precaution to avoid drug administration within the extrafo-raminal space.

This investigation has some weaknesses. Detractors will still criticize the current study because of its small sample size, because the body mass index was not taken into account, and because the experimental conditions do not match the clinical reality. The latter point is certainly true with the new approaches,[7,8] but is not far from the clinical reality when using the Winnie technique. This further highlights the potential danger associated with the classic Winnie technique.

What about the interscalene catheter? The results of this investigation let us fear that inadvertent catheterization of the epidural or spinal space can (too) easily occur. The catheter will go toward the direction of the needle. Sardesai *et al.*[1] showed that the use of the Winnie technique gives the catheter good conditions to go through the intervertebral foramen.

Another issue is to consider whether the new approaches (direction of the needle more caudad) will create new complications, such as pneumothorax. It is still too premature to give a definitive response, but initial studies of interscalene single-shot and catheter have reported only one case of pneumothorax occurring in a patient with Marfan syndrome.[7,15,16]

Should the Winnie technique be avoided for interscalene block? When considering the results of Sardesai *et al.*[1] and the safety of regional anesthesia, the answer is yes. First, alternatives do exist, because approaches that likely have a wider margin of safety have been described. Second, usual precautions, like the use of a short needle for performing this block, are not sufficient for all patients. Last, the safety margin is very small, an important issue for nonexperienced anesthetists. What about experienced anesthesiologists? Compared with nonexperienced colleagues, competent anesthetists have good tires to drive on an unsalted icy road, but the road is nevertheless still icy. It is therefore still recommended for all drivers to use the salted icy road! Primum non nocere.

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Postpneumonectomy Pulmonary Edema

Good News, Bad News

IN this issue of ANESTHESIOLOGY, Drs. Fernández-Pérez *et al.*[1] present a retrospective analysis of perioperative risk factors related to the development of respiratory failure necessitating mechanical ventilatory assistance beyond 48 h after pneumonectomy. Of 170 pneumonectomy patients studied during a 4-yr period at one institution, 30 developed postoperative respiratory failure. Half (15) of these respiratory failure cases were due to complications common to all major intrathoracic (and many nonthoracic) surgeries such as cardiogenic pulmonary edema, pneumonia, and pulmonary emboli. The other 15 cases (9% of pneumonectomies) were due to acute

This Editorial View is accompanied by the following article: Fernández-Pérez ER, Keegan MT, Brown DR, Hubmayr RD, Gajic O: Intraoperative tidal volume as a risk factor for respiratory failure after pneumonectomy. ANESTHESIOLOGY 2006; 105:14–8.

Accepted for publication February 14, 2006. The author is not supported by, nor maintains any financial interest in, any commercial activity that may be associated with the topic of this article.

lung injury (ALI). This latter 9% represent a dreaded complication both for anesthesiologists and thoracic surgeons because this "postpneumonectomy pulmonary edema,"[1] unrelated to other identifiable etiologies of respiratory failure, has a case-fatality rate of more than 50% in most reports.[2] The most significant perioperative factor that Fernández-Pérez *et al.* found to be associated with postpneumonectomy respiratory failure was larger intraoperative tidal volumes (median 8.3 ml/kg predicted body weight in failure patients *vs.* 6.7 ml/kg in nonfailure pneumonectomy controls). The other significant factor was larger amounts of intraoperative fluids administered (median 2.2 l for cases *vs.* 1.3 l for controls). Patients who developed respiratory failure had a higher 60-day mortality than controls (23% *vs.* 4%) and a longer hospital stay (22 *vs.* 6 days).

Before we conclude that large tidal volumes and intravenous fluids contribute to postpneumonectomy pulmonary edema, there are some caveats that we must place on the analysis and that the authors largely acknowledge. In their retrospective analysis, the authors were not able to get clear data on the exact tidal volumes or duration of one-lung ventilation. They could only document the largest intraoperative tidal volume; this could represent one- or two-lung ventilation. However, because it has been a common clinical practice to use the same tidal volume for one- and two-lung ventilation,[3] I believe these data are probably valid. Also, the authors do not provide a between-subgroup comparison of the associations with tidal volume and fluids for the ALI *versus* the non-ALI respiratory failure cases. It seems plausible that tidal volumes might impact ALI but would not have an effect on non-ALI cases, whereas fluids could impact both cardiogenic and noncardiogenic pulmonary edema.

The original description of postpneumonectomy pulmonary edema as a specific entity seems to have been in a series of 10 cases published in 1984 by Zeldin *et al.*[4] After retrospective comparison with controls, they identified three significant risk factors: right pneumonectomy (9 of 10 cases), increased perioperative intravenous fluids, and increased postoperative urine output. Zeldin *et al.* further demonstrated 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, ". . . the most important thing that we can do in terms of recognizing this problem is to watch our anesthetists as they start loading the patient up with fluid." In the 20+ yr since the article of Zeldin *et al.* was published, there have been at least a dozen similar case-series reviews of this topic, 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 proposed, such as the administration of fresh frozen plasma, mediastinal lymphatic damage,[5] serum cytokines, and oxygen toxicity.[6]

The largest study of postpneumonectomy pulmonary edema was by Turnage and Lunn.[7] In a retrospective survey of 806 pneumonectomies published in 1993 (from the same institution as Fernández-Pérez *et al.*), they found 21 cases (2.5%) of postpneumonectomy pulmonary edema, one of the lowest incidences reported of this complication. They found no differences in any measure of perioperative fluid balance between postpneumonectomy pulmonary edema cases (mean positive fluid balance at 24 h = 10 ml/kg) *versus* uncomplicated pneumonectomy controls (24-h positive balance = 13 ml/kg). However, the routine practice at their institution was rigorous fluid restriction, compared with many other reports where the 24-h fluid balance often exceeds 20 ml/kg.[8] This suggests that by limiting fluids the incidence of postpneumonectomy, ALI can be decreased but not eliminated.

Traditional teaching has been to use large tidal volumes, 10–12 ml/kg, during one-lung ventilation to prevent atelectasis in the dependent lung and to avoid hypoxemia.[3] However, the incidence of hypoxemia during one-lung ventilation has declined from 20–25% in the 1970s[9] to less than 1% currently.[10] This decrease can be attributed to several advances in thoracic anesthesia, including the use of fiberoptic bronchoscopy for positioning double-lumen endobronchial tubes and bronchial blockers and the use of newer volatile anesthetics[11] (isoflurane, sevoflurane, desflurane) that cause less inhibition of hypoxic pulmonary vasoconstriction and less shunt during one-lung ventilation than older volatile agents.[12] Before this study of Fernández-Pérez *et al.*, several other reports have also suggested that the use of large tidal volumes and pressures during one-lung ventilation may contribute to post–lung resection ALI. Van der Werff *et al.*[13] found ALI, diagnosed radiographically, in 42% of pneumonectomy patients who were ventilated with peak airway pressures greater than 40 cm H_2O. Licker *et al.*[14] found that the most significant predictor of ALI was the product of the airway pressure and the duration of one-lung ventilation. Also, bronchial lavage levels of some inflammatory markers were higher after one-lung ventilation with 10 ml/kg tidal volumes *versus* 5 ml/kg.[15]

Central to our current understanding of postpneumonectomy ALI is the appreciation that the patients develop a low-pressure, high-protein-content pulmonary edema, which indicates an endothelial injury.[7] It has been demonstrated that the nonoperated lung develops a capillary-leak injury after a pneumonectomy but not a lobectomy.[16] There is no single mechanism that can fully explain ALI after lung resection, and its etiology is likely multifactorial; it may represent one end of a spectrum of lung injury that occurs with all pulmonary resections and is proportional to the amount of lung tissue resected. Changes in plasma makers of oxidative damage after

pulmonary resection were found to be largest in pneumonectomy patients, less in lobectomy, and not significant in wedge resection or abdominal surgery.[17]

Understanding that lung endothelial injury occurs after major lung resection supports management principles similar to other conditions associated with ALI and acute respiratory distress syndrome.[18] As a general principle, it seems that the lung is least injured when a pattern of ventilation as close as possible to normal spontaneous ventilation can be followed: fraction of inspired oxygen as low as acceptable, variable tidal volumes, beginning inspiration at functional residual capacity, and avoiding atelectasis[19] with frequent recruitment maneuvers.[20] Studies in acute respiratory distress syndrome demonstrate that ALI is exacerbated by the use of large tidal volumes and that lung-protective ventilation strategies with low tidal volumes and positive end-expiratory pressure are less injurious.[21] The most important factor in the etiology of ventilator-induced lung injury is the end-inspiratory lung volume.[22] Many patients, particularly those with emphysema, develop auto–positive end-expiratory pressure during one-lung ventilation,[23] thus beginning inspiration at a lung volume above functional residual capacity. It is conceivable that routine use of large tidal volumes (10–12 ml/kg) during one-lung ventilation in such patients produces end-inspiratory lung volumes close to levels that contribute to ALI, particularly in the smaller left lung.

Based on our current appreciation of post–lung resection ALI, several management principles for pneumonectomy (and potential pneumonectomy) patients seem evident. Overinflation of the nonoperated (ventilated) lung should be avoided using lung-protective ventilation (tidal volumes 5–6 ml/kg), adding positive end-expiratory pressure to those patients without auto–positive end-expiratory pressure and limiting plateau and peak inspiratory pressures to less than 25 cm H_2O and less than 35 cm H_2O, respectively.[24] Minimizing pulmonary capillary pressures by avoiding overhydration for patients undergoing pneumonectomy is reasonable, while acknowledging that not all increases in pulmonary artery pressures perioperatively are due to intravascular volume replacement. Other factors, such as hypercapnia, hypoxemia, and pain, can all increase pulmonary pressures and must be treated.

It should be appreciated that not all hyperinflation of the residual lung occurs in the operating room. Overexpansion of the remaining lung after pneumonectomy may occur postoperatively either with or without a chest drain in place. This prolonged hyperinflation during the period of increased endothelial permeability may be one of the major causes of postpneumonectomy pulmonary edema. There is currently no consensus among thoracic surgeons on the best method to manage the postpneumonectomy chest cavity. There are at least four methods: chest closure without a chest drain, attachment of a chest drain to underwater seal, repeated unclamping of a chest drain, and use of a balanced chest drainage system to maintain the mediastinum in a neutral position.[25] Use of a balanced chest drainage system has been suggested to contribute to a marked decline in postpneumonectomy pulmonary edema in one center.[26] A sheep study (University of Western Australia, Perth, Australia) found a significant reduction in postpneumonectomy pulmonary edema with the use of a balanced chest drainage system compared with no drain or the other methods of chest drain management (personal communication, John M. Alvarez, M.B., B.S., F.R.A.C.S., Clinical Associate Professor, Department of Cardiothoracic Surgery, January 2006).

In summary, there is good news and bad news about postpneumonectomy ALI. The good news is that as the etiology begins to become clearer and we understand that there is a postresection lung endothelial injury, we can begin to use ventilation strategies that have been shown to improve survival in patients with other forms of ALI. Also good news is that we, as anesthesiologists, do not cause the injury with intravenous fluids (we can make it worse, but we do not cause it). And also good news is that the mortality of postpneumonectomy pulmonary edema seems to be decreasing. Fernández-Pérez *et al.* found that greater than 75% of patients survived. This compares to less than 50% survival in previous reports. However, this may be more related to better intensive care of established cases than to anesthetic management.[27]

The bad news is that the incidence of postpneumonectomy pulmonary edema does not seem to be decreasing. The incidence in the current study is 9%, compared with an incidence of less than 3% at the same institution 10 yr ago.[7] This could be due heightened awareness and more aggressive treatment. Also, few anesthesiologists have yet adopted lung-protective ventilation in thoracic anesthesia, so it may be too early to expect an improvement. Also bad news is that fluid restriction does seem to be indicated for anesthetic management of pneumonectomy patients. This complicates perioperative management in patients who often receive thoracic epidural analgesia and tend to be hypotensive. And finally, bad news is that much of the etiology of post–lung resection ALI may be related to the extent of the surgical resection and the postoperative chest drain management and thus may be out of the control of the anesthesiologist.

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