의학석사 학위논문

Comparison of intraoperative basal fluid requirements in distal pancreatectomy : laparotomy *vs.* laparoscopy

A retrospective cohort study

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의학과 마취통증의학

한 지 원

A thesis of the Degree of Master of Medical Science

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Comparison of intraoperative basal fluid requirements in distal pancreatectomy : laparotomy *vs.* laparoscopy

A retrospective cohort study

Directed by Ah-young Oh, M.D., Ph.D.

A thesis submitted to the Department of Anesthesiology in partial fulfillment of the requirement of the Degree of Master of Medical Science at Seoul National University College of Medicine

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Approved by Thesis Committee:

Professor _____ Chairman

Professor _____ Vice chairman

Professor _____

Abstract

Background: 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.

Methods: 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.

Results: More colloid was infused in laparotomy than in laparoscopy (1.5 ml/kg/h *vs*. 1.0 ml/kg/h, $P = 0.007$), while there were no significant differences in the volumes of crystalloid (7.6 ml/kg/h *vs*. 7.2 ml/kg/h, $P = 0.578$) or total fluids (1.5 times: 9.8 ml/kg/h *vs*. 8.7 ml/kg/h, $P = 0.136$; 2.0 times: 10.6 *vs*. 9.1 ml/kg/h, $P = 0.092$). The hospital stay was longer (18 day *vs*. 13.4 day, $P < 0.001$), and the rates of postoperative complications (63% *vs*. 45%, $P = 0.008$) and readmission (15% *vs*. 5.6%, $P = 0.02$) were higher in laparotomy.

Conclusions: In patients undergoing distal pancreatectomy, no significant difference was found in intraoperative basal fluid requirements between

laparotomy and laparoscopy.

Keywords: fluid therapy, laparoscopic surgery, distal pancreatectomy

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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.[1] Excessive fluid infusion can lead to postoperative complications such as anastomotic leakage, wound dehiscence, wound infection, and pulmonary edema, especially in major abdominal surgery.[2] However, the fluid requirements are dynamic, with great inter-individual 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 is that additional fluid administration is required at 2–6 mL/kg/min depending on the degree of the surgical procedure.[3,4] However, the new concept is that the insensible loss is at most 1 mL/kg/h in major abdominal surgery with maximal bowel exposure.[5,6] 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.[7,8]

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.[8]

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 two surgical methods.

MATERIALS AND METHODS

This retrospective cohort study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (Seongnam, Korea) and the need for informed consent was waived. The study protocol was registered at clinicaltrials.gov. (registration number: L2015932) 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 ASA physical status 4 or more were excluded. Data were collected on age, sex, weight, height, American Society of Anesthesiologists (ASA) physical status, pre- and postoperative hemoglobin levels, durations of surgery and anesthesia, volumes of crystalloid and colloid infused intraoperatively, intraoperative transfusion, urine output, and estimated blood loss. 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 intra-operatively, which was calculated as the sum of the volume of crystalloid plus the volume of colloid multiplied by 1.5 or 2.0.[9,10] This was based on the revised Starling equation and the glycocalyx model paradigm. According to the theory, 1.5 times volume of crystalloid is needed to obtain a similar volume effect of colloid.[10,19] The calculated value divided by the patient's weight and anesthesia

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.[11]

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_2 concentration, and urine output. Anesthesia was induced with intravenous (IV) propofol, remifentanil, and rocuronium and maintained with inhaled sevoflurane in addition to IV remifentanil 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 estimated blood loss 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.

Statistical analysis

SPSS was used for the statistical analyses. All data are presented as the mean (standard deviation) or number (% incidence). Patient characteristics and other clinical data were compared using the Student's *t*-test, chi-square test, and Fischer's exact test, as appropriate. All *P*-values were two-sided and were deemed to indicate statistical significance at $P = 0.05$. Correlation analysis was performed to identify factors associated with the volume of fluid administered. To determine the causes of complications after laparotomy and laparoscopic surgery, we divided the patients into two groups with and without complications and compared the possible variables using the Student's *t*-test, chi-square test, and Fischer's exact test, as appropriate. We also performed logistic regression analysis of the factors with $P < 0.1$ and those associated with fluid administration, such as the volumes of crystalloid, colloid, and total fluids per body weight and anesthesia time.

RESULTS

The records of 301 consecutive patients who underwent distal pancreatectomy under general anesthesia 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. We also excluded 13 patients who underwent another operation at the same time and one patient classified as ASA physical status 4. As a result, 253 patients (73 laparotomyand 180 laparoscopic surgeries) were evaluated (Figure 1).

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

Table 2 summarizes the outcome variables related to intraoperative fluid therapy. For those who were not transfused intraoperatively, no difference was found in the estimated blood loss during surgery (417 ml *vs*. 320 ml, $P = 0.143$). Both the operating and anesthesia times were about 30 min longer in the laparotomy group (260 min *vs*. 228 min, $P = 0.011$, 303 min *vs*. 273 min, $P = 0.018$).

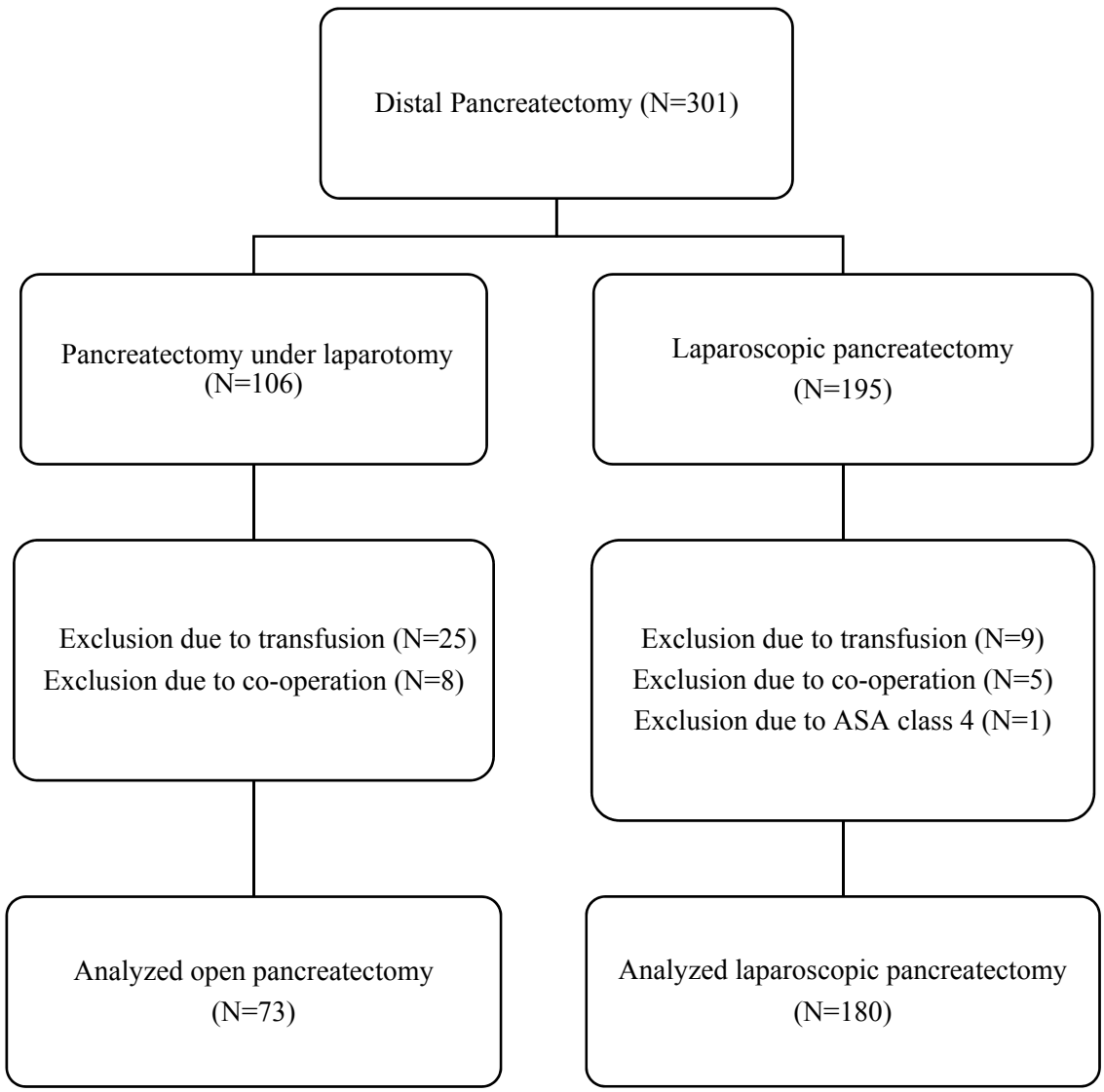
The volumes infused per body weight and per unit time were calculated, more colloid fluids were infused in the laparotomy group (1.5 ml/kg/h *vs*. 1.0 ml/kg/h, *P*

= 0.007), while no difference was found in the volumes of crystalloid (7.6 ml/kg/h *vs*. 7.2 ml/kg/h, $P = 0.578$) or total calculated fluids (1.5 Times: 9.8 ml/kg/h *vs*. 8.7 ml/kg/h, $P = 0.136$, 2.0 times: 10.6 ml/kg/h *vs*. 9.1 ml/kg/h, $P = 0.092$).

For potential confounders for fluid administration, such as age, gender, ASA class, surgeon, anesthesia time, preoperative hemoglobin value, and estimated blood loss, a correlation analysis was done for the total calculated fluid volume. Anesthesia time (1.5 times: Pearson coefficient 0.162, $P = 0.01$, 2 times: Pearson coefficient 0.187, $P = 0.003$) and estimated blood loss (1.5 times: Pearson coefficient 0.386, $P < 0.001$, 2 times: Pearson coefficient 0.416, $P < 0.001$) were the only factors related to the total calculated fluid volume. (Table 3)

Tables 4 and 6 list the numbers and kinds of postoperative complications, and Table 5 lists outcome variables with potential relationships to complications. Logistic regression analysis was done for operation type: laparotomy *vs*. laparoscopy, age, gender, operation and anesthesia times, crystalloid and colloid fluids per unit body weight and time, and calculated total fluids per unit body weight and time. No relationship was found between the volumes of infused fluid and complications. Operation type (laparotomy *vs*. laparoscopy, $P = 0.025$) and anesthesia time ($P = 0.002$) were related to complications.

Figure 1. Patient flow diagram illustrates number of exclusion and analyzed data.



ASA = American Society of Anesthesiologists

Table 1. Patient characteristics

	Laparotomy (N = 73)	**Laparoscopic (N = 180)**	***P* value**
Age (year)	67 (13)	58 (16)	< 0.001*
Gender (M/F)	43/30	68/112	0.003*
Weight (kg)	58(9)	62 (11)	0.017*
Height (cm)	161 (9)	161 (8)	0.896
BMI (kg/m^2)	22.5 (3)	23.9 (3)	0.002*
ASA class (1/2/3)	16/50/7	78/98/4	< 0.001

The data are presented as the mean (standard deviation) or number of patients.

**P* value < 0.05, BMI = Body mass index, ASA = American Society of Anesthesiologist

Table 2. Outcome variables related to intraoperative fluid therapy.

	Laparotomy (N=73)	**Laparoscopic (N=180)**	***P* value**
Operation time (min)	260 (94)	228 (89)	0.011*
Anesthesia time (min)	303 (93)	273 (89)	0.018*
Estimated blood loss (ml)	417 (347)	320 (514)	0.143
Urine output (ml)	371 (283)	226 (188)	< 0.001*
Crystalloid per weight and anesthesia time (ml/kg/h)	7.6 (3.5)	7.2 (4.7)	0.578
Colloid per weight and anesthesia time (ml/kg/h)	1.5 (1.3)	1.0 (1.5)	0.007*
Total fluids(1.5) per weight and anesthesia time (ml/kg/h)†	9.8 (4.0)	8.7 (6.1)	0.136
Total fluids(2.0) per weight and anesthesia time (ml/kg/h)‡	10.6 (4.2)	9.1 (6.6)	0.092

The data are presented as the mean (standard deviation). **P* value < 0.05

†Total fluids (1.5) = [crystalloids (ml) + 1.5 x colloids (ml)]/body weight (kg)/anesthesia time (hour), ‡Total fluids (2.0) = [crystalloids (ml) + 2.0 x colloids (ml)]/body weight (kg)/anesthesia time (hour).

Table 3. Potential confounders for fluid administration

	Total fluids(1.5) per weight and anesthesia time (ml/kg/hr)†		Total fluids(2.0) per weight and anesthesia time (ml/kg/hr) ‡	
	Pearson coefficient	***P* value**	**Pearson coefficient**	***P* value**
Age	0.06	0.340	0.059	0.354
Gender	0.071	0.263	0.057	0.364
ASA class	-0.038	0.551	-0.030	0.636
Surgeon	0.028	0.654	0.044	0.485
Anesthesia time	0.162	0.010*	0.187	0.003*
Preoperative Hemoglobin	-0.076	0.228	-0.073	0.248
Estimated blood loss	0.386	<0.001*	0.416	<0.001*

ASA = American Society of Anesthesiologists **P* value < 0.05

†Total fluids (1.5) = [crystalloids (ml) + 1.5 x colloids (ml)]/body weight (kg)/anesthesia time (hour), ‡Total fluids (2.0) = [crystalloids (ml) + 2.0 x colloids (ml)]/body weight (kg)/anesthesia time (hour).

Table 4. Postoperative outcome variables

	Laparotomy(N=73)	Laparoscopic (N=180)	*P* value
Postoperative complications, total	46 (63%)	81 (45%)	0.008*
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)	< 0.001*
Readmission	11 (15%)	10 (5.6%)	0.02*

Values are number of patients (% incidence) or mean (standard deviation). **P* value < 0.05

Postoperative complications are classified by grade: **Grade 1** = minor risk events unnecessary pharmacological treatment, **Grade 2** = requiring pharmacological treatment, **Grade 3** = requiring surgical, endoscopic, radiological intervention,

Grade 3A = Intervention not under general anesthesia, **Grade 3B** = Intervention under general anesthesia, **Grade 4** = life threatening complication, **Grade 5** = result in death

Table 5. Outcome variables related to complications

	No complications (N=127)	Complications (N=126)	*P* value
Operation type : laparotomy/laparoscopy	27/100	46/80	0.008*
Age (year)	59 (16)	64 (14)	0.016*
Gender (M/F)	47/80	64/62	0.031*
Weight (kg)	61(11)	61 (10)	0.74
Height (cm)	161 (8)	161 (9)	0.99
BMI (kg/m^2)	23.4 (3)	23.6 (3)	0.647
ASA class (1/2/3)	53/69/5	41/79/6	0.336
Surgeon (1/2/3/4)	56/11/53/7	42/11/67/6	0.292
Spleen preserving / with splenectomy	57/70	76/50	0.012*
Operation time (min)	219 (79)	257 (99)	< 0.001*
Anesthesia time (min)	263 (80)	301 (98)	< 0.001*
Preop Hemoglobin (g/dL)	13.4 (1.3)	13.6 (1.6)	0.632
Postop Hemoglobin (g/dL)	12.2 (1.5)	12.0 (1.8)	0.26
Estimated blood loss (ml)	340 (598)	357 (300)	0.78
Urine output (ml)	256 (235)	277 (221)	0.456
Crystalloid per weight and anesthesia time (ml/kg/h)	7.5 (4.6)	7.2 (4.2)	0.516
Colloid per weight and anesthesia time (ml/kg/h)	1.0(1.6)	1.2 (1.3)	0.193

Total fluids(1.5) per weight and anesthesia time (ml/kg/h)	9.0 (6.0)	9.0 (5.1)	0.996
Total fluids(2.0) per weight and anesthesia time (ml/kg/h)	9.6 (5.5)	9.5 (6.5)	0.881
Admission date (d)	11.2 (3.7)	18.3 (10.1)	< 0.001*

The data are presented as the mean (standard deviation) or number of patinets.

*P value < 0.05, BMI = Body mass index, ASA = American Society of Anesthesiologists

DISCUSSION

In this retrospective cohort study of patients who underwent distal pancreatectomy, we found that the basal fluid requirements did not differ according to the surgical method used, i.e., laparotomy or laparoscopy. Logistic regression analysis did not show a relationship between the volumes of infused fluid and complications, which means that the fluid management was within the tolerable range. Pancreatic resection is major abdominal surgery in which complications are common; the reported rate of complications is 38–59%.[12-14] The main reported complications are anastomotic leakage, wound or intraabdominal infection, fistula formation, and intra-abdominal fluid collection, similar to our findings. In our study, the complication rate was 63% in the laparotomy group and 45% in the laparoscopy group, and the total complication rate was 50.2%. Many studies have compared liberal and restrictive intraoperative fluid administration and revealed that liberal fluid administration increased postoperative complications and prolonged hospital stays.[15-18] In these studies, the restricted regimen consisted of crystalloid infusion at 4–6 mL/kg/h versus 12 mL/kg/h for the liberal regimen.[15] The calculated total fluid volumes in our study were between these two values in both groups. Although several studies have reported on fluid management in pancreatectomy, few have examined fluid management in laparoscopic pancreatectomy.

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 3–4 times the

volume to have a similar volume effect to colloid. This was based on the revised Starling equation and the glycocalyx model paradigm.[7] The endothelial glycocalyx layer is known to have a semipermeable barrier function and infused crystalloid fluids do not spread through the extracellular volume, but mainly remain in the intravascular space. To obtain a similar volume effect to that of 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.[10,19] We calculated both total fluid volumes by multiplying colloid volume 1.5 and 2.0 and neither value differed between the groups. The fluid kinetics are context sensitive so it is difficult to know exact total volume. But we assumed that exact total volume is between the two values.

The use of colloid is still controversial; the main concern is that it could result in renal damage.[20] However, this is mainly reported when large volumes of colloid are infused in critically ill patients. No evidence for renal dysfunction was observed in a meta-analysis of surgical patients.[21] Better resuscitation was reported with colloid compared with crystalloid in severely injured, hypovolemic patients.[19] In our patients, the estimated blood loss did not differ between the groups, but more colloid were infused in the laparotomy group. It is possible that the anesthesiologist in charge was more generous regarding colloid infusion in laparotomy in the belief that more fluids are needed in laparotomy and that colloid would fill the demand for fluid requirements more efficiently. However, our results found no differences in the basal fluid requirements according to the surgical

method used and there seems to be no reason for the generous colloid in laparotomy compared with laparoscopy in cases with similar estimated blood losses.

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 requiring 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 affect it and differed in each patients. We tried to minimize the effect of bleeding by excluding patients who had transfusions. And for the total volume of fluid, the calculated dose was used because crystalloid and colloid fluids have different volume effects and the possibility of bias exists.

In conclusion, in patients undergoing distal pancreatectomy under general anesthesia, there is no difference in the basal fluid requirements in laparoscopic surgery compared with laparotomy. And this finding may serve as a basis for guideline for fluid management in laparoscopic surgery.

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국 문 초 록

서론: 최근 몇 년 동안 수술 중 수액 관리 방법에 대한 개념이 진보하였다. 하지만 복강경 수술에서의 수액 관리에 대해서는 정립된 내용이 부족한 실정이다. 이 연구는 원위부 췌장절제술을 받은 환자에서의 수액 투여량을 조사하여 개복수술과 복강경수술에서의 기본 수액 요구량에 차이가 있는지 알아보고자 한다.

방법: 본 연구는 후향적 코호트 연구로서, 2006년 6월부터 2016년 3월까지의 전자의무기록 데이터를 검토하여 개복 혹은 복강경하 원위부 췌장절제술을 시행 받은 환자 253명의 정보를 분석하였다. 수술 중 수액 투여량, 수술 후 합병증, 재원기간, 재입원율을 비교하였으며, 총 수액 투여량은 교질액에 1.5 혹은 2를 곱한 후 정질액과 합산하여 계산하였다.

결과: 개복 수술에서 복강경 수술보다 많은 교질액이 투여되었으나(1.5 ml/kg/hr vs. 1.0 ml/kg/hr, P = 0.007) 정질액(7.6 ml/kg/hr vs. 7.2 ml/kg/hr, P = 0.578)과 총 수액 투여량에는 유의한 차이가 없었다.(1.5배: 9.8 ml/kg/hr vs. 8.7 ml/kg/hr, P = 0.136; 2.0배: 10.6 vs. 9.1 ml/lg/hr, P = 0.092)

결론: 원위부 췌장 절제술을 받은 환자에서 개복 수술과 복강경 수술에

서의 수술 중 기초 수액 요구량에는 차이가 없었다.

주요어: 수액 관리, 복강경 수술, 원위부 췌장 절제술

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