

## 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)

See related commentary on pages 321-2.

Supplemental material is available online.

Pulmonary resection is a major surgical procedure that carries a mortality risk of 1% to 7% depending on the extent of lung tissue removed.<sup>1</sup> 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.<sup>2-4</sup>

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.<sup>4-8</sup> 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,

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Disclosures: Authors have nothing to disclose with regard to commercial support.

Read at the 94th Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, April 26-30, 2014.

Received for publication April 9, 2014; revisions received Aug 8, 2014; accepted for publication Aug 20, 2014; available ahead of print Oct 8, 2014.

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0022-5223/\$36.00

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<http://dx.doi.org/10.1016/j.jtcvs.2014.08.071>

### Abbreviations and Acronyms

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

and the renin-angiotensin II system.<sup>9</sup> The association of excessive fluid administration and occurrence of pulmonary edema after pneumonectomy was reported in 10 patients by Zeldin and colleagues<sup>10</sup> 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.<sup>9</sup> 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).<sup>11,12</sup> 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.<sup>12</sup>

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  $56.8 \pm 11.6$  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.<sup>13</sup> 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  $\chi^2$  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.

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