Effect of the amount of intraoperative fluid administration on postoperative pulmonary complications following anatomic lung resections

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Objective: Excessive fluid administration during lung resections is a risk for pulmonary injury. We analyzed the effect of intraoperative fluids on postoperative pulmonary complications (PCs).

Methods: Patients who underwent anatomic pulmonary resections during 2012 to 2013 were included. Age, weight, pulmonary function data, smoking (pack-years), the infusion rate and the total amount of intraoperative fluids (including crystalloid, colloid, and blood products), duration of anesthesia, hospital stay, PCs, and mortality were recorded. PCs were defined as acute respiratory distress syndrome, need for intubation, bronchoscopy, atelectasis, pneumonia, prolonged air leak, and failure to expand. Univariate analyses and multivariate logistic regression were performed. A Lowess curve was drawn for intraoperative fluid threshold.

Results: In 139 patients, types of resections were segmentectomy-lobectomy (n = 69; extended n = 37; video-assisted thoracoscopic surgery n = 19) and pneumonectomy (n = 9; extended n = 5). One hundred sixty-one PCs were observed in 76 patients (acute respiratory distress syndrome [n = 5], need for intubation [n = 9], atelectasis [n = 60], need for bronchoscopy [n = 19], pneumonia [n = 26], prolonged air leak [n = 19], and failure to expand [n = 23]). Overall mortality was 4.3% (6 out of 139 patients). Mean hospital stay was 8.5 ± 4.8 days. Univariate analyses showed that smoking, intraoperative total amount of fluids, crystalloids, blood products, and infusion rate as well as total amount of crystalloids and infusion rate during the postoperative first 48 hours were significant for PCs ($P = .033$, $P < .0001$, $P = .001$, $P = .03$, $P < .0001$, $P = .002$, and $P < .0001$, respectively). In multivariate logistic regression analysis intraoperative infusion rate ($P < .0001$) and smoking were significant ($P = .023$). An infusion rate of 6 mL/kg/h was found to be the threshold.

Conclusions: The occurrence of postoperative PCs is seen more frequently if the intraoperative infusion rate of fluids exceeds 6 mL/kg/h. (J Thorac Cardiovasc Surg 2015;149:314-2)

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Pulmonary resection is a major surgical procedure that carries a mortality risk of 1% to 7% depending on the extent of lung tissue removed.[1] This is due to poor cardiopulmonary status secondary to the presence of tumor or infection, chronic obstructive pulmonary disease, or heavy smoking. This risk is further increased by surgical trauma with removal of lung tissue and perioperative factors such as single lung ventilation and increase in pulmonary vascular resistance. The main causes of morbidity and mortality following pulmonary resections are of pulmonary origin, mainly pneumonia, acute lung injury (ALI), and acute respiratory distress syndrome (ARDS), whereas cardiac and surgical complications have decreased over the decades.[2-4]

There are several well-designed, single center studies that show a significant correlation between the amount of intra- and postoperative fluid infused and postoperative ALI and ARDS.[4-8] Surgery causes a stress response of endocrine and inflammatory origin, which leads to conservation of sodium and water and excretion of potassium mediated by antidiuretic hormone, aldosterone,

Abbreviations and Acronyms

ALI = acute lung injury
ARDS = acute respiratory distress syndrome
PC = pulmonary complications

and the renin-angiotensin II system.[9] The association of excessive fluid administration and occurrence of pulmonary edema after pneumonectomy was reported in 10 patients by Zeldin and colleagues[10] and assumptions were shown to be correct in a subsequent dog model. As a result, the amount and type of fluid administered during and after pulmonary resection have been the subject of debate, but no randomized studies exist in the thoracic surgery literature that address the use of different fluid protocols.

There are randomized studies in the literature that evaluate the outcome of patients with liberal and restrictive fluid administration intraoperatively, 6 in major abdominal surgery patients and 1 in a knee arthroplasty patient.[9] Whereas 3 of these studies showed improved outcomes, 2 showed improvement in certain parameters and 2 showed no changes with restrictive fluid administration for pulmonary complications (PCs).[11,12] In a recent randomized study, restrictive intravenous fluid regimens in elderly patients with abdominal cancer showed better preservation of cellular immunity and a 50% decrease in pneumonia rate.[12]

Although there are several studies in that address the causes of ARDS in the postoperative period and its correlation with intraoperative fluid administration, there are no studies in the thoracic surgery literature that address the correlation between all types of PCs and intraoperative fluid administration. Thus we analyzed our results in patients who underwent anatomic pulmonary resections and the effect of intraoperative fluid management on PCs.

METHODS

One hundred thirty-nine patients (32 women, average age 56.8 ± 11.6 years) who underwent anatomic lung resection at Marmara University Hospital during January 2012 to September 2013 were included in the study. Detailed patient data of the whole cohort are shown in Tables 1 and E1. Indications for surgical resection were lung cancer (n = 124), bronchiectasis or destroyed lung (n = 13), lung metastasis (n = 1), and mesothelioma (n = 1). One hundred twelve patients had a history of smoking. The study was approved by the Ethical Council of Marmara University Faculty of Medicine. The study was initiated following a clinical observation of decreased pulmonary complications in patients who received fewer intraoperative fluids and the data were collected prospectively after that point, whereas some were retrieved from patient records. Demographic criteria (ie, age, gender, and comorbidities), pulmonary function tests, history and amount of smoking, type of resection, use of thoracic epidural analgesia, amount of intraoperative fluids (ie, crystalloid, colloid, and blood products separately recorded), length of operation, amount of fluids and rate of infusion of fluids during the postoperative 48 hours, postoperative pulmonary morbidities, other complications, in-hospital mortality, and length of hospital stay were recorded. We used hydroxyethyl starch and other artificial volume expanders as colloids. All patients received prophylactic first/second generation cephalosporins until removal of chest tubes, whereas patients with complex procedures (eg, postneoadjuvant treatment and extensive resections) typically received sulbactam ampicillin and ciprofloxacin. All patients started oral feedings in the sixth to eighth postoperative hour, unless they were intubated or at risk for aspiration.

Definition of PCs

Pulmonary morbidities were defined as ARDS, need for intubation, pneumonia, need for toilet bronchoscopy, atelectasis, prolonged air leak, and failure to expand. ARDS was defined as acute onset of hypoxemia with abnormal oxygenation ratios (arterial partial pressure of oxygen to fraction of inspired oxygen: ARDS < 300) and radiologic infiltrates characteristic of pulmonary edema according to the Berlin definition of ARDS guidelines.[13] Pneumonia was defined as a new pulmonary infiltrate with associated increase in white blood cells and fever. A sputum culture was obtained whenever possible; however, we did not specifically seek microbiologic proof. Atelectasis was defined as an area of no ventilation or collapse identified on chest radiograph that is reexpanded following chest physiotherapy or toilet bronchoscopy. All patients underwent bronchoscopy before extubation in the operating room and toilet bronchoscopy was accepted as an intervention to clear secretions in the lung following lung resection. Prolonged air leak was accepted as leak >7 days. Failure to expand was accepted as the inability of the remaining lung to completely fill the pleural cavity with or without air leak.

Comparative Analysis

The cohort was divided into 2 groups depending on the occurrence of pulmonary morbidity and 2 groups were analyzed using parametric Student *t* test and nonparametric χ^2 test and Mann-Whitney *U* tests. A multivariate stepwise logistic regression analysis was performed to determine factors affecting postoperative pulmonary morbidity. A Lowess smoothing curve was drawn with logit transformed values to determine the threshold value for the amount of intraoperative fluids that would be better associated with the occurrence of postoperative pulmonary complications.

RESULTS

Demographic characteristics, pulmonary function test results, and perioperative data and types of resections are shown in Tables 1 and E1. Eighty-two patients had preoperative comorbidities. There were only cardiac comorbidities in 15 patients; only pulmonary comorbidity in 15 patients, cardiopulmonary comorbidity in 7 patients, and multiple comorbidities in 45 patients. Diabetes mellitus was present in 20 patients. Seventy-two patients had thoracic epidural analgesia. Fifteen patients needed intraoperative infusion of blood products with 4 patients needing >1000 mL (range, 0-2400 mL). Ninety-three patients had bleeding <400 mL. Forty patients had intraoperative fluids at a >7 mL/kg/h rate and these were due to a combination of factors such as high preoperative creatinine values (>1 mg/dL) in 10 patients, bleeding in 8 patients, hypotension secondary to cardiac risk factors in 16 patients, and duration of anesthesia in 32 patients. Inotropes were used intraoperatively in 12 patients and duration of anesthesia was longer than 5 hours in 63 patients. After surgery, 55 patients were admitted to the intensive care unit, whereas 84 patients were followed in the thoracic surgery ward.

TABLE 1. Demographic and operative data of the entire cohort (n = 139)

Characteristic	Entire cohort
Age	56.8 ± 11.6
Gender (female/male)	32/107
Weight (kg)	76.9 ± 14.9
Forced expiratory volume in 1 second, L	2.73 ± 0.69
Forced vital capacity, L	3.58 ± 0.82
Smoking, pack-years	33 ± 26
Type of lung resection	
Lobectomy/segmentectomy	69
Video-assisted thoracoscopic surgery lobectomy/ segmentectomy	19
Extended lobectomy	37
Pneumonectomy	9
Extended pneumonectomy	5
Amount of intraoperative fluids, mL	
Total	2174 ± 1371
Crystalloid	1789 ± 953
Colloid*	0 (500)
Rate of infusion of intraoperative fluids, mL/kg/h	5.69 ± 3.24
Intraoperative bleeding, mL*	300 (350)
Urine output, mL*	250 (270)
Length of anesthesia, min	311 ± 83
Amount of postoperative crystalloid fluids, mL	1507 ± 553
Rate of infusion of postoperative fluids, mL/kg/h	0.42 ± 0.19
Patients with pulmonary complications, n	76
Total number of pulmonary complications	161
Acute respiratory distress syndrome	5 (3)
Need for intubation	9 (6)
Atelectasis	60 (37)
Need for toilet bronchoscopy	19 (12)
Pneumonia	26 (16)
Prolonged air leak	19 (12)
Failure to expand	23 (14)
In-hospital mortality, n	6
Length of hospital stay, d	8.5 ± 4.8

Values are presented as mean ± standard deviation, n, or n (%). *These variables had standard deviations higher than average, thus median and interquartile percentages are presented.

One hundred sixty-one pulmonary complications occurred in 76 patients (Table 1). Six patients died, 4 patients died secondary to respiratory failure/ARDS, 1 patient died secondary to respiratory failure and ARDS following right main bronchial stapler line disruption and unsuccessful subsequent repairs, and 1 patient died due to sepsis secondary to empyema. Surgical resections in those patients were left lower lobectomy (n = 2), right pneumonectomy (n = 1), right upper lobectomy with chest wall resection (n = 1), right upper lobectomy with Dartevelle approach (n = 1), and left upper bronchial and arterial sleeve lobectomy (n = 1).

Comparative Univariate and Multivariate Analysis

Total amount of smoking (pack-years); intraoperative total amount of crystalloids, blood products, and other types of fluids; infusion rate of intraoperative fluids; total amount of crystalloid fluids; infusion rate of fluids during the postoperative 48 hours; and mortality were significantly higher in the patients who developed pulmonary complications. Hospital stay was significantly longer in patients who developed pulmonary complications compared with those who did not (Table 2). There was no difference in the frequency of pulmonary complications between patients who had extended resections or pneumonectomy and standard lobectomy/segmentectomy.

We included statistically significant factors, namely total amount of smoking, the infusion rate of intraoperative fluids, intraoperative total amount of crystalloid fluids and blood products, and the total amount of crystalloid fluids during the postoperative 48 hours, to our multivariate logistic regression model to determine the degree of contribution of intraoperative fluids on postoperative pulmonary complications (odds ratios [OR], 1.02; 95% confidence interval [CI], 1.003-1.037; OR, 1.203; 95% CI, 0.99-1.461; OR, 1, 95% CI, 1-1.001; OR, 1; 95% CI, 0.999-1.002; and OR, 1.001; 95% CI, 1-1.002, respectively). Only 2 factors were found to be significant in stepwise analysis: total amount of smoking and rate of infusion of intraoperative fluids (OR, 1.019; 95% CI, 1.003-1.035 and OR, 1.3; 95% CI, 1.125-1.501; $P = .023$ and $P = .0001$, respectively).

Determination of Threshold Value for Infusion Rate of Intraoperative Fluids

Lowess curve for presence of pulmonary complications per patient and intraoperative infusion rate (Figure 1) showed a break value of 6 mL/kg/h. Additionally we analyzed intraoperative fluids as a continuous variable and calculated ORs for 3, 4, 5, 6, 7, and 8 mL to find the threshold value to predict postoperative pulmonary complications. ORs for infusion rates of 3, 4, 5, 6, 7, and 8 mL/kg/h were 2.3, 1.96, 1.92, 2.6, 2.6, and 6.4, respectively ($P = .04$, $P = .06$, $P = .06$, $P = .009$, $P = .02$, and $P < .001$, respectively). The initial break value for intraoperative infusion rate was found to be 6 mL/kg/h, whereas pulmonary complication rate was very high after 8 mL/kg/h.

DISCUSSION

Undergoing lung resection is a dynamic process that involves several pre-, intra- and postoperative variables. Pulmonary complications are the most important causes of morbidity and mortality in the postoperative period. In a series of 1139 patients who underwent lung resection in Royal Brompton Hospital during 1991 to 1997, overall mortality was 3.5%.[14] However, 72.5% of all postoperative deaths were due to ALI/ARDS. Better assessment of preoperative pulmonary functions and routine use of thoracic epidural analgesia has led to a lower incidence of pulmonary complications following thoracotomy. Licker and

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TABLE 2. Univariate analysis of results in patients who experienced pulmonary complications and who did not

Characteristic	Pulmonary complication (n = 76)	No pulmonary complication (n = 63)	*P* value
Age	57 ± 12.2	56.4 ± 10.9	.75
Gender (female/male)	17/59	15/48	.99
Weight, kg	77 ± 15.4	76.2 ± 13.1	.62
Forced expiratory volume in 1 second, L	2.64 ± 0.7	2.83 ± 0.67	.11
Forced vital capacity, L	3.49 ± 0.86	3.68 ± 0.76	.2
Smoking, pack-years	37 ± 29	28 ± 20	.033
Total amount of infused fluids, mL	2502 ± 1510	1778 ± 1064	.0001
Amount of crystalloid, mL	2030 ± 1004	1499 ± 804	.001
Amount of colloid, mL*	0 (500)	0 (500)	.49
Amount of blood products, mL†	0 (0-2400)	0 (0-2200)	.03
Intraoperative infusion rate of fluids, mL/kg/h	6.58 ± 3.64	4.61 ± 2.28	.0001
Intraoperative bleeding, mL*	350 (400)	250 (270)	.11
Intraoperative urine output, mL	380 ± 280	301 ± 203	.08
Patients with infusion of blood products	12	3	.053
Thoracic epidural analgesia (yes/no)	35/41	37/26	.23
Types of resections			.09
Lobe-segment	43	26	
Video-assisted thoracoscopic surgery lobe-segment	8	11	
Extended lobectomy	19	18	
Pneumonectomy	2	7	
Extended pneumonectomy	4	1	
Total intravenous crystalloid infusion in the postoperative 48 h, mL	1632 ± 601	1351 ± 444	.002
Intravenous fluid infusion rate in the postoperative 48 h, mL/kg/h	0.47 ± 0.21	0.35 ± 0.15	.0001
Length of anesthesia, min	312 ± 90	310 ± 75	.86
In-hospital mortality	6	0	.03
Length of hospital stay, d	10.4 ± 5.5	6.2 ± 2	.0001

Values are presented as mean ± standard deviation or n. *These variables had standard deviations higher than average, thus median and interquartile percentages are presented. †Median and interquartile range values were 0 in both groups, thus range is presented.

colleagues[3] showed a decrease in the incidence of pulmonary complications in various periods (18.7% vs 15.2% between 1990-1994 and 2000-2004, respectively). In the recent analysis of a Society of Thoracic Surgeons database of 18,800 patients (including 3621 wedge resections) who underwent lung cancer resections, major complications occurred in 7.9% of patients and mortality was 2.2%.[1] Pneumonia was observed in 722 patients, reintubation in 654 patients, and ARDS in 220 patients. Thus PCs are still the major cause of mortality following lung resection.

Several preoperative risk factors were identified for postoperative PCs. Licker and colleagues[3] showed that an forced expiratory volume in 1 second of <60% was associated with an increase in respiratory complications. In a study by Ferguson and Vigneswaran,[15] carbon monoxide diffusion capacity was found to be the most important predictor of postoperative PCs in patients with and without chronic obstructive pulmonary disease. A similar analysis of the Society of Thoracic Surgeons database in patients without chronic obstructive pulmonary disease reproduced the same results.[16] The study showed a 1.12-times increase in complications for each 10-points decrease in carbon monoxide diffusion capacity.[16] In other studies,[14,17] age > 60 years, preoperative chemotherapy, radiotherapy, male gender, and presence of lung cancer were found to be important. A more recent study[18] drew attention to the extent of perfusion in the lung that will be removed surgically. If the lung perfusion was <35%, incidence of ARDS was much lower.

In our patients, the only preoperative factor that was significantly different between patients with and without PCs was the amount of smoking. One hundred twelve of 139 patients had a history of smoking (61 out of 76 patients vs 51 out of 63 patients; not significant). Pulmonary function tests were similar (Table 2). We did not perform carbon monoxide diffusion capacity measurements. In patients with limited forced expiratory volume, we performed quantitative ventilation perfusion scans and stair climbing tests.

The intraoperative period involves a series of interventions that affect postoperative outcome during lung resections. These include double lumen intubation and single lung ventilation, use of thoracic epidural analgesia, duration of anesthesia, invasiveness of the surgical procedure (video-assisted thoracoscopic surgery vs open), magnitude of lung resection (segmentectomy, lobectomy, or pneumonectomy), intraoperative fluid resuscitation, and bleeding.[19]

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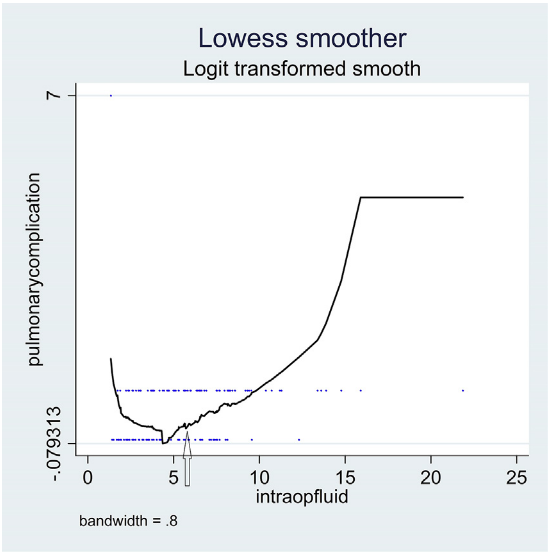

FIGURE 1. A logit-transformed Lowess smoothing curve shows a break value of intraoperative infusion rate of 6 mL/kg/h associated with the occurrence of postoperative pulmonary complications (*arrow*). The initial increased frequency of pulmonary complications (mainly pneumonia) was thought to be secondary to renal complications (need for dialysis or high creatinine values) due to very limited intraoperative fluid infusion.

It has been shown that single lung ventilation leads to an alteration in the endoepithelial interface of alveoli, thus decreasing the rate of fluid clearance in the alveoli.[19] Ventilator-induced lung injury during anesthesia is due to barotrauma (eg, pneumothorax or bronchopleural fistula), volutrauma (eg, ARDS/ALI), or contamination secondary to intubation (eg, pneumonia). One recent study demonstrated that protective lung ventilation during single lung ventilation (tidal volume 5.3 ± 1.1 vs 7.1 ± 1.2 mL/kg) resulted in a lower incidence of ALI and atelectasis, fewer admissions to the intensive care unit, and shorter hospital stay.[20] In all of our patients, we used a protective lung ventilation strategy with tidal volume 5 to 6 mL/kg with peak plateau pressure <30 mm H_2O.

Intraoperative infusion rate and type of fluids have been studied in various major surgeries and randomized studies have been performed to determine the outcomes and effects on pulmonary complications (Table 3).[3,5,6,12,20-23] One of the first studies to draw attention to the importance of intraoperative fluids was by Zeldin and colleagues.[9] They identified right pneumonectomy, excessive intraoperative fluid infusion, and increased postoperative urine output as the risk factors for postpneumonectomy pulmonary edema. However the study was criticized for lack of fluid input and output data in 6 of 10 patients. A study by Parquin and colleagues[6] found that infusion >2 L fluid intraoperatively was associated with a significantly higher incidence of postpneumonectomy pulmonary edema.

In thoracic surgery, we do not have adequate data to suggest a critical intraoperative fluid threshold, but Licker and colleagues[3,20] reported a total infusion volume of 1533 mL crystalloid and colloid intraoperatively in their initial report in 2006[3] and then an infusion rate of 5.8 ± 2.9 mL/kg/h in 2009.[20] Alam and colleagues[5] reported an intraoperative fluid volume of 2775 mL for patients undergoing lung resection for cancer. Our data show that an intraoperative infusion rate of 6 mL/kg/h is critical (Figure 1) and in our patients who had pulmonary complications total volume of intraoperative fluids was >2500 mL and average infusion rate was 6.6 ± 3.6 mL/kg/h (Table 2). The debate on restrictive, normal, or a liberal approach in intraoperative fluids has not been settled in thoracic surgery.[24] A strategy targeting normovolemia (1.5 mL/kg/h plus intraoperative losses) was found to be adequate in terms of maintaining normal creatinine levels.[24] A randomized study showed the role of protective lung ventilation (6 mL/kg tidal volume) as an important determinant of fluid responsiveness compared with conventional lung ventilation.[25] Another study[26] showed that goal-directed fluid therapy did not result in fluid overload in patients undergoing thoracotomy. Gao and colleagues[12] showed that in elderly patients with abdominal cancer, an intraoperative infusion rate of 7 mL/kg in the first hour, followed by 5 mL/kg in the consecutive hours, resulted in fewer overall and pulmonary complications and did not increase renal dysfunction. In our study, 2 patients experienced acute renal failure with the need for temporary dialysis. Both patients restored their renal functions within 3 months after thoracic surgery.

Amount of postoperative fluid infusion during the first 48 hours has also been linked with pulmonary edema.[27,28] In our study, although the amount of crystalloid infusion and the infusion rate of fluids was significant in univariate analysis, they were not significant in multivariate analysis. Postoperatively, our protocol includes intravenous infusion of 75 mL/kg crystalloid and free oral intake. Once a patient fully starts oral intake of liquids and semisolids (usually during the first 24-48 hours), we stop intravenous infusion. Our postoperative fluid data only includes the amount of the infusate and not oral intake.

The type of fluid to be used in patients undergoing thoracic surgery was analyzed by Ishikawa and colleagues[22] and colloids were found to increase postoperative acute kidney injury, which resulted in pulmonary complications and increased hospitalization as well. However we do not have studies that address the type of fluid that should be used in pulmonary resections and in routine thoracic surgical practice.

Our study has several weaknesses. It was a single-arm study that is partly retrospective and the number of patients was limited. The surgical procedures were variable (ie, open

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TABLE 3. Studies that show data between pulmonary complications and the type and amount of fluid used intraoperatively

Author, year	Type of study and surgery	No. of patients/ average age	Pulmonary complication	No patients with pulmonary complications	Type of fluid/ intraoperative infusion rate, mL/kg/h	Total amount of intraoperative fluids, mL
Parquin, 1996[6]	Retrospective patient series, pneumonectomy	146/61	Edema	22	Colloid and blood/NS	1039 ± 938 vs 729 ± 859*
Licker, 2006[3]	Prospective patient series, thoracotomy for various pathologies	1222/64	Prolonged drainage, BPF, ALI, reintubation, pneumonia, atelectasis	224	Crystalloid and colloid/NS	1533 (1470-1580)
Alam, 2007[5]	Retrospective case control, lung resection for cancer	76/71	Pneumonitis, ALI, ARDS	76	NS/NS	2775 (1350-5000)
Licker, 2009[20]	Retrospective patient series, thoracotomy for cancer	558/63	ALI, ARDS	5	Crystalloid and colloid/5.8 ± 2.9	NS
Mizuno, 2012[21]	Retrospective patient series, lung resection (excluding pneumonectomy and wedge)	52/71	PAE of IPF	7	NS/7.71 ± 3.11 vs 10.3 ± 3.66 in PAE patients	NS
Gao, 2012[12]	Prospective randomized, major gastrointestinal oncologic surgery	93 vs 86/72 vs 73	Emboli, edema, pneumonia	9 vs 20	Lactated Ringers/7 in the first hour, 5 afterward vs 12	1555 ± 410 vs 3050 ± 800
Ishikawa, 2012[22]	Retrospective patient series, lung (including wedges)	1129/61	Intubation, need for mechanical ventilation	65	Crystalloid and colloid/NS	1847 ± 907
Matot, 2013[23]	Prospective randomized video-assisted thoracoscopic surgery segmentectomy-lobectomy	51 vs 51/64 vs 65	Edema, atelectasis, pneumonia, PAL, embolism	6 vs 7	Lactated Ringers/2 vs 8	1035 ± 652 vs 2131 ± 850
Current study	Retrospective patient series, anatomic lung resection	139/57	ARDS, ALI/need for intubation, atelectasis, need for bronchoscopy, pneumonia, prolonged air leak, failure to expand	76	Crystalloid and colloid/5.69 ± 3.24	2174 ± 1371

NS, Not stated; *BPF*, bronchopleural fistula; *ALI*, acute lung injury; *ARDS*, adult respiratory distress syndrome; *PAE of IPF*, postoperative acute exacerbation of idiopathic pulmonary fibrosis; *PAL*, prolonged air leak. *The amount of fluids infused in patients who developed pulmonary edema versus who did not. The difference was not statistically significant. However 10 out of 22 patients had received fluids >2 L, whereas 25 out of 124 patients received <2 L ($P < .01$).

and minimally invasive approaches) and the rate of thoracic epidural analgesia was also lower when compared with other contemporary series (72 out of 139 patients; 52%). Our lower rate of thoracic epidural analgesia may in part explain the relatively high rate of minor (67 out of 139 patients; 48%) and major (9 out of 139 patients; 6.5%) PCs. On the other hand in our study group, the frequency of thoracic epidural analgesia was not different between the patients who had pulmonary complications and those who did not. We included prolonged air leak and failure to expand as PCs, because both complications are related to the elasticity of the lung tissue that is affected in case of a fluid overload. As a novel feature, our study is one of the few studies to show an association between all types of PCs with the infusion rate of intraoperative fluids and provide objective values of infusion volume and rate of intraoperative fluids. However, this association can only be shown with a prospective randomized trial and such a study should be performed in thoracic surgery, given the results of similar randomized control trials in general and orthopedic surgery.[11,12] Data in the literature show that higher infusion of intraoperative fluids can contribute to the occurrence of all PCs through increasing capillary hydrostatic pressure, which would readily increase with lung resection.[19] Additionally excess fluid can reach alveoli via increased capillary permeability secondary to surgical trauma or decreased alveolar clearance secondary to conventional lung ventilation.[19]

CONCLUSIONS

Intraoperative fluid infusion rate together with excessive smoking history are independently associated with an

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increased occurrence of postoperative pulmonary complications and infusion rate should be kept <6 mL/kg/h.

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Discussion

Dr Eric Seeley *(San Francisco, Calif).* Dr Batirel, that was a fabulous talk. I have a couple of questions for you. One thing that is very difficult about this kind of retrospective cohort design is that it is hard to tell the chicken from the egg, meaning were the patients sicker and they thus got more fluid and were more likely to have postoperative complications? Going into surgery they had shock or they had longer operative courses, is that why they got more fluid? Or was it more the choice of the anesthesiologist?

Dr Batirel. The patients who had pulmonary complications had the same preoperative figures and had similar operating times. All of these patients were in relatively good condition, their average forced expiratory volume in 1 second was 2.5 to 2.7 L, and none were oxygen dependent. We have clarified comorbidities, especially pulmonary and cardiopulmonary comorbidities. We had a high-risk group of patients, but the number of pulmonary complications was not higher in this group. One of the most important factors was the amount of smoking.

Dr Seeley. Do you have a sense for how the intraoperative fluid was delivered? Was this a maintenance dose of intravenous fluids or was it bolus dosing?

Dr Batirel. The anesthesia strategy is to give intraoperative fluids around 300 cc/h and they usually start with crystalloids. They use colloids if there is blood loss up to a unit. If it is more than a unit, then they start to give blood. And this has been a big discussion among us. I'm a surgeon, so it's always a big discussion between the anesthesiologist and the surgeon whether or not to give fluids or to give less or more. If a patient has more bleeding or the patient is not responding to fluids, vasopressors are used to keep up blood pressure and urine output.

Dr Seeley. I know you had a composite end point as your outcome. Was it clear which of those components drove the *P* value? Was there 1 component of your composite end point that really stuck out?

Dr Batirel. In multivariate analysis it was the infusion rate of intravenous fluids.

Dr Seeley. Right, but your composite end point was actually pulmonary complication, atelectasis, and pneumonia.

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Dr Batirel. Atelectasis and pneumonia were the most significant.

Dr Seeley. If you were to design a randomized controlled trial around your investigation, how would you design it?

Dr Batirel. We should only focus on certain postoperative complications, namely atelectasis and pneumonia. We had 2 patients who had kidney failure after surgery secondary to low infusion rate during surgery, but both were temporary. I would probably determine a value, which is likely to be 5 or 6 mL, and a relatively liberal, like 8 to 10 mL, and then look at the postoperative pulmonary complications.

Dr Daniel L. Miller *(Marietta, Ga).* I enjoyed your presentation. Someone is finally putting some objective numbers on the operating room experience for fluids. These are very long procedures, and 2100 cc actually is not a lot of fluid. But the big thing I think you are getting into trouble with is within that first 48 hours. You are still giving patients intravenous fluid a lot of times. At my institution, we are on the Epic medical record system (Epic Systems Corporation, Verona, Wis); we have an automatic discontinuation of intravenous fluid at 12 and 18 hours. So we have really cut down the fluid immediately after surgery.

Also, we do not allow patients to eat unless they have been seen by a speech pathologist—not on the straightforward lobe but if a patient has had neoadjuvant treatment, induction therapy (a pneumonectomy especially), is older than the age 70 years, or has a history of head and neck cancer. We get them involved very early; the family feeds them ice chips and water, which is the worst thing to aspirate. What's very important in that whole picture is that first 24 to 48 hours.

Dr Batirel. Dr Miller, thank you very much for your comments. Fifty-five of our patients went to the intensive care unit, so typically even patients undergoing pneumonectomy go to the ward. If we believe they don't have any recurrent laryngeal nerve palsy at all, we start oral feeds 6 to 8 hours after surgery, and we don't offer intravenous fluids >1 L in the first 24 to 48 hours. If it's not a patient undergoing pneumonectomy we don't limit oral fluid intake because we believe oral intake is different than intravenous fluid administration.

EDITORIAL COMMENTARY

A dry lung is a happy lung: More supporting evidence

Eric J. Seeley, MD

See related article on pages 314-21.

Emerging data from multiple subspecialties, including surgery, medicine, and anesthesia, suggest that even mild fluid overload has adverse physiologic effects on lung function and leads to worsened pulmonary and nonpulmonary outcomes after surgery and during the resolution phase of acute respiratory distress syndrome (ARDS).[1,2] The study conducted by Arslantas and colleagues[3] and published in this month's edition of the *Journal of Thoracic and Cardiovascular Surgery* adds to the body of literature supporting a fluid conservative approach during lung resection. The counterargument to a fluid conservative approach to medical or operative management of fluids is that inadequate right atrial filling pressures lead to a decrease in stroke volume, with a subsequent decrease in cardiac output and mean arterial pressure. Prolonged subnormal cardiac outputs and hypotension may cause decreased oxygen delivery to the kidneys, which may in turn lead to renal ischemia and acute kidney injury. Thus fluid administration in any setting, from the operating room to the intensive care unit, requires a fine balance between fluid overload and renal hypoperfusion.

Unfortunately, the current toolbox for hemodynamic measurement is not sufficiently sophisticated to allow clinicians to find the sweet spot in this balance between lung and kidney. In addition, studies within the last 8 years, most notably the Fluids and Catheters Treatment Trial,[4] which was a randomized trial of fluid therapy in patient with ARDS after the resolution of shock, suggests that a fluid conservative approach may actually decreases the risk of continuous renal replacement therapy, rather than increasing it. The observational study conducted by Arslantas and colleagues supports the concept that we should err on the side of keeping patients dry to preserve lung function and decrease postoperative complications in patients undergoing lung resection.

The study by Arslantas and colleagues is notable for several reasons. First, they initially used a univariate

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TABLE E1. The distribution and types of lung resections in the entire cohort (n = 139)

Lung resection	n
Extended lobectomy	
Postneoadjuvant treatment*	11
Sleeve†	16
Superior sulcus/en bloc chest wall‡	9
Intrapericardial	1
Lobectomy/segmentectomy (video-assisted thoracoscopic surgery cases)	
RUL	25 (4)
RML	3
RUBL	5
RLBL	1
RLL	10 (4)
LUL	16 (4)
LLL	23 (4)
LLL + lingulectomy	1
LUL trisegmentectomy	2 (2)
Lingulectomy	2 (1)
Pneumonectomy (extended cases)	
Right	3 (1§)
Left	11 (4‖)

RUL, Right upper lobectomy; *RML*, right middle lobectomy; *RUBL*, right upper bilobectomy; *RLBL*, right lower bilobectomy; *RLL*, right lower lobectomy; *LUL*, left upper lobectomy; *LLL*, left lower lobectomy. *Six following chemoradiotherapy and 5 chemotherapy. †Four cases with bronchial and arterial sleeve lobectomy. ‡Three cases of superior sulcus tumors (1 with Dartevelle approach and postneoadjuvant chemoradiotherapy). §Intrapericardial. ‖Three completion (1 following chemotherapy) and 1 extrapleural.

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