Intraoperative fluid therapy and postoperative complications during minimally invasive esophagectomy for esophageal cancer: a single-center retrospective study

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Abstract

PURPOSE: Compared with open thoracotomy, minimally invasive esophagectomy (MIE) methods, such as transhiatal or thoracoscopic esophagectomy, likely have lower morbidity. However, the relationship between intraoperative fluid management and postoperative complications after MIE remains unclear. Thus, we investigated the association of cumulative intraoperative fluid balance and postoperative complications in patients undergoing MIE.

METHODS: This single-center retrospective cohort study examined patients undergoing thoracoscopic esophagectomy for esophageal cancer in the prone position. Postoperative complications included pneumonia, arrhythmia, thrombotic events and acute kidney injury (AKI). We compared patients with higher and lower intraoperative fluid balance (higher and lower than the median). Multivariable logistic regression analyses were performed to estimate the odds ratio of intraoperative fluid balance status on the incidence of postoperative complications.

RESULTS: In total, 135 patients were included in the study. Postoperative complications occurred in 43 (32%), including cardiac arrhythmia (n = 12, 9%), thrombosis (n = 20, 15%), pneumonia (n = 13, 10%), and AKI required hemodialysis (n = 1, 1%). Patients with a higher fluid balance had higher incidence of complications than those with a lower fluid balance (46% vs. 18%, $p < 0.001$). After adjusting for age, ASA-PS ≥ III, blood loss, and the use of radical surgery, the higher intraoperative fluid balance group was significantly and independently associated with postoperative complications (adjusted OR 5.31, 95% CI 2.26 to 13.6, $p < 0.0001$).

CONCLUSIONS: In patients undergoing thoracoscopic esophagectomy in the prone position, a greater intraoperative positive fluid balance was independently associated with a higher incidence of complications.

Introduction

Minimally invasive esophagectomy (MIE) methods, such as transhiatal esophagectomy and thoracoscopic esophagectomy are associated with lower morbidity than open thoracotomy [1-4]. However, the number of complications remained non-negligible compared to other types of surgery. Moreover, postoperative complications increase health care costs and worsen long-term mortality [5-10].

Many studies have shown that intraoperative fluid management like goal-directed fluid therapy (GDFT) and restricted fluid therapy contribute to better outcomes [11-14]. Liberal intraoperative fluid management during esophagectomy with open thoracotomy for carcinoma led to a positive fluid balance and respiratory disturbances [15]. However, the relationship between intraoperative fluid management and postoperative complications after MIE remains unclear.

Therefore, the aim of this study was to investigate the association between intraoperative fluid management and postoperative complications in patients undergoing thoracoscopic esophagectomy in the prone position. We hypothesized that patients with complications had a significantly greater cumulative positive intraoperative fluid balance.

Methods

Study design

This was a single-center retrospective observational study at Okayama University Hospital. Ethical approval for this study was provided by the Ethical Committee of Okayama University Hospital (Okayama, Japan), with an informed consent waiver. All consecutive patients who underwent thoracoscopic esophagectomy for esophageal cancer, in the prone position, from 1/1/2011 to 31/3/2014 were eligible for inclusion. Patients with missing data were excluded from the study.

Anesthetic managements and postoperative care

All patients received only general anesthesia or general anesthesia combined with epidural analgesia, unless otherwise contraindicated. The choice of anesthetic agent, fluid management, and administration of a vasopressor (ephedrine, phenylephrine, or norepinephrine) or inotropic agents (dopamine) were left to the discretion of the attending anesthesiologist. The patients undergoing radical esophagectomy were kept sedated and intubated overnight in intensive care units (ICU) following surgery. If there were no clinical problems, the patients were routinely extubated on postoperative day 1 and enteral nutrition through jejunal feeding tube was initiated after they were extubated. Contrast-enhanced computed tomography was routinely performed on postoperative day 3, and the decision to discharge the patients from ICU was made.

Data collection

We collected patients' baseline demographics such as age, sex, body mass index, and ASA-physical status (ASA-PS) from electronic medical records. We also collected intraoperative variables, such as operative time, fluid administration, use of albumin, transfusion of blood, bleeding, and urine output. Intraoperative fluid balance was determined by subtracting fluid eliminated from total fluid administered, referencing electronic anesthesia records. Fluid balance was indicated as follows (infusion + transfusion) – (urinary output + blood loss).

The outcome of interest

The primary outcome was the incidence of postoperative complications. We defined postoperative complications as the extended Clavian-Dindo classification grade II or greater [16]. We defined anastomotic leakage, gastric tube or flap necrosis, thoracic fistula, abscess, recurrent laryngeal nerve paresis, and chyle leakage as surgical complications. Pneumonia, cardiac complications, thrombotic events, and others including acute kidney injury (AKI) were considered medical complications. All complications were identified from the patient's electronic medical record. Each complication was confirmed and graded by radiography, computed tomography, or electrocardiogram findings; required pharmacological treatment (e.g., antibiotics, antiarrhythmics, or anticoagulants); required surgical, endoscopic, or radiological intervention; or required organ support (e.g., mechanical ventilation or renal replacement therapy). To assess the detailed association between fluid balance and postoperative complications, we investigated only medical complications and excluded complications likely related to surgical technique from analysis.

Statistical analysis

Continuous variables were compared using the Wilcoxon rank sum test and are reported as medians (interquartile range). Categorical variables were compared using chi-square tests and reported as n (%). To determine the clinical ramifications based on fluid balance status, patients were dichotomized into two groups: patients with a higher fluid balance and those with a lower fluid balance. A higher fluid balance was defined as receiving more than the median fluid balance. We also compared the intraoperative fluid management between patients with complications and those without complications.

Unadjusted and adjusted regression analyses were conducted to estimate the odds ratio (OR) with 95% confidence intervals (CIs) for the incidence of postoperative complications. The adjusted OR was estimated by multivariable logistic regression analyses. First, we included intraoperative fluid balance group and *a priori* determined possible confounding factors including age, ASA-PS ≥ III, blood loss during surgery, and performance of radical surgery (one-stage resection and reconstruction) in the model using the forced entry method (Model 1). Next, we performed a multivariate logistic regression analysis where the higher fluid balance group was replaced with the total amount of intraoperative fluid balance per hour as a continuous variable (Model 2). According to several previous studies [17, 18], we adopted intraoperative fluid balance as the most relevant information regarding intraoperative fluid management. Moreover, we selected other covariates as preoperative physical status of the patient (namely age and ASA-PS ≥ III) and severity of the procedure (blood loss during surgery and performance of radical surgery) are well-known risk factors for postoperative complications. We used the Hosmer–Lemeshow goodness-of-fit test to examine whether the multivariable model was fit of data. Collinearity was assessed by calculating the variance inflation factor. Statistical significance was accepted at a two-sided P value <0.05. Data were analyzed using JMP version 12 (SAS Institute, Cary, NC, USA) and EZR (Version 1.36, Saitama Medical Center, Jichi Medical University, Saitama, Japan) [19], which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).

Post hoc analyses

To further reduce the possibility that non-anesthesia-related complications that occurred in the later postoperative period influenced the results, early complications were defined as those that occurred within 7 days following surgery. This window is likely to restrict complications to those that are anesthesia-related. All above analyses were repeated for early complications.

Intraoperative fluid management might be associated with postoperative AKI [20], Therefore, we focused on the incidence of AKI in this cohort. Serum creatinine data reported within 7 days following surgery was collected from electronic medical records. AKI was defined using the serum creatinine criterion from the Kidney Disease: Improving Global Outcomes (KDIGO) group [21], which is widely used for detecting and staging AKI.

Results

Study population

A total of 136 patients underwent thoracoscopic esophagectomy in the prone position during the study period and 1 was excluded due to missing data. There were 124 (92%) males with a median age of 65 (Interquartile range [IQR] 62–71) years, and 75 (56%) patients received preoperative chemotherapy and radiation. Most patients (85%) had an ASA-PS of I or II. A total of 130 (96%) patients were inserted epidural catheter. The median surgical time was 653 (IQR 595–731) minutes. The median amount of intraoperatively administered crystalloid was 5100 (IQR 4198–6000) ml, and median hydroxyethyl starch volume was 500 (IQR 500–1000) ml. Albumin was administered in 34 (25%) patients and packed red blood cell (PRBC) was transfused in 12 (9%) patients. Intraoperative bleeding volume was 230 (IQR 110–380) ml. The fluid balance during operation was 4311 (IQR 3455–5310) ml.

Primary outcome

Overall, 43 patients (32%) had medical complications during hospital stay and 3 of them had 2 medical complications. Medical complications included cardiac arrhythmia (n = 12, 9%), deep venous thrombosis/other thrombosis (n = 20, 15%), pneumonia (n = 13, 10%), and other complications, including AKI that required continuous renal replacement therapy (n = 1, 1%) (Table 1). Thirteen patients (10%) had surgical complications, including anastomotic leak, gastric necrosis, chyle leak, pleural effusion in need of drainage, and recurrent nerve palsy.

Comparison of patients with higher and lower fluid balance.

Table 2 shows the comparisons between patients with higher and lower fluid balance. There were no significant differences in the demographic characteristics except for ASA-PS classification. Patients with a higher fluid balance had a larger median intraoperative crystalloid administration (5898 ml [IQR 5370–6893] vs. 4250 ml [IQR 3600–4800]; $p < 0.0001$) and more blood loss (243 ml [IQR 133-403] vs. 190 ml [IQR 60-340]; $p = 0.03$) than those with lower fluid balance. Patients with higher fluid balance were more likely to have used albumin during surgery than those with a lower fluid balance. (37% vs. 13%, $p < 0.01$). There was no significant difference for the use of hydroxyethyl starch between the two groups. Patients with higher fluid balance had a higher incidence of complications than those with lower fluid balance (46% vs. 18%, $p < 0.001$). There was no difference between the groups in the length of ICU stay, hospital stay and mechanical ventilation days, and the use of vasopressor and inotropic agents.

Comparison of patients with and without complications.

Table 3 shows the comparisons between patients with and without medical complications. There were no significant between-group differences in baseline patient characteristics.

With regard to intraoperative fluid management, patients with complications had a larger median intraoperative crystalloid administration than those without complications (5670 ml [IQR 4400–6300] vs. 4875 ml [IQR 4030–5714]; $p = 0.02$). However, the group differences in hydroxyethyl starch administration were not statistically significant. Although the difference was not statistically significant, the use of albumin (33% vs 22%, $p = 0.18$) and PRBC transfusion (12% vs 8%, $p = 0.44$) tended to be more frequent in patients with complications. Furthermore, the group differences in blood loss, urine output, or surgery time were not statistically significant.

Patients with complications had a larger median intraoperative fluid balance than those without complications (4715 ml [IQR 4180–5615], vs. 4095 ml [IQR 3239–5150], $p < 0.01$). Patients with complications tended to exhibit increases in intraoperative fluid balance per hour (404 ml/h [IQR 352–478] vs. 374 ml/h [IQR 305–463], $p = 0.08$).

In the complication group, the median length of intensive care unit stay after operation was significantly longer than non-complication group (6 days [IQR 5–8] vs. 6 days [IQR 5–6], $p < 0.001$). The complication group tended to have longer hospital stays (22 days [IQR 17–30] vs. 20 days [IQR 16–24], $p = 0.08$). In both groups, all patients were alive at one year.

Multivariable logistic regression analyses for postoperative complications

After adjusting for age, ASA-PS ≥III, blood loss, and the use of radical surgery, there was a significant and independent association between a higher fluid balance group and postoperative medical complications in model 1 (adjusted OR 5.31, 95% CI 2.26 to 13.6, $p < 0.0001$) (Table 4). Similarly, a total amount of intraoperative fluid balance was also significantly and independently associated with postoperative medical complications in model 2 (adjusted OR 1.47, 95% CI

1.06 to 2.10, p = 0.02) (Table 4).

Post hoc analyses

Restricting analyses to complications that occurred within 7 days of surgery did not change the overall direction of the results (summarized in Electronic Supplementary Material; Supplemental Tables 1, 2, and 3)

Over the first 7 days following surgery, postoperative AKI identified using serum creatine levels occurred in 3 (2%) patients: 2 patients with stage 1 and 1 patient with stage 3. Due to the small number of postoperative KDIGO-defined AKI events, statistical analysis was not performed.

Discussion

Key findings

We conducted a single-center retrospective observational study of 135 patients who underwent thoracoscopic esophagectomy for esophageal cancer in the prone position to examine the association between intraoperative fluid management and postoperative complications. Overall, 43 patients (32%) had medical complications. We found that intraoperative positive fluid balance was independently associated with postoperative complications.

Relationship to previous studies

Incidence of postoperative complications after MIE

Previous studies have described postoperative complications in patients undergoing MIE. Tsujimoto et al. reported the incidence of medical complications after video-assisted thoracoscopic esophagectomy was 9%. They also reported pneumonia was the most frequent medical complication among them [4]. Petri R et al. also described the incidence of medical complications after thoracoscopic esophagectomy in the prone position and found that 15.2% of patients developed pneumonia, which was the most common complication [22]. Other studies reported that the incidence of arrythmia after thoracoscopic esophagectomy was 13–26% [23, 24]. These findings are consistent with our observations where the incidence of postoperative medical complications was still relatively high (32%), and they mainly consisted of respiratory and cardiac complications.

Excessive fluid administration and postoperative complications

Excessive fluid administration promotes postoperative complications or poor outcomes like lung injury after pulmonary resection and gastrointestinal cancer surgeries, and pancreatic fistula after pancreaticoduodenectomy [25-28]. Similarly, intraoperative positive fluid balance was associated with increased postoperative medical complications in patients who underwent thoracoscopic esophagectomy in the prone position for esophageal cancer. In the current study, most complications were pulmonary. Excessive fluid administration can cause increased extravascular fluid in the lung tissue and pulmonary edema, which can impair oxygen exchange and increase the risk of postoperative respiratory failure and pneumonia [29]. Interstitial edema can also develop in several organs, which can lead to prolonged ileus and impaired wound healing [29].

Notably, 15% of patients had deep venous thrombosis/other thrombosis.

Hypercoagulability was significantly enhanced by crystalloid hemodilution *in vitro* and *in vivo* [30, 31]. In an early randomized controlled trial of 60 patients who underwent laparotomy, the incidence of postoperative deep venous thrombosis was significantly higher among patients who received fluids (30%), compared with only 7% in patients who did not receive fluids [32]. Thus, theoretically, excessive intraoperative fluid administration can have deleterious effects on several organs.

Effect of intraoperative restricted fluid therapy

An increasing number of reports have reported beneficial effects from use of a restrictive fluid regimen during abdominal surgery, with faster return of bowel function, fewer complications, and shorter hospital stays [27, 33, 34]. Olivers et al. showed that patients who received more intraoperative fluids (>17.26 ml/kg/h) had significantly more major complications (CD classification ≥Ⅲ) compared to patients who received less intraoperative fluids (<17.26 ml/kg/h) during transhiatal esophagecgtomy [35]. In the current study, most patients had lower rates of fluid administration (median rate 9.1 ml/kg/h, IQR 7.29–11.1) than those that were previously reported. Thus, a more restrictive approach to fluid management may be feasible and beneficial during MIE.

Clinical implications

We found that higher fluid balance during thoracoscopic esophagectomy for esophageal cancer, in the prone position, was associated with increased postoperative complications. These findings are important because GDFT strategies to optimize intraoperative fluid management decrease postoperative complications in patients undergoing major elective surgery [12, 36-38]. Given that MIE has been widely used over the last decade, our findings support the need for further interventional trials to evaluate the safety and feasibility of GDFT in patients undergoing thoracoscopic esophagectomy in prone position.

Additionally, most of these strategies use dynamic parameters including stroke volume variation and pulse pressure variation to detect fluid responsiveness. However, such parameters are non-validated during thoracoscopic esophagectomy in the prone position, or during special circumstances like one-lung ventilation with a CO_2 pneumothorax procedure. Thus, future studies should also focus on the predictive validity of such dynamic indices for fluid responsiveness (trial registration number: UMIN000027264).

Strengths and limitations

To our knowledge, ours is the first study to examine the association between intraoperative fluid management and postoperative complications in patients undergoing thoracoscopic esophagectomy for esophageal cancer in the prone position.

However, this study had several limitations. First, this was a single-center retrospective study and our findings may not be generalizable. Similar studies should be performed in other hospitals to confirm or refute our findings. However, we note that our hospital is a high-volume esophagectomy center in a developed country, suggesting a degree of external validity. This notion is supported by the fact that our incidence of postoperative medical complications was similar to those values reported in the literature. Secondly, although statistically significant, the group differences in intraoperative fluid balance may not affect occurrence of postoperative complications in a clinically relevant manner. However, this was a preliminary study to assess the necessity and feasibility of further research and trials. Thus, the current study represents an initial step towards developing intraoperative fluid management during minimally invasive esophagectomy. Thirdly, post hoc analysis of postoperative AKI was assessed using serum creatinine levels, but not urine output. In addition, the small number of KDIGO-defined AKI events did not allow for statistical analysis. Fourth, the relationship between cancer staging and postoperative outcomes was not evaluated. Fifthly, because there was a lack of previous studies regarding fluid management in patients undergoing thoracoscopic esophagectomy in the prone position, we were unable to determine the required sample size *a priori*. Finally, our regression analysis included 5 independent variables, although the number of events was 43. This indicates that the number of independent variables in the logistic regression model exceeded the allowable number [39]. Therefore, these results must be interpreted with caution. However, the Hosmer–Lemeshow goodness-of-fit test revealed a satisfying level of fitness, and all the variance inflation factor scores in this study were <2.0, which indicated that multi-collinearity was not a concern.

Conclusion

In patients undergoing thoracoscopic esophagectomy in the prone position, a greater intraoperative positive fluid balance was independently associated with a higher incidence of medical complications. Optimizing fluid administration during surgery may reduce the risk of complications following thoracoscopic esophagectomy. Our findings justify further study.

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Table 1. Postoperative medical complications

（Extended Clavien-Dindo classification ≥ II）

Complication	**n (%)**
Pneumonia*	13 (10)
Cardiac arrhythmia**	12 (9)
Deep venous thrombosis/other thrombosis***	20 (15)
Others****	1 (1)

*Pneumonia: Patients who received medical management (such as antibiotics); bronchoscopic aspiration; tracheal puncture; tracheostomy under general anesthesia, sedation, or mechanical ventilation; or mechanical ventilation indicated.

**Cardiac arrhythmia: Patients who received medical management (such as antiarrhythmic drugs) or medical intervention (such as catheter ablation or synchronized cardioversion) under local anesthesia. Patients only included those who acquired arrhythmias after surgery and did not include those who received antiarrhythmic drugs before operation.

***Thrombosis: Patients who received medical management (such as anticoagulants) and presented with thrombosis indicated by a contrast-enhanced computerized tomography scan on postoperative day 3.

****Others：Acute kidney injury that required continuous renal replacement therapy

Table 2. Comparison of higher fluid balance group and lower fluid balance group

Variable	**Higher fluid balance (≥4311ml) n = 68**	**Lower fluid balance (<4311ml) n = 67**	**p value**
Demographic characteristic			
Age (years)	65 [62–72]	65 [62–71]	0.76
Gender (male), n (%)	62 (91)	62 (93)	0.77
Body weight (kg)	58.2 [53.1-64.3]	57.3 [50.7-66.7]	0.99
BMI (kg/m^2)	21.8 [19.9–23.9]	21.5 [19.3–24.5]	0.87
ASA-PS ≥III, n (%)	6 (9)	14 (21)	0.05
FVC (L)	3.5 [3.1–4.0]	3.4 [2.9–4.1]	0.75
$FEV_{1.0}$ (L)	2.6 [2.1–3.0]	2.5 [2.1–2.9]	0.72
Preoperative Chemotherapy, n (%)	42 (62)	33 (49)	0.14
Preoperative Hemoglobin (g/dl)	12.3 [11.3–13.6]	12.8 [12.0–13.7]	0.24
Preoperative Albumin (g/dl)	4.0 [3.8–4.3]	4.1 [3.8–4.4]	0.81
Preoperative Creatinine (mg/dl)	0.76 [0.69-0.91]	0.79 [0.68-0.88]	0.62
Preoperative comorbidity			
Hypertension n (%)	34 (50)	25 (37)	0.14
Arrhythmia n (%)	2 (3)	3 (4)	0.64
Past smoking n (%)	65 (96)	62 (93)	0.45
Diabetes n (%)	9 (13)	11 (16)	0.60
Intraoperative management			
Operative time (min)	701 [614–781]	626 [573–682]	<0.0001
Radical surgery n (%)	62 (91)	54 (81)	0.08
Epidural anesthesia n (%)	65 (96)	65 (97)	0.66
Crystalloid (ml)	5898 [5370–6893]	4250 [3600–4800]	<0.0001
Hydroxyethyl starch use n (%)	59 (87)	53 (79)	0.24
amount (ml)	600 [500–1000]	500 [500–1000]	0.63
Albumin use n (%)	25 (37)	9 (13)	<0.01
Amount (ml)	0 [0-273]	0 [0-0]	<0.001
Crystalloid only* n (%)	5 (7)	13 (19)	0.04
Use of Red blood cell n (%)	9 (13)	3 (4)	0.07
Use of Noradrenaline n (%)	2 (3)	2 (3)	0.99
Use of Dopamine n (%)	0 (0)	1 (1)	0.31

Blood loss (ml)	243 [133–403]	190 [60–340]	0.03
Urine output (ml)	1035 [720–1494]	1140 [820–1750]	0.14
Postoperative outcome			
Complication n (%)	31 (46)	12 (18)	<0.001
Pneumonia n (%)	8 (12)	5 (7)	0.40
Arrhythmia n (%)	9 (13)	3 (4)	0.07
Thrombosis n (%)	16 (24)	4 (6)	<0.01
Others** n (%)	0 (0)	1 (1)	0.31
Early complication*** n (%)	30 (44)	12 (18)	0.001
Length ICU stay (days)	6 [5–7]	6 [5–6]	0.60
Length of postoperative hospital stay (days)	21 [17–26]	18 [16–27]	0.28
Mechanical ventilation (days)	1 [1–1]	1 [1–1]	0.53
Use of Noradrenaline n (%)	23 (34)	15 (22)	0.14
Use of Dopamine n (%)	9 (13)	11 (16)	0.60
Use of Adrenaline n (%)	0 (0)	1 (1)	0.31
SOFA score on ICU admission	2 [2–3]	2 [1–3]	0.61
SOFA score after 48 hours	2 [1–3]	2 [1–3]	0.44

Data are presented as median [interquartile range] or n (%).

BMI, body mass index; ASA-PS, American Society of Anesthesiologist Physical Status classification; FVC, forced vital capacity; $FEV_{1.0}$, forced expiratory volume in 1 s; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment score

Higher fluid balance was defined as receiving higher than the median fluid balance (4311ml).

*Patients who only received crystalloid during the surgery.

**Acute kidney injury that required continuous renal replacement therapy

***Postoperative complications in the first 7 days after surgery

Table 3. Comparison of complication and non-complication groups

Variable	**Complications (+)** n = 43	**Complications (−)** n = 92	**p value**
Demographic characteristic			
Age (years)	64 [61–69]	66 [63–72]	0.20
Gender (male), n (%)	39 (91)	85 (92)	0.74
Body weight (kg)	58.0 [53.2-64.5]	57.7 [51.0-66.4]	0.72
BMI (kg/m²)	21.7 [19.7–24.0]	21.6 [19.6–24.4]	0.94
ASA-PS ≥III, n (%)	8 (19)	12 (13)	0.40
FVC (L)	3.5 [3.0–4.1]	3.4 [3.1–4.0]	0.81
$FEV_{1.0}$ (L)	2.5 [2.3–3.0]	2.6 [2.1–3.0]	0.73
Preoperative Chemotherapy, n (%)	27 (63)	48 (52)	0.25
Preoperative Hemoglobin (g/dl)	12.5 [11.1–13.5]	12.7 [11.7–13.7]	0.43
Preoperative Albumin (g/dl)	4.0 [3.8–4.4]	4.0 [3.8–4.4]	0.95
Preoperative Creatinine (mg/dl)	0.78 [0.67-0.95]	0.77 [0.70-0.88]	0.90
Preoperative comorbidity			
Hypertension n (%)	17 (40)	42 (46)	0.50
Arrhythmia n (%)	1 (2)	4 (4)	0.56
Past smoking n (%)	42 (98)	85 (92)	0.23
Diabetes n (%)	10 (23)	10 (11)	0.06
Intraoperative management			
Operative time (min)	668 [598–771]	650 [592–726]	0.30
Radical surgery n (%)	39 (91)	77 (84)	0.28
Epidural anesthesia n (%)	40 (93)	90 (98)	0.17
Crystalloid (ml)	5670 [4400–6300]	4875 [4030–5714]	0.02
Hydroxyethyl starch use n (%)	34 (79)	78 (85)	0.41
amount (ml)	500 [500–1000]	650 [500–1000]	0.47
Albumin use n (%)	14 (33)	20 (22)	0.18
Amount (ml)	0 [0-250]	0 [0-0]	0.16
Crystalloid only* n (%)	6 (14)	12 (13)	0.88
Use of Red blood cell n (%)	5 (12)	7 (8)	0.44
Use of Noradrenaline n (%)	0 (0)	4 (4)	0.17
Use of Dopamine n (%)	0 (0)	1 (1)	0.49
Blood loss (ml)	200 [110–310]	235 [110–428]	0.40
Urine output (ml)	1155 [720–1675]	1025 [765–1670]	0.76

Fluid balance (ml)	4715 [4180–5615]	4095 [3239–5150]	<0.01
Fluid balance (ml/h)	404 [352–478]	374 [305–463]	0.08
Postoperative outcome			
Length ICU stay (days)	6 [5–8]	6 [5–6]	<0.001
Length of postoperative hospital stay (days)	22 [17–30]	20 [16–24]	0.08
Mechanical ventilation (days)	1 [1–1]	1 [1–1]	0.66
Use of Noradrenaline n (%) Use of Dopamine n (%) Use of Adrenaline n (%)	13 (30) 3 (7) 1 (2)	25 (27) 17 (18) 0 (0)	0.71 0.08 0.14
SOFA score on ICU admission	2 [2–3]	2 [1–3]	0.85
SOFA score after 48 hours	2 [1–4]	2 [1–3]	0.24

Data are presented as median [interquartile range] or n (%).

BMI, body mass index; ASA-PS, American Society of Anesthesiologist Physical Status classification; FVC, forced vital capacity; $FEV_{1.0}$, forced expiratory volume in 1 s; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment score

*Patients who only received crystalloid during the surgery.

Table 4. Unadjusted and adjusted odds ratios and 95% confidence intervals for postoperative complications

Variable	Unadjusted Odds ratio (95%CI)	P value	Model 1*		Model 2**	
			Adjusted Odds ratio (95%CI)	P value	Adjusted Odds ratio (95%CI)	P value
Higher fluid balance	3.84 (1.79-8.68)	<0.001	5.31 (2.26-13.6)	<0.0001	-	
Total amount of Intraoperative fluid balance (100 ml/h)	1.33 (0.98-1.85)	0.07	-		1.47 (1.06–2.10)	0.02
Age	0.98 (0.93-1.02)	0.27	0.96 (0.91-1.02)	0.18	0.97 (0.93–1.02)	0.30
ASA-PS ≥ III	1.52 (0.55-4.02)	0.40	3.52 (1.10-11.5)	0.03	2.69 (0.89–8.21)	0.08
Blood loss (ml/h)	0.99 (0.97-1.01)	0.20	0.98 (0.96-1.00)	0.05	0.98 (0.96–1.00)	0.07
Radical Surgery	1.90 (0.64-7.01)	0.26	1.80 (0.51-7.56)	0.38	2.70 (0.79–11.3)	0.12

CI, confidence interval; ASA-PS, American Society of Anesthesiologist Physical Status classification

Total amount of intraoperative fluid balance was calculated as: [(total amount of fluid administration (ml) + transfusion (ml)) – (total amount of blood loss (ml) + urine output (ml))]/100/operative time (h).

Higher fluid balance was defined as receiving higher than the median fluid balance (4311ml).

Blood loss was calculated as: total amount of blood loss (ml)/operative time (h).

* Hosmer and Lemeshow goodness-of-fit P value = 0.82 The maximum variance inflation factor was 1.20.

**Hosmer and Lemeshow goodness-of-fit P value = 0.11. The maximum variance inflation factor was 1.17.

Supplementary table 1. Postoperative early medical complications（Extended Clavien-Dindo classification ≥ ）in the first 7 days after surgery

Complication	**n (%)**
Pneumonia*	13 (10)
Cardiac arrhythmia**	11 (8)
Deep venous thrombosis/other thrombosis***	20 (15)
Others****	1 (1)

*Pneumonia: Patients who received medical management (such as antibiotics); bronchoscopic aspiration; tracheal puncture; tracheostomy under general anesthesia, sedation, or mechanical ventilation; or mechanical ventilation indicated.

**Cardiac arrhythmia: Patients who received medical management (such as antiarrhythmic drugs) or medical intervention (such as catheter ablation or synchronized cardioversion) under local anesthesia. Patients only included those who acquired arrhythmias after surgery and did not include those who received antiarrhythmic drugs before operation.

***Thrombosis: Patients who received medical management (such as anticoagulants) and presented with thrombosis indicated by a contrast-enhanced computerized tomography scan on postoperative day 3.

****Others：Acute kidney injury that required continuous renal replacement therapy

Supplementary table 2. Comparison of early complication and non-early complication groups

Variable	**Early Complications (+) n = 42**	**Early Complications (−) n = 93**	**p value**
Demographic characteristic			
Age (years)	65 [61-69]	65 [63-72]	0.30
Gender (male), n (%)	39 (93)	85 (91)	0.77
Body weight (kg)	58.5 [53.4-64.9]	57.7 [50.8-66.3]	0.54
BMI (kg/m²)	21.8 [19.9-24.0]	21.5 [19.5-24.4]	0.92
ASA-PS ≥III, n (%)	8 (19)	12 (13)	0.35
FVC (L)	3.5 [3.0-4.1]	3.4 [3.1-4.0]	0.71
$FEV_{1.0}$ (L)	2.5 [2.3-3.0]	2.6 [2.1-3.0]	0.68
Preoperative Chemotherapy, n (%)	26 (62)	49 (53)	0.32
Preoperative Hemoglobin (g/dl)	12.5 [11.1-13.6]	12.7 [11.7-13.7]	0.39
Preoperative Albumin (g/dl)	4.0 [3.8-4.4]	4.0 [3.8-4.4]	0.84
Preoperative Creatinine (mg/dl)	0.78 [0.67-0.96]	0.77 [0.70-0.88]	0.74
Preoperative comorbidity			
Hypertension n (%)	17 (41)	42 (45)	0.61
Arrhythmia n (%)	1 (2)	4 (4)	0.58
Past smoking n (%)	41 (98)	86 (92)	0.24
Diabetes n (%)	10 (24)	10 (11)	0.05
Intraoperative management			
Operative time (min)	668 [597-772]	650 [593-724]	0.30
Radical surgery n (%)	38 (90)	78 (84)	0.31
Epidural anesthesia n (%)	39 (93)	91 (98)	0.16
Crystalloid (ml)	5660 [4400-6305]	4900 [4033-5732]	0.03
Hydroxyethyl starch use n (%)	33 (79)	79 (85)	0.36
amount (ml)	500 [500-1000]	700 [500-1000]	0.37
Albumin use n (%)	13 (31)	21 (23)	0.30
Amount (ml)	0 [0 -250]	0 [0-0]	0.28
Crystalloid only* n (%)	6 (14)	12 (13)	0.83
Use of Red blood cell n (%)	5 (12)	7 (8)	0.41
Use of Noradrenaline n (%)	0 (0)	4 (4)	0.17
Use of Dopamine n (%)	0 (0)	1 (1)	0.50

Blood loss (ml)	205 [110-320]	230 [110-425]	0.50
Urine output (ml)	1148 [720-1604]	1030 [770-1700]	0.99
Fluid balance (ml)	4798 [4160-5626]	4100 [3243-5140]	<0.01
Fluid balance (ml/h)	408 [351-480]	375 [306-463]	0.08
Postoperative outcome			
Length ICU stay (days)	6 [6-8]	5 [5-6]	<0.001
Length of postoperative hospital stay (days)	22 [17-30]	20 [16-24]	0.11
Mechanical ventilation (days)	1 [1-1]	1 [1-1]	0.67
Use of Noradrenaline n (%) Use of Dopamine n (%) Use of Adrenaline n (%)	13 (31) 3 (7) 1 (2)	25 (27) 17 (18) 0 (0)	0.63 0.09 0.14
SOFA score on ICU admission	2 [2-3]	2 [1-3]	0.68
SOFA score after 48 hours	2 [1-4]	2 [1-3]	0.18

Data are presented as median [interquartile range] or n (%).

BMI, body mass index; ASA-PS, American Society of Anesthesiologist Physical Status classification; FVC, forced vital capacity; $FEV_{1.0}$, forced expiratory volume in 1 second; SOFA, Sequential Organ Failure Assessment score

*Patients who received only crystalloid during the surgery.

Supplementary Table 3. Unadjusted and adjusted odds ratios and 95% confidence intervals for early postoperative complications

Variable	Unadjusted Odds ratio (95%CI)	P value	Model 1*		Model 2**	
			Adjusted Odds ratio (95%CI)	P value	Adjusted Odds ratio (95%CI)	P value
Higher balance fluid	3.62 (1.68-8.19)	<0.001	4.85 (2.01-11.7)	<0.001	-	
Total amount of Intraoperative fluid balance (100 ml/h)	1.34 (0.98-1.86)	0.07			1.47 (1.05–2.11)	0.02
Age	0.98 (0.94-1.03)	0.39	0.97 (0.92-1.02)	0.28	0.98 (0.93–1.03)	042
ASA-PS ≥ III	1.59 (0.58-4.19)	0.36	3.44 (1.09-10.9)	0.04	2.73 (0.90–8.31)	0.08
Blood loss (ml/h)	0.99 (0.97-1.01)	0.26	0.98 (0.96-1.00)	0.08	0.98 (0.96–1.00)	0.10
Radical Surgery	1.83 (0.61-6.74)	0.29	1.78 (0.47-6.65)	0.40	2.62 (0.77–10.9)	0.13

CI, confidence interval; ASA-PS, American Society of Anesthesiologist Physical Status classification

Total amount of intraoperative fluid balance was calculated as: [(total amount of fluid administration (ml) + transfusion (ml)) – (total amount of blood loss (ml) + urine output (ml))]/100/operative time (h).

Higher fluid balance was defined as receiving higher than the median fluid balance (4311ml).

Blood loss was calculated as: total amount of blood loss (ml)/operative time (h).

* Hosmer and Lemeshow goodness-of-fit P value = 0.12 The maximum variance

inflation factor was 1.19.

**Hosmer and Lemeshow goodness-of-fit P value = 0.13. The maximum variance inflation factor was 1.17.