

# Acute Lung Injury After Pulmonary Resection: More Pieces of the Puzzle

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**A**cute lung injury (ALI) without obvious etiology after pulmonary resection has been described intermittently over the past 50 yr (1). Perhaps the most widely known report is a multicenter compilation of 10 cases after pneumonectomy published in 1984 by Zeldin et al. (2). After a retrospective comparison with controls, they identified 3 significant risk factors: right pneumonectomy (9 of 10 cases), increased perioperative IV fluids, and increased postoperative urine output. Zeldin et al. went on to further demonstrate their thesis that this was an anesthetic complication caused by overhydration by producing postpneumonectomy pulmonary edema in a dog model with fluid overload. In their recommendations, they wrote that "...the most important thing that we can do in terms of recognizing this problem is to watch our anesthesiologists as they start loading the patient up with fluid."

In the 19 yr since Zeldin et al.'s landmark article (2), there have been at least a dozen similar case-series reviews of this topic in the literature, with varied conclusions about the role of fluid administration as a cause of this complication. Also, a variety of other associated and potentially causative factors have been suggested, such as the intraoperative airway pressure during one-lung ventilation (3), the administration of fresh frozen plasma, mediastinal lymphatic damage (4), serum cytokines, and oxygen toxicity (5).

The study by Licker et al. (6) in this issue of *Anesthesia & Analgesia* adds new insights to this problem of unexplained lung injury in the early postoperative period after pulmonary resection. Licker et al. present a retrospective analysis of factors associated with ALI in an 11-yr period in their practice, which included >800 pulmonary resection procedures. As with any retrospective study that covers an extended period, there is the potential that management changed in the interval between the start and end of the study period. Surgical case selection, adjuvant therapy, and nursing

care have all evolved over the period of the study, and this may affect the conclusions. Also, less severe cases may not have been detected in the retrospective screening process. Despite these limitations, some of the information adds weight to previous theories, and some previously unappreciated factors must now be included in any consideration of this problem.

The authors found a bimodal distribution of ALI after pulmonary resection. Late-onset cases (3–10 days postoperatively) (incidence of 10 in 879; 1%) were secondary to other obvious causes, such as bronchopneumonia or aspiration. "Primary" ALI (27 of 879; 3% of cases) presented on Days 0–3, and this includes the subgroup with postpneumonectomy pulmonary edema, which has been the focus of Zeldin et al. (2) and previous investigators. Licker et al. (6) found four factors to be independently significant predictors of primary ALI. These four were excessive intravascular volume, pneumonectomy, high intraoperative ventilation pressures, and preoperative alcohol abuse.

Before this new information, the known facts about ALI (and acute respiratory distress syndrome (ARDS)) after lung surgery included the following: 1) an incidence of 2%–4% after pneumonectomy (it does occur postlobectomy, but with a less frequent incidence and better outcome); 2) an increased incidence in right versus left pneumonectomies; 3) symptomatic onset on postoperative Days 1–4, with radiologic changes preceding clinical signs by 24 h; 4) large mortality rates (25%–50%) and resistance to standard therapies for pulmonary edema; 5) association with fluid overload, but not clearly cause and effect; and 6) association with low or normal pulmonary artery wedge pressures and high-protein edema fluid, suggesting endothelial damage (low-pressure pulmonary edema). As there is no single mechanism that can fully explain all these findings, the cause must be multifactorial.

Perhaps the most useful information in the search for the underlying causes of postpneumonectomy pulmonary edema in the past decade comes from a study by Waller et al. (7). These authors studied the postoperative permeability, assessed by scintigraphy with technetium-99m-labeled albumin, of the nonoperated lung in pulmonary resection patients. In the early postoperative period, the permeability of the nonoperated lung increased in pneumonectomy, but not lobectomy, patients. Even though the exact reasons may

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not be clear, just knowing that a pneumonectomy patient has a "leaky lung" has enormous implications for the anesthesiologist. Also, even though we do not understand the exact etiology of this complication, knowing that the pulmonary resection patient, particularly the pneumonectomy patient, probably has a degree of endothelial injury in the nonoperated lung leads to obvious management principles based on what we have learned from the outcomes of therapy for ARDS patients in other settings (8).

First, we should try to avoid overinflation of the nonoperated lung. Traditionally, anesthesiologists have been taught to use large tidal volumes (10–12 mL/kg) during one-lung anesthesia to prevent atelectasis in the dependent lung, and this practice is still followed in many centers (9). However, many clinicians have become aware of the fact that most patients during one-lung ventilation develop auto-positive end-expiratory pressure (PEEP) and have an increased functional residual capacity (10). The use of a large tidal volume in a lung that is starting at an increased volume can lead to end-inspiratory lung volumes that approach the theoretical limits associated with ventilator-induced lung injury. Because of this concern, some anesthesiologists have backed down from the traditional large tidal volumes for one-lung anesthesia and are using more physiologic volumes (e.g., 5 mL/kg), adding PEEP to those patients without auto-PEEP and limiting plateau inspiratory pressures to <25 cm H<sub>2</sub>O.

Not all hyperinflation of the residual lung occurs in the operating room. Overexpansion of the remaining lung after a pneumonectomy may occur postoperatively, either with or without a chest drain in place. Alvarez et al. (11) presented an abstract at a surgical meeting in Australia in 2001 on their use of a balanced chest drainage system to keep the mediastinum in a neutral position and avoid hyperinflation of the residual lung after a pneumonectomy. Although the numbers were small and the controls historical, they have seen a marked decline in this complication in their practice since the introduction of this system of chest drainage.

Second, we should try to minimize the pulmonary intravascular pressures. This has often been attempted by fluid restriction, as suggested originally by Zeldin et al. (2). Those managing thoracic cases are well aware that fluid management is a contentious issue between anesthesiologists and surgeons. Anesthesiologists tend to focus on the undesirable consequences of the regional hypoperfusion of potentially compromised organs (brain, heart, and kidneys), whereas surgeons worry about the complications due to volume overload on the respiratory system. Perhaps the most thorough study of this controversy was an investigation by Turnage and Lunn (12). In a retrospective survey of 806 pneumonectomies from the Mayo Clinic, these

authors found 21 cases (2.5%) of postpneumonectomy pulmonary edema—one of the smallest incidences reported of this complication. They found no differences in any measure of perioperative fluid balance between postpneumonectomy pulmonary edema cases (positive fluid balance at 24 h, 10 mL/kg) versus age- and sex-matched pneumonectomy controls (positive balance, 13 mL/kg.). However, the routine practice at their institution was rigorous fluid restriction. This suggests that by limiting fluids, the incidence of ALI can be decreased but not eliminated. Avoidance of fluid overload in pneumonectomy patients is logical, but this must be appreciated in the context that severe fluid restriction can precipitate renal dysfunction, which also has a high postoperative mortality in the thoracic surgical population (13). Not all increases in pulmonary pressures postoperatively are related to intravascular volume. Other factors under the influence of the anesthesiologist, such as hypercarbia, hypoxemia, and pain, can all increase pulmonary pressures and must be treated.

The identification of the correlation between alcohol abuse and ALI after lung resection is new. It is not easy to directly link the two. Alcohol has been implicated in many other perioperative complications. My personal anecdotal experience agrees with this finding, and this factor must obviously be taken into consideration in any future studies of this problem. The fact that some factors noted as significant in other series, such as right-sided pneumonectomy, were not corroborated in this study is possibly due to the small number of cases. Even though this is one of the larger series reports, there were still only 27 cases of primary ALI and only 14 in pneumonectomies.

One of the reasons that the topic of ALI after lung resection has received more interest in the past several years is that the other major causes of respiratory morbidity and mortality (atelectasis, pneumonia, etc.) after lung resection have declined. Much of this reduction is coincident with better postoperative analgesic techniques, such as the introduction of thoracic epidural infusions (14). However, the incidence of ALI has not shown any noticeable decrease. In some centers, it has now become the major cause of mortality after lung resection (15). Although aggressive nonspecific treatment for ARDS, including the use of nitric oxide, has decreased the case-fatality rate, it still remains exceedingly high (16). At this time our efforts seem better directed to prevention than cure.

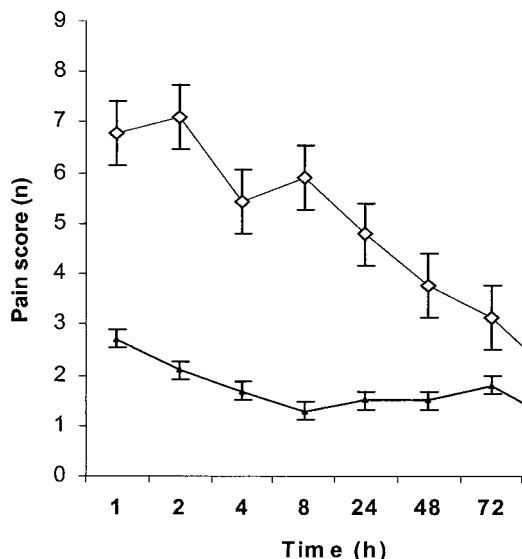
The study of this problem has always been hampered by the small number of actual cases that any one center sees. It may be time for a large prospective multicenter study. I would like to thank Licker et al. for the information they have provided in their retrospective study. They have added some new pieces that we should be able to use as we try to put together the

puzzle of primary ALI after pulmonary resection surgery.

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## Erratum



In the November 2003 issue, in the article by White et al., "The Use of a Continuous Popliteal Sciatic Nerve Block After Surgery Involving the Foot and Ankle: Does It Improve the Quality of Recovery?" (*Anesth Analg* 2003;97:1303-9), there was an error in the legend for Figure 2 on page 1307. The symbols for the control and bupivacaine groups were incorrect. The legend should read: "Figure 2. A verbal rating scale was used to assess postoperative pain (with 0 = no pain to 10 = worst pain imaginable) at specific intervals after the end of surgery in the control (◇-) and bupivacaine (▲-) treatment groups (n = 10 patients in each group). Values are mean ± SD. \*P < 0.05 versus control." Figure 2 is reproduced above. The publisher apologizes for the error.