomy tended to be older, included a higher proportion of males, and had higher ASA physical status scores compared with those undergoing laparoscopic surgery. However, correlation analysis showed that the effect of these factors on the fluid requirement was minimal. Operation time and EBL had effect on fluid administration.

We calculated the total fluid volume as sum of the volume of crystalloid plus the volume of colloid multiplied by 1.5 or 2.0. This differs from the previous concept of crystalloid spreading through the extracellular space and needing 3 to 4 times the volume to have a similar volume effect to colloid. This was based on the revised Starling equation and the glycocalyx model paradigm.<sup>17</sup> The endothelial glycocalyx layer is known to have a

**Table 6****Backward stepwise (Wald) logistic regression of individual factors on the postoperative complications.**

	$\beta$ (SE)	Wald	<i>P</i>	OR (95% CI)
<b>Step 1</b>				
Operation type: laparotomy	0.472 (0.307)	2.358	.125	1.603 (0.878–2.926)
Age, y	0.014 (0.009)	2.357	.125	
Gender: male	0.289 (0.273)	1.122	.290	1.335 (0.782–2.279)
Operation time, min	0.005 (0.002)	7.490	.006	
EBL, mL	-0.001 (0)	1.165	.280	
Colloid, mL/kg per h	0.001 (0.002)	0.621	.431	
<b>Step 5 (last)</b>				
Operation type: laparotomy	0.642 (0.292)	4.833	.028	1.900 (1.072–3.368)
Operation time, min	0.004 (0.001)	8.437	.004	

For brevity, only the first and last step of the logistic regression was included.

CI=confidence interval, EBL=estimated blood loss, OR=odds ratio, SE=standard error.

semipermeable barrier function and infused crystalloid fluids do not spread through the extracellular volume, but mainly remain in the intravascular space. The fluid kinetics are context sensitive so it is difficult to know exact total volume needed. That is, when the patient is in hypovolemic status, more infused crystalloid remain in the intravascular space compared with euvolemic or hypervolemic status. To obtain a similar volume effect as colloid, 1.5 times volume of crystalloid is needed in a low-capillary-pressure situation but this should not exceed 2.0 times in euvolemic status.<sup>[7,10,11]</sup> We calculated total fluid volumes by multiplying colloid volume by 1.5 and 2.0 expecting the real volume to be between the 2 values.

The use of colloid is still controversial; the main concern is that it could result in renal damage.<sup>[13]</sup> However, this was mainly reported when large volumes of colloid are infused in critically ill patients. Recently, it is known that the origin of HES matters and in contrast to potato-derived HES, the most modern, 3rd generation, waxy maize-derived HES does not do harm to kidney. No evidence for renal dysfunction was observed after intraoperative use of waxy maize-derived HES in a meta-analysis of surgical patients.<sup>[14]</sup> Better resuscitation was reported with colloid compared with crystalloid in severely injured, hypovolemic patients.<sup>[11]</sup> The colloid used in our institution, Voluven or Volulyte, is waxy maize-derived HES and no patient had renal damage due to colloid. The EBL was larger and more colloid was infused in laparotomy group.

There is consensus about the importance of fluid management in major hepatobiliary surgery. The reason why we chose distal pancreatectomy was that it was the most in number among pancreas surgery. Liver surgery was excluded because it was mainly laparoscopic and laparotomy was very rare. Pancreatic resection is major abdominal surgery in which postoperative complications are common; the reported rate of complications is 38% to 59%.<sup>[15–17]</sup> The main reported complications are anastomotic leakage, wound or intra-abdominal infection, fistula formation, and intra-abdominal fluid collection, similar to our findings. In our study, the complication rate was similar to the previous report and was higher in laparotomy group compared with laparoscopy group. We investigated if total fluid amount, especially colloid amount had effect on the occurrence of complications but found that the effect of fluid or colloid was minimal. Operation time and the operation type (laparotomy vs. laparoscopy) were the most related factors in this study.

Many studies have compared liberal and restrictive intraoperative fluid administration in pancreas surgery and revealed that liberal fluid administration increased postoperative complications and prolonged hospital stays.<sup>[18–21]</sup> In these studies, the restricted regimen consisted of crystalloid infusion at 4 to 6 mL/kg per h versus 12 mL/kg per h for the liberal regimen.<sup>[18]</sup> The crystalloid infused in our study was between these 2 values in both groups. Although several studies have reported on fluid management in pancreatectomy, few have examined fluid management in laparoscopic pancreatectomy. In this retrospective analysis, we showed that EBL was smaller, less colloid and hence less total fluid is administered, and less postoperative complications developed in laparoscopic distal pancreatectomy surgery compared with laparotomy.

This study had several limitations. First, it was a retrospective study and could not control for all factors that might affect the fluid requirements. The type of surgery (i.e., laparotomy or laparoscopy) was determined by the patient's condition, so the demographics differed between the groups. The surgeons tended to choose laparotomy when the lesion seemed to be more complicated.

Hence, the laparotomies took longer and had more bleeding and also had more transfusion. The patients who underwent laparotomy were older, had a higher proportion of males, weighed less, and had higher ASA physical status scores compared with those undergoing laparoscopy. However, it is difficult to design a randomized-controlled study for this purpose and we could exclude the effects of these factors with the correlation analysis. Second, it was difficult to measure fluid requirement because there are so many factors affecting it and those were differed in each patients. The calculated total fluid amount is not a real but a virtual concept. However, we thought that it would better reflect the fluid amount than simple sum of crystalloid and colloid do.

## 6. Conclusion

In patients undergoing distal pancreatectomy, basal fluid requirements were larger in laparotomy compared with laparoscopy. Operation time and EBL had effects on fluid administration. Postoperative complications were more frequent in laparotomy but we could not find relationships with infused colloid or total calculated fluid volumes. Operation type (laparotomy vs. laparoscopy) and operation time were the only related factors to postoperative complications.

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