Original Article

Effects of 24-hour postoperative intravenous fluid on postoperative outcomes after lobectomy: a retrospective observational study

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Background: Postoperative fluid management plays a key role in providing adequate tissue perfusion, stabilizing hemodynamics, and reducing morbidities related to hemodynamics. This study evaluated the dose-response relationship between postoperative 24-hour intravenous fluid volume and postoperative outcomes in patients with non-small cell lung cancer (NSCLC) undergoing video-assisted thoracoscopic surgery (VATS) lobectomy.

Methods: A retrospective analysis of adult patients with NSCLC undergoing VATS lobectomy between May 2016 and April 2017 was performed. The primary exposure variable was total intravenous crystalloid infusion in the 24-hour postoperative period. The observation outcomes were postoperative pulmonary complications, acute kidney injury (AKI), in-hospital mortality, readmission within 30 days, prolonged hospital stay, postoperative length of stay, and total hospital care costs. Univariate and multivariate analyses were performed.

Results: Of the 563 patients, 136 (24.2%) with pulmonary complications were observed. Binary logistics regression showed that, relative to the group with moderate postoperative 24-hour crystalloid infusion, the risk for postoperative pulmonary complications was significantly increased in the restrictive [odds ratio (OR) 1.815, 95% CI: 1.083–3.043; P=0.024] and liberal (OR 2.692, 95% CI: 1.684–4.305; P<0.001) groups.

Conclusions: In patients with NSCLC undergoing VATS lobectomy, both restrictive and liberal 24-hour postoperative crystalloid infusions were related to adverse effects on postoperative outcomes and the optimal volume of 24-hour postoperative intravenous crystalloid infusion was 1,080–<1,410 mL.

Keywords: Perioperative fluid management; video-assisted thoracoscopic surgery (VATS); lobectomy; postoperative; pulmonary complications

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Introduction

Lobectomy with systematic mediastinal lymph node dissection is the gold standard surgical treatment for early non-small cell lung cancer (NSCLC) (1). Lobectomy performed by video-assisted thoracoscopic surgery (VATS) has been shown to reduce postoperative pain, inflammatory response, and length of hospital stay (2). Although the overall mortality from lobectomy has declined to approximately 0.5–1% with the improvement of surgical techniques and perioperative management (3), the

morbidity after lobectomy for lung cancer remains between 26.0% and 54.7% (3-5). The main causes of morbidity following pulmonary resections are of pulmonary origin and mainly include pneumonia, acute lung injury, and acute respiratory distress syndrome (ARDS) (3-5). These postoperative complications are, in part, related to intra- and postoperative fluid management (6).

Healthy people have a certain preload reserve capacity, and they have the ability to self-regulate on the ascending limb of the Frank-Starling curve without the need for additional fluid supplementation (7). Insufficient intravascular volume to patients who are fluid responsive can be adapted by self-adjustment, and excessive perioperative fluid administration to these patients may increase the risks of fluid overload without conferring additional benefit (8,9). Liberal fluid management often leads to a variety of negative outcomes, but restrictive fluid management also carries important risks, such as organ hypoperfusion leading to organ dysfunction and failure (8). Among them, the kidney is an organ that is particularly susceptible to changes in volume status, and hypovolemia often leads to renal impairment (8). During the perioperative period of a lobectomy, maintenance of intravascular volume via intravenous fluid is necessary to mitigate the hypovolemia caused by osmotic loss and bleeding (4). However, the upper bound and the lower limit of safe intravenous fluid in this setting remain unclear (8). For these reasons, the dosing of perioperative intravenous fluid varies widely among medical centers, and physicians may adopt a restrictive or liberal fluid management strategy based on their habits. Therefore, more evidence-based medical evidence is needed to guide clinical fluid management in lung surgery patients.

Postoperative fluid management plays a key role in ensuring adequate tissue perfusion, stabilizing hemodynamics, and reducing morbidities related to hemodynamics (10,11). We hypothesized that variation in 24-hour postoperative fluid administration within the range of standard clinical practice would be associated with differences in postoperative pulmonary complications, acute kidney injury (AKI), in-hospital mortality, and readmission within 30 days in patients with NSCLC who underwent VATS lobectomy. We sought to quantify the dose-response relationship between the 24-hour postoperative fluid volume and each of these outcomes across three groups of practice that spanned the range of restrictive to liberal fluid dosing. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-707/rc).

Methods

Patients

During a period of 1 year between May 2016 and April 2017, 592 consecutive adult patients with NSCLC who underwent VATS lobectomy were included for this observational retrospective study. The patients were treated on a routine basis in the First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China. VATS lobectomy was conducted through 3 ports, and systematic mediastinal lymph node dissection was performed. The patient fasted for 8 hours before surgery, and a lung protective strategy (low tidal volume) was implemented. Patients with preoperative renal dysfunction, history of thoracic surgery, congestive heart failure, sleeve lobectomy, a simultaneous resection of more than 2 lobes, and second surgery were excluded (*Figure 1*). All patients received prophylactic first- or second-generation cephalosporins before chest tube removal. If postoperative pulmonary infection is diagnosed, sulbactam ampicillin or ciprofloxacin is administered. All patients started eating 6 to 8 hours after resuscitation from anesthesia unless they were intubated or at risk of aspiration. The TNM classification (seventh edition) proposed by the International Union Against Cancer was applied in this cohort. Demographic, intraoperative, postoperative, and outcome data were extracted from medical records (summarized in *Table 1* and available online in Table S1). The amount of intraoperative total fluids was defined as the sum of crystalloids, colloids, and blood products administered between the onset of anesthesia care and resuscitation from anesthesia (12). The infusion rate of intraoperative total fluids was an average fluid administration rate, defined as the intraoperative total fluid volume per kilogram of weight divided by the operation duration (hours).

The Medical Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China, approved the study (No. 2017-58). Due to the retrospective research method used in this study, no intervention was taken, and the Medical Ethics Committee agreed to waive the patients' informed consent. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Exposure variable

Total intravenous crystalloid infusion in the 24-hour postoperative period was derived from the medical record

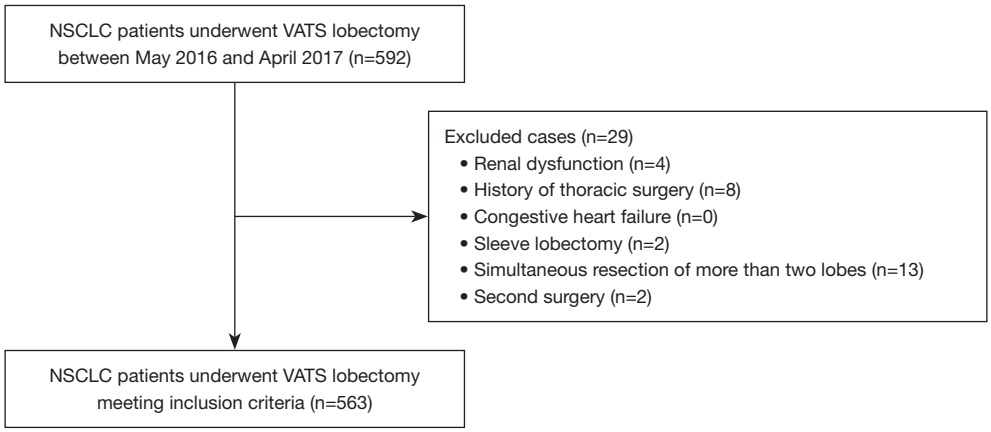

Figure 1 Study enrolment flow chart. NSCLC, non-small cell lung cancer; VATS, video-assisted thoracoscopic surgery.

and defined as the volume of crystalloid administered in the 24-hour postoperative period. Initially, patients were classified into four groups representing incremental quartiles of the exposure variable of the total intravenous crystalloid infusion in the 24-hour postoperative period (8,12). The results eventually showed that the middle two groups were very similar in terms of the incidence of postoperative pulmonary complications. Therefore, we merged the middle two groups into a single group. Finally, patients were classified into three groups: quartile 1 (restrictive group: R group), quintile 2+3 (moderate group: M group), and quartile 4 (liberal group: L group).

Outcome measures

The primary outcomes were postoperative pulmonary complications and AKI. Postoperative pulmonary complications included ARDS, reintubation, pulmonary embolism, need for bedside bronchoscopy, prolonged air leak, failure of the lung to expand, atelectasis, and pneumonia within the period of postoperative hospitalization (4,8). Pulmonary embolism was confirmed by pulmonary computed tomography angiography (4,12). A prolonged air leak was defined as a leak lasting >1 week (4,12). The failure to expand was defined as an inability of the remaining lung to fill the pleural cavity on a chest X-ray, with or without air leak (4,12). Atelectasis was diagnosed by chest radiograph documentation (4,12). The diagnosis of postoperative pneumonia was made if a new pulmonary infiltrate, with leukocytosis and fever (ear temperature >38.0 ℃), was evident on chest X-ray (4,12). AKI refers to the increase of serum creatinine level by at least 0.3 mg/dL or 50% compared with the preoperative level within 48 hours postoperatively (8).

Secondary outcomes included in-hospital mortality, readmission within 30 days, prolonged hospital stay, postoperative length of stay, and total hospital care costs (yuan renminbi) (8). A prolonged hospital stay was defined as hospitalization for more than 7 days after surgery.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation and were compared using 1-way analysis of variance. In the case of uneven variance, a nonparametric test (Kruskal-Wallis H test for multiple independent samples) was used. Categorical variables are expressed as percentages, which were compared using an R×C chi-square test. When the theoretical frequency was <5, Fisher's exact test was used. Binary logistic regression analyses were performed to determine the relationship between total intravenous crystalloid infusion in the 24-hour postoperative period with postoperative pulmonary complications, AKI, in-hospital mortality, readmission within 30 days, and prolonged hospital stay, respectively. Multiple linear regression analyses were conducted to determine the relationship between total intravenous crystalloid infusion in the 24-hour postoperative period with postoperative length of stay and total hospital care costs. Confounders were included according to univariate analysis (12). Odds ratios (ORs) were calculated from these models, together with their 95% CIs. The assignment of the variables in multivariate analysis is shown in the online Table S2. For all tests, a 2-tailed P value ≤0.05 was considered statistically

Table 1 The clinical characteristics of patients in the three groups treated with different total intravenous crystalloid infusions in the 24-hour postoperative period

Characteristics	Total intravenous crystalloid infusion 24 h postoperatively				P value
	Total (n=563)	Restrictive group (n=136), <1,080 mL	Moderate group (n=272), 1,080–<1,410 mL	Liberal group (n=155), ≥1,410 mL	
ASA score, n (%)					0.001
I	472 (83.8)	100 (73.5)	244 (89.7)	128 (82.6)	
II	68 (12.1)	29 (21.3)	21 (7.7)	18 (11.6)	
III	23 (4.1)	7 (5.1)	7 (2.6)	9 (5.8)	
Age (year)	63.2±10.7	64.1±11.3	62.7±10.5	63.4±10.5	0.439
Gender (female/male)	336/227	76/60	164/108	96/59	0.553
Weight, kg	61.4±9.8	62.3±10.3	60.6±9.6	61.9±9.7	0.198
Smoking, n (%)	156 (27.7)	35 (25.7)	83 (30.5)	38 (24.5)	0.346
Diabetes mellitus, n (%)	48 (8.5)	25 (18.4)	15 (5.5)	8 (5.2)	<0.001
Coronary heart disease, n (%)	9 (1.6)	3 (2.2)	4 (1.5)	2 (1.3)	0.813
FEV1, L	2.3±0.6	2.3±0.6	2.3±0.6	2.3±0.6	0.799
FVC, L	2.9±0.7	2.9±0.8	2.9±0.7	2.9±0.8	0.994
PEF, L/s	4.7±1.9	4.9±1.8	4.6±1.9	4.7±1.9	0.190
FEV1%	(91.1±17.2)%	(90.9±18.5)%	(91.3±17.3)%	(90.8±16.1)%	0.932
FVC%	(91.3±15.7)%	(89.8±15.8)%	(91.5±15.7)%	(92.1±15.6)%	0.417
PEF%	(67.6±24.0)%	(70.4±20.4)%	(66.1±25.3)%	(67.9±24.3)%	0.056
Intraoperative bleeding, mL	48.8±45.1	49.4±69.1	47.4±35.5	50.6±31.9	0.764
Intraoperative blood transfusion, mL	0	0	0	0	–
Length of operation, min	133.3±36.4	125.6±33.0	136.1±39.7	135.1±32.2	0.010
Amount of intraoperative fluids, mL	1,545.3±415.2	1,500.7±386.1	1,578.4±433.6	1,526.0±404.4	0.164
Infusion rate of intraoperative total fluids, mL/kg/h	11.6±3.8	12.2±3.7	12.3±4.0	11.6±3.8	0.158
Total intravenous crystalloid infusion 24 h postoperatively, mL	1,254.7±278.0	877.4±120.2	1,259.3±82.2	1,577.8±163.5	<0.001
Total intravenous colloid infusion 24 h postoperatively, mL	0	0	0	0	–
NSCLC staging, n (%)					0.245
IA	455 (80.8)	107 (78.7)	224 (82.4)	124 (80.0)	
IB	39 (6.9)	8 (5.9)	21 (7.7)	10 (6.5)	
IIA	34 (6.0)	9 (6.6)	10 (3.7)	15 (9.7)	
IIB	2 (0.4)	1 (0.7)	1 (0.4)	0 (0.0)	
IIIA	33 (5.9)	11 (8.1)	16 (5.9)	6 (3.9)	
Postoperative pathology, n (%)					0.976
Adenocarcinoma	513 (91.1)	125 (91.9)	247 (90.8)	141 (91.0)	
Squamous cell carcinoma	43 (7.6)	10 (7.4)	21 (7.7)	12 (7.7)	
Adenosquamous carcinoma	7 (1.2)	1 (0.7)	4 (1.5)	2 (1.3)	

Values are presented as mean ± standard deviation, n or n (%). ASA, American Society of Anesthesiologists; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; PEF, peak expiratory flow; FEV1%, FEV1 as percentage of predicted; FVC%, FVC as percentage of predicted; PEF%, PEF as percentage of predicted; NSCLC, non-small cell lung cancer.

Table 2 Effect of total intravenous crystalloid infusion 24 hours postoperatively on postoperative outcomes (three groups)

Postoperative outcome	Total intravenous crystalloid infusion 24 h postoperatively			Total P value
	Restrictive group (n=136), <1,080 mL	Moderate group (n=272), 1,080–<1,410 mL	Liberal group (n=155), ≥1,410 mL	
Postoperative pulmonary complications				
Acute respiratory distress syndrome, n (%)	2 (1.5)	1 (0.4)	1 (0.6)	0.291
Reintubation, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	–
Pulmonary embolism, n (%)	2 (1.5)	1 (0.4)	0 (0.0)	0.344
Need for bedside bronchoscopy, n (%)	4 (2.9)	0 (0.0)	0 (0.0)	1.000
Prolonged air leak, n (%)	5 (3.7)	6 (2.2)	2 (1.3)	0.529
Failure to expand, n (%)	1 (0.7)	6 (2.2)	6 (3.9)	0.261
Atelectasis, n (%)	6 (4.4)	2 (0.7)	5 (3.2)	0.083
Pneumonia				<0.001
N (%)	24 (17.6)	37 (13.6)	49 (31.6)	
OR (95% CI)	1.390 (0.779–2.478)	1	2.869 (1.750–4.703)	
P value	0.265	–	<0.001	
Patients with pulmonary complications				<0.001
N (%)	36 (26.5)	45 (16.5)	55 (35.5)	
OR (95% CI)	1.815 (1.083–3.043)	1	2.692 (1.684–4.305)	
P value	0.024	–	<0.001	
Acute kidney injury, n (%)	3 (2.2)	8 (2.9)	2 (1.3)	0.464
In-hospital mortality, n (%)	0	0	0	–
Readmission within 30 days, n (%)	0 (0.0)	1 (0.4)	5 (3.2)	0.114
Prolonged hospital stay, n (%)	25 (18.4)	31 (11.4)	14 (9.0)	0.077
Postoperative length of stay, days	5.9±1.9	5.8±2.1	5.9±2.3	0.572
Total hospital care costs (yuan renminbi)	58,388.4±8,998.8	57,830.2±10,036.1	59,133.9±9,808.9	0.262

Results of binary logistics regression are presented as adjusted OR, 95% CI, and P value. The best-performing moderate group served as the reference group. OR, odds ratio; CI, confidence interval.

significant. All analyses were performed using SPSS 25.0 (IBM Corp., Armonk, NY, USA) (8,12).

Results

Patient selection and comparative univariate analysis

A total of 563 patients were deemed eligible for analysis after our inclusion and exclusion criteria were applied (*Figure 1*). Of these, 136 (24.2%) patients with pulmonary complications and 13 (2.3%) patients with AKI were observed (Table S1). No patient died during the postoperative hospitalization (Table S1). *Table 1* and Table S1 list the baseline characteristics of the cohort and the results of comparative univariate analysis.

Comparative multivariate analysis of three groups of different total intravenous crystalloid infusion in the 24-hour postoperative period

We included statistically significant factors in univariate analysis in our multivariate regression model in order to determine the degree of contribution of total intravenous crystalloid infusion 24 hours postoperatively on postoperative outcomes (Table S3).

Binary logistics regression analysis demonstrated the incidence of postoperative pulmonary complications was lowest in the moderate group (*Table 2* and Table S3). In comparison, the risk for postoperative pulmonary complications was significantly increased in the restrictive group (OR 1.815, 95% CI: 1.083–3.043; P=0.024) and

liberal group (OR 2.692, 95% CI: 1.684–4.305; P<0.001; *Table 2*). AKI incidence among the three groups was similar (P=0.464; *Table 2*).

No deaths occurred in the three groups during hospitalization. Binary logistics regression analysis demonstrated that the incidences of readmission within 30 days (P=0.114) and prolonged hospital stay (P=0.077) were similar among the three groups (*Table 2*). There were also no statistical differences in postoperative length of stay (P=0.572) or total hospital care costs (P=0.262) among the three groups according to the multiple linear regression model (*Table 2*).

A separate binary logistics regression analysis was performed for each of the postoperative pulmonary complications. The results showed that the incidence of pneumonia was lowest in the moderate group (*Table 2* and Table S3). Compared with that in the moderate group, the risk for pneumonia in the liberal group was significantly increased (OR 2.869, 95% CI: 1.750–4.703; P<0.001) while that in the restrictive group was increased but not significantly so (P=0.265; *Table 2*). The incidences of other postoperative pulmonary complications (including ARDS, reintubation, pulmonary embolism, need for bedside bronchoscopy, prolonged air leak, failure of the lung to expand, and atelectasis) were similar among the three groups (*Table 2*).

In addition, we also classified patients into four groups representing the incremental quartiles of the exposure variable of the total intravenous crystalloid infusion in the 24-hour postoperative period. The baseline characteristics and comparative univariate results of the 4 groups are presented in Table S4 and Table S5 while the results of multivariate analysis are presented in Tables S6-S8.

Discussion

In an analysis of 563 patients with NSCLC who underwent VATS lobectomy, we observed a robust association between total intravenous crystalloid infusion in the 24-hour postoperative period and postoperative pulmonary complications (*Table 2*). The major finding of this study was that for patients with NSCLC who underwent VATS lobectomy, restrictive (<1,080 mL) or liberal (≥1,410 mL) 24-hour postoperative crystalloid infusion led to an increased incidence of postoperative pulmonary complications, while moderate 24-hour postoperative crystalloid infusion (1,080–<1,410 mL) led to optimal outcomes (*Table 2*).

In clinical practice, patients undergoing surgery display large differences in postoperative fluid volume. This variability results from the diversity in habits of clinicians and the occurrence of some emergencies that require increased infusions (e.g., postoperative bleeding and hypotension). As there is currently no clinically applicable standard for the amount of 24-hour postoperative fluid to be administered after VATS lobectomy, clinicians use a relatively random amount of 24-hour postoperative fluid volume (6). Institution-specific protocols for postoperative fluid therapy should be developed, and our present study provides some references for clinical 24-hour postoperative fluid management.

Perioperative intravenous-fluid therapy serves to restore and maintain body water, electrolytes, and organ perfusion to achieve homeostasis (13). Avoiding excessive intravenous fluid is commonly recommended in programs for enhanced recovery after surgery (14). The harmful effects of fluid excess frequently manifest in the lungs, especially after pulmonary resections (4,8). Fluid overload can precipitate pulmonary edema and impair gas exchange, leading to postoperative pulmonary complications such as pneumonia, respiratory failure, and reintubation (8). Arslantas *et al.* reported that excessive perioperative infusion fluid during pulmonary resection results in an increased incidence of postoperative pulmonary complications (4). Pang *et al.* conducted a meta-analysis of perioperative fluid administration, and the results showed that perioperative liberal fluid administration could increase postoperative pulmonary and cardiac complications compared with perioperative restrictive fluid administration (15). However, excessive perioperative fluid restriction can be harmful (11,16); for instance, fluid restriction can cause hypovolemia and postoperative organ dysfunction (17). Shin *et al.* found that both the restrictive and liberal types of perioperative fluid administration are associated with an increased risk of postoperative pulmonary complications and increased 30-day mortality (8). Our previous study also indicated both restrictive and liberal intraoperative fluid administration to be related to adverse effects on postoperative outcomes in patients undergoing minimally invasive lobectomy (12). In our previous study, postoperative pneumonia was defined as a new pulmonary infiltrate on chest X-ray with leukocytosis and fever (ear temperature >37.5 ℃) (12). However, after the article was published, some readers pointed out that the incidence of postoperative pneumonia (37.9%) was too high. Therefore, in this study, the diagnosis of postoperative pneumonia was made if a new pulmonary infiltrate, with

leukocytosis and fever (ear temperature >38.0 ℃), was evident on chest X-ray. This change led to the absence of a significant correlation between the infusion rates of intraoperative total fluid and postoperative pulmonary complications in multivariate analysis (Table S8), but we did find that the total intravenous crystalloid infusion in the 24-hour postoperative period was significantly associated with postoperative pulmonary complications. Our current study further suggests that moderation rather than extremes of fluid balance in the 24-hour postoperative period produces optimal outcomes.

Another finding of this study was that postoperative pneumonia, atelectasis, prolonged air leak, and failure of the lung to expand were the main 4 postoperative pulmonary complications in patients undergoing minimally invasive lobectomy, with incidences of 19.5%, 2.3%, 2.3%, and 2.3%, respectively (Table S1). Binary logistics regression analysis showed significant differences in the incidence of postoperative pneumonia across the three groups, with the result of the moderate group being the best (*Table 2*). This statistical difference regarding postoperative pneumonia was similar to the difference regarding the total postoperative pulmonary complications among the three groups of different total intravenous crystalloid infusion in the 24-hour postoperative period.

In recent years, the safety of perioperative fluid restriction has been questioned by many clinicians (15), with AKI being considered as the main adverse outcome of perioperative fluid restriction (16,18). AKI can be induced by renal hypoperfusion, and inadequate perioperative fluid administration is detrimental to kidney function (19,20). However, in our study, there were no differences in postoperative AKI incidence among the groups treated with the restrictive, moderate, and liberal 24-hour postoperative fluid therapies. This may be related to our research population. For one, we excluded patients with preoperative renal dysfunction, so the included cases had a good reserve of renal function. For another, all patients began to eat freely after 6–8 hours of postoperative recovery and therefore were unlikely to experience excessive organ hypoperfusion.

There were no deaths during hospitalization in this study, and this result is consistent with a previous report (3). Differences in the incidence of postoperative pulmonary complications did not result in significant differences in readmission within 30 days, prolonged hospital stay, postoperative length of stay, or total hospital care costs among the groups treated with the restrictive, moderate, or liberal 24-hour postoperative fluid therapy (*Table 2*). This may be because, among the pulmonary complications, pneumonia has the highest incidence. Most of the patients with postoperative pneumonia recovered quickly after short-term antibiotic treatment, which did not affect the postoperative length of stay. However, the diagnosis of postoperative pneumonia, especially the occurrence of postoperative fever >38.0 ℃, may cause discomfort and anxiety in the patient and should be paid attention to by the surgeon.

Limitations

Several limitations in our study should be noted. First, due to the retrospective nature of our current analyses, our findings should be regarded as step toward hypothesis generation, and a causal relationship between the postoperative fluid therapy and risk of postoperative complications could not be determined. Theoretically, the amount of fluid therapy can be greatly affected by postoperative complications. Therefore, we only selected 24-hour postoperative fluid therapy as an exposure variable, and most of the postoperative complications did not occur during the 24 hours postoperatively. Second, the American Society of Anesthesiologists (ASA) score, diabetes mellitus, and length of operation among groups were uneven. This imbalance can only be resolved through a prospective randomized trial. Therefore, we included all the above variables as potential confounders in the multivariate regression model to obtain reliable results. Third, we did not count the total fluid intake in the 24-hour postoperative period because the amount of oral fluid was not recorded in the medical records. However, the most important influence on cardiopulmonary function is the intravenous fluid infusion, and the effect of oral fluid is limited. Finally, we could not control the perioperative administration of drugs. The crystalloid used after surgery includes 5% glucose or 0.9% NaCl. In addition to these fluids, each patient was treated with antibiotics and the antiphlegmatic drug Mucosolvan until the removal of chest tubes; these actions were closely related to postoperative pulmonary complications. Although our study has these drawbacks, because the patients are a relatively homogeneous population and were treated uniformly at a single center, we believe that our data and the analysis results are reliable. To address these limitations, a subsequent, well-designed, randomized controlled study is necessary.

Conclusions

In conclusion, total intravenous crystalloid infusion in the 24-hour postoperative period was associated with postoperative pulmonary complications in patients with NSCLC undergoing VATS lobectomy. We have found both the restrictive and liberal 24-hour postoperative crystalloid infusions to be related to adverse effects on postoperative outcomes. In patients undergoing VATS lobectomy, the optimal volume of 24-hour postoperative intravenous crystalloid infusion is 1,080–<1,410 mL. Our current study provides evidence for clinicians to reconsider the management of postoperative fluid during VATS lobectomy.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-707/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-707/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-707/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The Medical Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China, approved the study (No. 2017-58). Due to the retrospective research method used in this study, no intervention was taken, and the Medical Ethics Committee agreed to waive the patients' informed consent. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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Supplementary

Table S1 Univariate analysis of postoperative outcomes based on the three groups treated with different total intravenous crystalloid infusions 24 hours postoperatively

Postoperative outcome	Total intravenous crystalloid infusion 24 h postoperatively				P value
	Total (n=563)	Restrictive group (<1,080 mL) (n=136)	Moderate group (1,080–<1,410 mL) (n=272)	Liberal group (≥1,410 mL) (n=155)	
Postoperative pulmonary complications	160	44	53	63	–
Acute respiratory distress syndrome	4 (0.7%)	2 (1.5%)	1 (0.4%)	1 (0.6%)	0.494
Reintubation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
Pulmonary embolism	3 (0.5%)	2 (1.5%)	1 (0.4%)	0 (0.0%)	0.189
Need for bedside bronchoscopy	4 (0.7%)	4 (2.9%)	0 (0.0%)	0 (0.0%)	0.003
Prolonged air leak	13 (2.3%)	5 (3.7%)	6 (2.2%)	2 (1.3%)	0.403
Failure to expand	13 (2.3%)	1 (0.7%)	6 (2.2%)	6 (3.9%)	0.179
Atelectasis	13 (2.3%)	6 (4.4%)	2 (0.7%)	5 (3.2%)	0.035
Pneumonia	110 (19.5%)	24 (17.6%)	37 (13.6%)	49 (31.6%)	<0.001
Patients with pulmonary complications	136 (24.2%)	36 (26.5%)	45 (16.5%)	55 (35.5%)	<0.001
Acute kidney injury	13 (2.3%)	3 (2.2%)	8 (2.9%)	2 (1.3%)	0.523
In-hospital mortality	0	0	0	0	–
Readmission within 30 days	6 (1.1%)	0 (0.0%)	1 (0.4%)	5 (3.2%)	0.011
Prolonged hospital stay	70 (12.4%)	25 (18.4%)	31 (11.4%)	14 (9.0%)	0.042
Postoperative length of stay, days	5.9±2.1	5.9±1.9	5.8±2.1	5.9±2.3	0.819
Total hospital care costs (yuan renminbi)	58,324.0±9730.7	58,388.4±8998.8	57,830.2±10,036.1	59,133.9±9,808.9	0.411

Values are presented as mean ± standard deviation, n or n (%).

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Table S2 Assignment of variables in multivariate analysis of the three groups treated with different total intravenous crystalloid infusions 24 hours postoperatively

Variable	Assignment instruction
ASA score	ASA I =1, ASA II =2, ASA III =3
Diabetes mellitus	No =0, yes =1
Length of operation	<2 h =1, 2 h– =2
Total intravenous crystalloid infusion in the postoperative 24 h	<1,080 mL =1, 1,080–<1,410 mL =2, ≥1,410 mL =3

ASA, American Society of Anesthesiologists.

Table S3 Full-model multivariate results of the three groups treated with different total intravenous crystalloid infusions 24 hours postoperatively

Variables	Pneumonia			Pulmonary complications		
	OR	95% CI	P value	OR	95% CI	P value
ASA score			0.007			<0.001
I	1.000			1.000		
II	3.251	1.466–7.211	0.004	4.164	1.883–9.208	<0.001
III	0.469	0.103–2.131	0.327	0.363	0.081–1.630	0.186
Diabetes mellitus						
No	1.000			1.000		
Yes	0.188	0.056–0.628	0.007	0.246	0.086–0.702	0.009
Length of operation						
<2 h	1.000			1.000		
2 h–	0.940	0.599–1.475	0.788	1.122	0.735–1.713	0.594
Total intravenous crystalloid infusion 24 h postoperatively			<0.001			<0.001
<1,080 mL	1.390	0.779–2.478	0.265	1.815	1.083–3.043	0.024
1,080–<1,410 mL	1.000			1.000		
≥1,410 mL	2.869	1.750–4.703	<0.001	2.692	1.684–4.305	<0.001

Results of binary logistics regression are presented as adjusted OR, 95% CI, and P value. ASA, American Society of Anesthesiologists; OR, odds ratio.

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Table S4 Clinical characteristics of patients in the 4 groups treated with different total intravenous crystalloid infusions 24 hours postoperatively

Characteristic	Total intravenous crystalloid infusion 24 h postoperatively					P value
	Total (n=563)	Quartile 1 (n=136), <1,080 mL	Quartile 2 (n=136), 1,080–<1,290 mL	Quartile 3 (n=136), 1,290–<1,410 mL	Quartile 4 (n=155), ≥1,410 mL	
ASA score						0.001
I	472 (83.8%)	100 (73.5%)	127 (93.4%)	117 (86.0%)	128 (82.6%)	
II	68 (12.1%)	29 (21.3%)	6 (4.4%)	15 (11.0%)	18 (11.6%)	
III	23 (4.1%)	7 (5.1%)	3 (2.2%)	4 (2.9%)	9 (5.8%)	
Age (year)	63.2±10.7	64.1±11.3	63.3±9.9	62.0±11.0	63.4±10.5	0.440
Gender (female/male)	336/227	76/60	82/54	82/54	96/59	0.756
Weight, kg	61.4±9.8	62.3±10.3	60.5±9.6	60.7±9.6	61.9±9.7	0.354
Smoking	156 (27.7%)	35 (25.7%)	47 (34.6%)	36 (26.5%)	38 (24.5%)	0.227
Diabetes mellitus	48 (8.5%)	25 (18.4%)	2 (1.5%)	13 (9.6%)	8 (5.2%)	<0.001
Coronary heart disease	9 (1.6%)	3 (2.2%)	2 (1.5%)	2 (1.5%)	2 (1.3%)	0.937
FEV1, L	2.3±0.6	2.3±0.6	2.3±0.6	2.3±0.5	2.3±0.6	0.930
FVC, L	2.9±0.7	2.9±0.8	3.0±0.8	2.9±0.7	2.9±0.8	0.898
PEF, L/s	4.7 ±1.9	4.9 ±1.8	4.8 ±2.0	4.3 ±1.8	4.7 ±1.9	0.033
FEV1%	(91.1±17.2)%	(90.9±18.5)%	(91.4±18.2)%	(91.3±16.4)%	(90.8±16.1)%	0.986
FVC%	(91.3±15.7)%	(89.8±15.8)%	(92.6±16.6)%	(90.5±14.8)%	(92.1±15.6)%	0.410
PEF%	(67.6±24.0)%	(70.4±20.4)%	(69.9±27.4)%	(62.4±22.6)%	(67.9±24.3)%	0.011
Intraoperative bleeding, mL	48.8±45.1	49.4±69.1	42.1±22.0	52.6±44.5	50.6±31.9	0.239
Intraoperative blood transfusion, mL	0	0	0	0	0	-
Length of operation, min	133.3±36.4	125.6±33.0	133.8±41.5	138.4±37.7	135.1±32.2	0.012
Amount of intraoperative fluids, mL	1,545.3±415.2	1,500.7±386.1	1,609.3±446.4	1,547.8±419.8	1,526.0±404.4	0.165
Infusion rate of intraoperative total fluids, mL/kg/h	12.1±3.9	12.2±3.7	12.8±4.2	11.7±3.7	11.6±3.8	0.028
Total intravenous crystalloid infusion 24 h postoperatively, mL	1,254.7±278.0	877.4±120.2	1,194.5±61.8	1,324.0±36.2	1,577.8±163.5	<0.001
Total intravenous colloid infusion 24 h postoperatively, mL	0	0	0	0	0	-
NSCLC staging						0.003
IA	455 (80.8%)	107 (78.7%)	112 (82.4%)	112 (82.4%)	124 (80.0%)	
IB	39 (6.9%)	8 (5.9%)	9 (6.6%)	12 (8.8%)	10 (6.5%)	
IIA	34 (6.0%)	9 (6.6%)	1 (0.7%)	9 (6.6%)	15 (9.7%)	
IIB	2 (0.4%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	
IIIA	33 (5.9%)	11 (8.1%)	14 (10.3%)	2 (1.5%)	6 (3.9%)	
Postoperative pathology						0.180
Adenocarcinoma	513 (91.1%)	125 (91.9%)	118 (86.8%)	129 (94.9%)	141 (91.0%)	
Squamous cell carcinoma	43 (7.6%)	10 (7.4%)	14 (10.3%)	7 (5.1%)	12 (7.7%)	
Adenosquamous carcinoma	7 (1.2%)	1 (0.7%)	4 (2.9%)	0 (0.0%)	2 (1.3%)	

Values are presented as mean ± standard deviation, n or n (%). ASA, American Society of Anesthesiologists; FEV1, forced expiratory volume in 1 s; FEV1%, FEV1 as percentage of predicted; FVC, forced vital capacity; FVC%, FVC as percentage of predicted; NSCLC, non-small cell lung cancer; PEF, peak expiratory flow; PEF%, PEF as percentage of predicted.

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Table S5 Univariate analysis of postoperative outcomes based on the 4 groups treated with different total intravenous crystalloid infusions 24 hours postoperatively

Postoperative outcome	Total intravenous crystalloid infusion 24 h postoperatively					P value
	Total (n=563)	Quartile 1 (n=136), <1,080 mL	Quartile 2 (n=136), 1,080–<1,290 mL	Quartile 3 (n=136), 1,290–<1,410 mL	Quartile 4 (n=155), ≥1,410 mL	
Postoperative pulmonary complications	160	44	29	24	63	-
Acute respiratory distress syndrome	4 (0.7%)	2 (1.5%)	1 (0.7%)	0 (0.0%)	1 (0.6%)	0.423
Reintubation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Pulmonary embolism	3 (0.5%)	2 (1.5%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0.193
Need for bedside bronchoscopy	4 (0.7%)	4 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.010
Prolonged air leak	13 (2.3%)	5 (3.7%)	2 (1.5%)	4 (2.9%)	2 (1.3%)	0.473
Failure to expand	13 (2.3%)	1 (0.7%)	3 (2.2%)	3 (2.2%)	6 (3.9%)	0.329
Atelectasis	13 (2.3%)	6 (4.4%)	0 (0.0%)	2 (1.5%)	5 (3.2%)	0.024
Pneumonia	110 (19.5%)	24 (17.6%)	22 (16.2%)	15 (11.0%)	49 (31.6%)	<0.001
Patients with pulmonary complications	136 (24.2%)	36 (26.5%)	25 (18.4%)	20 (14.7%)	55 (35.5%)	<0.001
Acute kidney injury	13 (2.3%)	3 (2.2%)	4 (2.9%)	4 (2.9%)	2 (1.3%)	0.730
In-hospital mortality, n	0	0	0	0	0	-
Readmission within 30 days	6 (1.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	5 (3.2%)	0.015
Prolonged hospital stay	70 (12.4%)	25 (18.4%)	18 (13.2%)	13 (9.6%)	14 (9.0%)	0.066
Postoperative length of stay, days	5.9±2.1	5.9±1.9	6.0±2.3	5.7±2.0	5.9±2.3	0.628
Total hospital care costs (yuan renminbi)	58,324.0±9,730.7	58,388.4±8,998.8	56,969.0±11,300.1	58,691.4±8544.4	59,133.9±9,808.9	0.272

Values are presented as mean ± standard deviation, n or n (%).

Table S6 Assignment of variables in multivariate analysis of the 4 groups treated with different total intravenous crystalloid infusions 24 hours postoperatively

Variable	Assignment instruction
ASA score	ASA I =1, ASA II =2, ASA III =3
Diabetes mellitus	No =0, Yes =1
Length of operation	<2 h =1, 2 h– =2
Infusion rate of intraoperative total fluids (quartile)	<9.3 mL/kg/h =1, 9.3–<11.6 mL/kg/h =2, 11.6–<14.2 mL/kg/h =3, ≥14.2 mL/kg/h =4
NSCLC staging	IA =1, IB =2, IIA =3, IIB =4, IIIA =5
PEF%	<60% =2, 60%– =1
Total intravenous crystalloid infusion 24 h postoperatively (quartile)	<1,080 mL =1, 1,080–<1,290 mL =2, 1,290–<1,410 mL =3, ≥1,410 mL =4

ASA, American Society of Anesthesiologists; NSCLC, non-small cell lung cancer; PEF%, peak expiratory flow as a percentage of predicted.

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Table S7 Effect of total intravenous crystalloid infusion 24 hours postoperatively on postoperative outcomes (4 groups)

Postoperative outcome	Total intravenous crystalloid infusion 24 h postoperatively				TOTAL P value
	Quartile 1 (n=136), <1080 mL	Quartile 2 (n=136), 1080–<1290 mL	Quartile 3 (n=136), 1290–<1410 mL	Quartile 4 (n=155), ≥1410 mL	
Postoperative pulmonary complications					
Acute respiratory distress syndrome, n (%)	2 (1.5%)	1 (0.7%)	0 (0.0%)	1 (0.6%)	0.660
Reintubation, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
Pulmonary embolism, n (%)	2 (1.5%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0.903
Need for bedside bronchoscopy, n (%)	4 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.000
Prolonged air leak, n (%)	5 (3.7%)	2 (1.5%)	4 (2.9%)	2 (1.3%)	0.518
Failure to expand, n (%)	1 (0.7%)	3 (2.2%)	3 (2.2%)	6 (3.9%)	0.458
Atelectasis, n (%)	6 (4.4%)	0 (0.0%)	2 (1.5%)	5 (3.2%)	0.490
Pneumonia					<0.001
n (%)	24 (17.6%)	22 (16.2%)	15 (11.0%)	49 (31.6%)	
OR (95% CI), P value	1.716 (0.812–3.628), 0.157	1.566 (0.741–3.312), 0.240	1	3.702 (1.908–7.186), <0.001	
Patients with pulmonary complications					<0.001
n (%)	36 (26.5%)	25 (18.4%)	20 (14.7%)	55 (35.5%)	
OR (95% CI), P value	2.007 (1.036–3.889), 0.039	1.331 (0.667–2.654), 0.417	1	3.250 (1.774–5.956), <0.001	
Acute kidney injury, n (%)	3 (2.2%)	4 (2.9%)	4 (2.9%)	2 (1.3%)	0.414
In-hospital mortality, n (%)	0	0	0	0	–
Readmission within 30 days, n (%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	5 (3.2%)	0.656
Prolonged hospital stay, n (%)	25 (18.4%)	18 (13.2%)	13 (9.6%)	14 (9.0%)	0.150
Postoperative length of stay, days	5.9±1.9	6.0±2.3	5.7±2.0	5.9±2.3	0.239
Total hospital care costs (yuan renminbi)	58,388.4±8,998.8	56,969.0±11,300.1	58,691.4±8,544.4	59,133.9±9,808.9	1.000

Results of binary logistics regression are presented as adjusted OR, 95% CI, and P value. The best-performing quartile 3 served as the reference group. OR, odds ratio.

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Table S8 Full-model multivariate results of the 4 groups treated with different total intravenous crystalloid infusions 24 hours postoperatively

Variables	Pneumonia			Pulmonary complications		
	OR	95% CI	P value	OR	95% CI	P value
ASA score			0.001			<0.001
I	1.000			1.000		
II	4.955	2.048–11.988	<0.001	5.930	2.483–14.163	<0.001
III	0.414	0.084–2.045	0.279	0.344	0.072–1.647	0.182
Diabetes mellitus						
No	1.000			1.000		
Yes	0.122	0.034–0.432	0.001	0.174	0.057–0.530	0.002
Length of operation						
<2 h	1.000			1.000		
2 h–	1.106	0.662–1.846	0.701	1.272	0.785–2.061	0.329
Infusion rate of intraoperative total fluids (quartile)			0.751			0.419
<9.3 mL/kg/h	1.000			1.000		
9.3–<11.6 mL/kg/h	0.747	0.398–1.404	0.365	0.654	0.364–1.175	0.156
11.6–<14.2 mL/kg/h	0.763	0.404–1.441	0.405	0.650	0.358–1.180	0.157
≥14.2 mL/kg/h	0.742	0.377–1.462	0.389	0.795	0.428–1.477	0.469
NSCLC staging			0.101			0.199
IA	1.000			1.000		
IB	0.084	0.011–0.659	0.018	0.299	0.095–0.940	0.039
IIA	1.272	0.470–3.443	0.636	1.060	0.400–2.808	0.907
IIB	6.079	0.345–107.022	0.217	5.469	0.309–96.751	0.246
IIIA	1.366	0.565–3.305	0.489	1.274	0.547–2.967	0.575
PEF%						
60%–	1.000			1.000		
<60%	1.278	0.806–2.029	0.297	1.159	0.750–1.789	0.506
Total intravenous crystalloid infusion in the postoperative 24 h (quartile)			<0.001			<0.001
<1,080 mL	1.716	0.812–3.628	0.157	2.007	1.036–3.889	0.039
1,080–<1,290 mL	1.566	0.741–3.312	0.240	1.331	0.667–2.654	0.417
1,290–<1,410 mL	1.000			1.000		
≥1,410 mL	3.702	1.908–7.186	<0.001	3.250	1.774–5.956	<0.001

Results of binary logistics regression are presented as adjusted OR, 95% CI, and P value. ASA, American Society of Anesthesiologists; NSCLC, non-small cell lung cancer; OR, odds ratio; PEF%, peak expiratory flow as a percentage of predicted.

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