Purpose of review
This review presents the current available data to date regarding the perioperative risks associated with fluid management in thoracic surgery and its implications on the development of acute lung injury (ALI) as well as acute kidney injury (AKI).

Recent findings
The debate over the adequate fluid management during lung resection surgery has not been settled. Recent findings question the relationship between fluid administration and the development of ALI after lung resection surgery. New concepts including the capillary glycocalyx and the ‘baby lung’ model have reshaped thinking and therapy. Currently, there has been a growing interest in tissue hypoperfusion resulting from inadequate fluid resuscitation and the development of AKI after lung resection surgery.

Summary
Alternative fluid regimens to the traditional restrictive protocols used during thoracic surgery are being explored. These include normovolemic and goal-directed therapy protocols and the use of newer colloid solutions.

Keywords
acute kidney injury, acute lung injury, fluid management, thoracic surgery

INTRODUCTION
The landscape of thoracic surgery is undergoing significant changes. The rate of surgical resection for nonsmall cell lung cancer has increased worldwide over the past decade owing to increased detection efforts and surgeries on high-risk patients who in the past would not have been deemed fit for surgery. Early detection and screening have effectively reduced the rate of pneumonectomy in favor of lesser resections, such as lobectomy and wedge resections. Last but not least, improvements in surgical technique and technology in conjunction with improvements in perioperative care have reduced the early mortality rate [1–3].

The evolution of lung resection surgery reveals a track leading from open surgery to video-assisted thoracoscopic surgery and most recently to robotic lung resection. Disappointingly, despite this evolution in surgical technology, there have been no significant changes in regard to the mortality rate, length of hospital stay, or rate of pulmonary complications between the three approaches [4,5].

Pulmonary complications after lung resection remain a prime cause of mortality and present a spectrum of disease processes ranging from mild complications, such as atelectasis and pneumonia, to the more severe presentations of acute lung injury (ALI) and adult respiratory distress syndrome (ARDS). The incidence of ALI and ARDS varies according to the extent of resection with pneumonectomy carrying the highest incidence of 3–10% compared to 2–5% for lesser resections and a mortality rate of 25–60%. Multiple factors have been shown to be associated with pulmonary complications, of which the volume of intravenous fluids administered has attracted much attention [6–9].

Concern that intravenous fluids may exacerbate or even cause pulmonary complications has led to the widespread adoption of perioperative restriction of fluids for thoracic surgical patients. Restrictive fluid management incurs risks such as a hypovolemic state with impaired tissue perfusion which may result in organ dysfunction and in particular postoperative acute kidney injury (AKI). The risk of AKI has been underappreciated until recently. Data now show that the risk of AKI after lung resection surgery varies between 6 and 24% with a mortality rate from 0 to 19% [10,11,12,13].

The aim of this review is to highlight the impact of fluid management strategies on ALI and AKI in patients undergoing thoracic surgery.
KEY POINTS

- Protective lung ventilation (PLV) strategies have the most support as a means to reduce the incidence of ALI after lung resection.
- The use of restrictive fluid therapy in pulmonary wedge resections and lobectomies raises concerns over hypovolemia, hypoperfusion, and the risk of AKI.
- Alternative fluid administration protocols, such as goal-directed therapy (GDT), are being explored to improve outcome in lung resection surgery.
- Emerging data on newer synthetic colloid solutions show promise to reduce the severity of ALI.

THE CASE FOR RESTRICTIVE FLUID MANAGEMENT

The association between excessive fluid administration and development of ALI, ‘previously known as postpneumonectomy pulmonary edema (PPE)’, was first studied by Zeldin et al. [14] in their report of 10 patients who developed this complication following pneumonectomy. This was followed by an experimental dog model and was shown that after right pneumonectomy, PPE developed in six of 13 dogs following a Ringers lactate fluid bolus of 100 mL/kg followed by 100 mL/kg h⁻¹ for 24 h. Of note, these dogs were ventilated with a tidal volume of 15 mL/kg. Clinical studies have subsequently corroborated these findings. Parquin et al. [6] reported that high intraoperative fluid load in excess of 2000 mL is an independent risk factor for PPE. Blank et al. [15] studied the incidence of all pulmonary complications including ALI/ARDS in 129 patients undergoing pneumonectomy and found perioperative administration of parenteral fluids of 2.7 liters followed by 1 mL/kg h⁻¹ for 24 h to be an independent risk factor in a univariate analysis but not in a multivariable analysis and that 1 Unit of blood product increased the risk of pulmonary complication by 47%. In a multivariate analysis, Licker et al. [16] found two independent risk factors for ALI: the extent of lung resection with pneumonectomy carrying the highest risk and excessive fluid infusion consisting of 9.1 mL/kg h⁻¹ intraoperatively followed by 1 mL/kg h⁻¹ for 24 h. Although the authors attempted to limit the peak inspiratory pressure to less than 50 cmH₂O, they did not adopt a protective lung ventilation (PLV) strategy. Interestingly, when the authors compared this group of patients to a more recent group after implementation of PLV, they showed that the incidence of ALI/ARDS was markedly decreased despite no change in their fluid regimen between the earlier and later groups.

In patients who developed ALI/ARDS, excessive fluid volume administered was a common finding and has led to the widespread practice of perioperative restrictive fluids management. Recent literature, however, has further advanced our understanding of ALI and its relationship to fluid therapy. These findings have impacted current opinion that now views the optimal fluid regimen as more complex than simply restriction.

THE GENESIS OF PULMONARY EDEMA IN THORACIC SURGERY

The two main mechanisms for pulmonary edema development are an increase in pulmonary capillary hydrostatic pressure and/or an increase in capillary permeability. Addressing these mechanisms is critical to improve outcomes.

Hydrostatic edema and Starling forces

The mechanism of fluid exchange between the microvascular and interstitial spaces remained poorly understood until 1896 when Ernest Starling presented the results of his experiment in an animal model. He concluded that fluid filtration and reabsorption between the capillaries and the interstitial space is determined by the difference between the capillary hydrostatic and osmotic pressures, and that, the capillary walls act as semipermeable membranes [17]. Starling’s forces are summarized in the following equation:

\[
\frac{J_v}{A} = L_f[\left(P_c - P_l\right) - \sigma(\Pi_c - \Pi_i)]
\]

Where \(J_v/A\) is the rate of fluid exchange per unit area of the vessel, \(L_f\) is the hydraulic permeability of the vessel wall, \(P_c - P_l\) is the difference in hydrostatic pressures between the capillary and interstitial fluid while \(\Pi_c - \Pi_i\) is the difference in osmotic pressures between the capillary and interstitial fluid, \(\sigma\) is the reflection coefficient of the vessel wall to plasma proteins.

Conceptually, capillary hydrostatic pressure represents the chief filtration force, whereas capillary oncotic pressure represents the chief reabsorption force.

The pulmonary circulation is able to adapt substantial changes in cardiac output without an increase in pulmonary capillary pressure. This is achieved by several mechanisms including capillary recruitment and distention [18]. In fact, until the left atrial pressure is doubled, the pulmonary capillary filtration does not markedly increase [19]. If adaptive mechanisms are overwhelmed, fluid starts to accumulate in the interstitium, in which the lymphatics then play an important role in fluid clearance. Lymph flow can increase five-fold to 10-fold in response to chronic elevations in...
interstitial pressure [20]. Following an acute increase in hydrostatic edema, the rise in interstitial volume is limited by the low compliance of the interstitial compartment, limiting further accumulation of interstitial fluid. This protective mechanism is short-lived secondary to fragmentation of the proteoglycan skeleton of the interstitial matrix [21]. The alveolar epithelial cells represent the last line of defense against pulmonary edema. Through the epithelial sodium channels (ENaCs), alveolar fluid clearance is enhanced and helps in the rapid resolution of alveolar edema. ENaCs are stimulated by β-adrenergic agonists with a potential future therapeutic role of these agents [22] and inhibited by endothelin-1 [23].

**Pneumonectomy versus lesser resections**
In a series of 1139 patients, ALI was diagnosed in 3.9%. The highest frequency was in patients who had extensive resections (12.9%) followed by pneumonectomy (6%), whereas in patients who had lobectomy, the risk was 3.7% [24].

It seems that the extent of the resection plays a very important role in the development of ALI after lung resection. In pneumonectomy, the whole cardiac output will be directed to the remaining lung. This volume in the presence of a decreased vital capacity may overwhelm the remaining lung's protective mechanisms resulting in a rise in the pulmonary capillary filtration pressure. And hence, a perioperative restrictive fluid management may be logical; this might not be the case following lesser resections. This was shown by the study by Waller et al. [25], in which pulmonary capillary pressure steadily declined after lobectomy compared to pneumonectomy (Table 1).

**Nonpulmonary thoracotomy surgery**
In surgeries like esophagectomy, the risk of pulmonary complications was related to the surgical approach with transthoracic carrying the highest risk and poor preoperative pulmonary status [26]. In transthoracic approach for esophagectomy, an intraoperative and 5-day postoperative fluid regimen in excess of 8 liters was an independent risk factor for pulmonary complications [27].

**Increased capillary permeability and acute lung injury**
The American-European Consensus Conference on ARDS defined ALI and ARDS as a syndrome of inflammation and increased permeability that is acute in onset, associated with bilateral infiltrates on chest radiograph and hypoxemia [\(P_{AaO_2} \leq 300\) mmHg for ALI and \(P_{AaO_2} \leq 200\) for ALI regardless of positive end-expiratory pressure (PEEP)] with no evidence of left atrial hypertension or pulmonary capillary occlusion pressure of 18 mmHg or less [28]. Therefore, pulmonary edema secondary to ALI is primarily the result of increased pulmonary capillary permeability and is associated with an increased ratio of edema to plasma protein content compared to cardiogenic pulmonary edema [29]. Consequently, ALI can occur despite normovolemia and is exacerbated in states of fluid overload.

Fluid transport across capillary endothelium takes place through several pathways that include tight junctions, breaks in tight junctions, vesicular transport, and leaky junctions. The tight junctions allow transport of small water-soluble solutes (<2 nm in diameter) and are sealed by proteins linked to the cytoskeleton. Breaks in the tight junctions allow transport of larger water-soluble solutes up to 20 nm in diameter. Vesicular transport carries molecules up to 80 nm in diameter. Finally, leaky junctions associated with cell death allow transport of solutes up to 1330 nm in diameter. The luminal side of the capillary endothelium and the intercellular junction is lined by a complex network of glycosaminoglycans (GAGs) and proteins called the glyocalyx. The most prominent GAGs are heparan sulfate, chondroitin sulfate, and hyaluronic acid. The glyocalyx layer was recently found to play several important roles in capillary fluid dynamics. First, it acts as a molecular sieve for plasma proteins and hence, the difference in oncotic pressure between plasma proteins and interstitial space has been revised from the original Starling’s equation with the glyocalyx now acting as the actual membrane. Second, it acts as a mechanosensor responsive to fluid shear stress (FSS) such that increases in capillary blood flow result in increases in capillary permeability. Heparan sulfate plays an important role in the transmission of this FSS through stimulation of endothelial nitric oxide synthesis (eNOs) [30,31].

<table>
<thead>
<tr>
<th>Time</th>
<th>Pneumonectomy</th>
<th>Lobectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>14.5 (9.2–28.4)</td>
<td>14.2 (9.2–18.4)</td>
</tr>
<tr>
<td>Pulmonary artery clamped</td>
<td>17.9 (12–39)</td>
<td>11.6 (8.8–22)</td>
</tr>
<tr>
<td>End of operation</td>
<td>15.3 (9.8–21)</td>
<td>11.8 (9.8–20.4)</td>
</tr>
<tr>
<td>2-h postoperative</td>
<td>15.3 (4.4–22)</td>
<td>8.8 (7.2–12.8)</td>
</tr>
<tr>
<td>18-h postoperative</td>
<td>12.2 (7.6–20.8)</td>
<td>7.6 (4.4–13.0)</td>
</tr>
</tbody>
</table>

*Values are shown as median mmHg with range in parentheses. P < 0.01 versus pneumonectomy at 2-h postoperative. Adopted with permission from [25].*
VENTILATOR-INDUCED LUNG INJURY

The role of mechanical ventilation in precipitating increased capillary permeability and ALI has been the focus of interest for the last decade. The causative factors in ventilator-induced lung injury (VILI) involve both end-inspiratory and end-expiratory lung volumes.

End-inspiratory lung volumes

Gattinoni et al. [32] debated that high tidal volumes used during mechanical ventilation of normal lungs can increase the risk of VILI. They suggested that for stress rupture (barotraumas) to occur, the alveoli must be stretched beyond their maximal physiologic strain, that is, beyond total lung capacity. Importantly, Gattinoni et al. argue that such stress rupture can occur in ARDS patients mechanically ventilated at tidal volumes far below the 70 ml/kg total lung capacity. Gattinoni and Pesenti [33] publicized the concept of ‘baby lung’ based on computed tomography images, which showed that in adults with severe ARDS, the amount of lung that is actually aerated is only 200–500 g, which is equivalent to the lung tissue of a 5–6-year old. As the ‘baby lung’ is actually the lung that is at risk for VILI, tidal volumes needed to cause physical strain will be much lower than if calculated based on body weight. In fact, if this strain does not reach the level of physical rupture (barotrauma), it still causes stretch of the alveolar wall leading to upregulation of pulmonary cytokine production (bietrauma) and local inflammatory process of the lungs causing increased permeability and pulmonary edema as well as systemic inflammatory response and multiorgan system failure [34,35].

End-expiratory lung volume

Mead et al. [36] found in a theoretical model that the pressure required to open a collapsed alveoli is far higher than those acting on an aerated alveoli and thus maintaining an open alveoli will cause far less stress (atelectrauma) on the alveolar walls. This concept led to the widespread adoption of PEEP, a ‘open up the lung and keep it open’ strategy ventilation [37,38].

Role of protective lung ventilation in mitigating ventilator-induced lung injury

The ARDS network study showed reduced mortality in ARDS patients who received PLV consisting of low tidal volumes, low inspiratory pressure, and PEEP [39]. Instituting PLV into the intraoperative period as a prophylactic measure in patients requiring one-lung ventilation (OLV) was associated with a reduction in the incidence of ALI/ARDS from 3.7 to 0.9% together with a reduction in the incidence of atelectasis, fewer ICU admission, and shorter hospital stay [16]. Large V_T either alone or in conjunction with high intraoperative fluid load was an independent risk factor for postpneumonectomy respiratory failure in a retrospective study [40]. This finding was also confirmed in a retrospective study on patients undergoing cardiac surgery in which V_T more than 10 ml/kg of predicted body weight was associated with multiple organ failure and prolonged hospital stay [41]. In a prospective study of cardiac and non-cardiac surgical patients, large V_T was not an independent risk factor for ALI, but a higher peak airway pressure was [42]. Surfactant protein-D is an early marker for ALI/ARDS. Interestingly, application of PLV in ALI/ARDS patients was shown to attenuate the rise of this protein [43,44]. In an animal model, baseline capillary permeability increased by five-fold when P_{al} pressure increased from 7.5 to 15 cmH_2O under PLV. Under standard ventilation (V_T 6–8 ml/kg), the same rise of P_{al} resulted in an increase in capillary permeability by 15-fold [19^*]. These data show that although PLV may reduce the risk of permeability edema, it does not prevent it.

The case against restrictive fluid management in thoracic surgery

In concert with the current evidence questioning the value of restrictive fluid therapy as a prophylactic measure for ALI, recent literature brings in this debate the issue of AKI after lung resection surgery. Historically, the incidence of renal injury in thoracic surgical patients has been regarded as very low, with the Society of Thoracic Surgeons Database citing a rate of 1.4%. However, these data report only the incidence of patients requiring renal replacement therapy [45]. As discussed below, the incidence of AKI as assessed by standardized criteria appears to be much higher.

In 2002, The Acute Dialysis Quality Initiative Group introduced a classification system of AKI termed RIFLE (risk, injury, failure, and loss and multiorgan system disease) [46]. This classification system is based on increases in serum creatinine (SCr) and concomitant decreases in glomerular filtration rates (GFRs) and urinary output and has been validated in multiple studies [47]. More recently, a new classification system of renal injury was described, namely the Acute Kidney Injury Network (AKIN) criteria [48] (Table 2). The difference between the two classification systems is that the AKIN introduced an absolute increase in SCr of 0.3 mg/dl as a diagnostic criterion for stage 1 disease. Using these criteria Ishikawa et al. recently reported an incidence of 5.9% in thoracic surgery patients [10^*]. Hobson examining a high-risk group of lung resection patients reported a 33% incidence of AKI [49].
Many clinicians question the clinical relevance of an apparently trivial increase in SCR (0.3 mg/dl). In a retrospective study, Basile showed worsened long-term outcomes in cardiothoracic patients developing postoperative AKI, even in stage 1, as compared to those patients with normal SCR values. In this study, the presence of post-thoracotomy AKI was associated with a hazard ratio of 1.6 for long-term survival. Of particular concern is the fact that even patients in whom the perioperative AKI resolved partially or completely still had a decreased long-term survival when compared to patients who maintained normal SCR values. This fact may be due to a progression of renal damage after normalization of the SCR, manifested by a decrease in the peritubular capillary density [50]. In summary, it is important to recognize that mild perioperative rises in SCR represent an important outcome factor. To date, the cause of perioperative AKI remains elusive. It is likely that, similar to the lung injury, kidney injury is a multifactorial process. In general, it is currently accepted that anesthetics negatively impact the kidneys by decreasing GFR, urinary output, and sodium excretion [51]. The operative procedure per se may unmask latent kidney disease caused by the patient’s comorbidities such as hypertension, diabetes, or atherosclerosis. In addition, the general inflammatory state described after thoracic surgery may also impact the kidney. However, among all these causes, the perioperative fluid management is an important factor to consider in the cause of AKI. Both states of hypervolemia and hypovolemia may be associated with the development of AKI. In states of hypervolemia, the kidney’s functional demands are increased. In the study of Hobson et al. [49], the incidence of AKI after thoracic surgery was associated with an increased amount of crystalloid administration. However, those patients who received higher intraoperative fluid volumes had also longer surgical times. It remains unclear which factor had more negative impact on the kidney function. However, significant volume depletion with subsequent hypotension and decreased renal perfusion, in a high-risk patient and in the setting of a generalized inflammatory state (surgery), may promote the development of AKI such that it appears prudent to maintain adequate perioperative hemodynamics and avoid prolonged episodes of renal hypoperfusion [52,53].

**THE CASE FOR ALTERNATIVE FLUID REGIMENS**

Given the concerns with excess and inadequate fluid administration, alternative fluid practices are being explored.

**Targeting normovolemia**

One strategy to minimize both lung and kidney injuries during lung resection surgery is to apply PLV with a standardized fluid protocol targeting normovolemia. This approach resulted in no increase in the extravascular lung water (EVLW) compared to baseline and was associated with an improvement in cardiac index (CI) [54] and SCR. The fluid regimen consisted of maintenance fluids at 1.5 ml/kg h⁻¹ in addition to replacement of deficit and blood losses. This maintenance rate continued in the postoperative period till patients are allowed to have oral intake [55]. Although this approach was not goal-directed, it was able to maintain normal kidney function as shown by the stable SCR without an increase in EVLW.

**Goal-directed therapy**

The approach of goal-directed therapy (GDT) has been utilized in several types of surgeries to improve outcome with conflicting results. Recent meta-analyses on patients undergoing major abdominal and cardiovascular surgery showed decreased incidence of pneumonia, AKI, and other renal complications in patients who utilized GDT compared to

### Table 2. Comparison between the RIFLE and Acute Kidney Injury Network criteria of acute kidney injury

<table>
<thead>
<tr>
<th>RIFLE criteria</th>
<th>Common criteria</th>
<th>AKIN criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage</strong></td>
<td><strong>GFR</strong></td>
<td><strong>Creatinine</strong></td>
</tr>
<tr>
<td>Risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss</td>
<td>Complete loss of kidney function for &gt;4 weeks</td>
<td></td>
</tr>
<tr>
<td>End-stage</td>
<td>End-stage kidney disease &gt;3 months</td>
<td></td>
</tr>
</tbody>
</table>

AKIN, Acute Kidney Injury Network; GFR, glomerular filtration rate; RIFLE, risk, injury, failure, and loss and end-stage renal disease; SCR, serum creatinine.
those who received conventional or restrictive therapy [56–59]. In contrast, two recent randomized controlled studies on patients undergoing open abdominal aortic surgery and colorectal surgery failed to show benefit of GDT over conventional non-GDT on intensive care stay or length of hospital stay [60,61].

Although GDT showed controversial benefit in nonthoracic surgery, it is our opinion that it is a valuable approach in thoracic surgery, given the complexity of the problem of fluid resuscitation in this type of surgery.

CI has been the most common goal to achieve in GDT. Several methods were used to measure CI including thermodilution method using pulmonary artery catheter (PAC), transpulmonary thermodilution method (TTD) using PiCCO monitor (Fig. 1), transesophageal Doppler monitoring (TDM). GDT utilizing transpulmonary thermodilution was recently shown to be superior to thermodilution using PAC in a randomized controlled study on patients undergoing valve surgery [62]. The utilization of TDM to achieve GDT in intubated patients undergoing abdominal surgery was shown to be associated with shorter hospital stay, faster return of gastrointestinal function, and fewer ICU admissions [63,64]. Diaper et al. [65] showed the utility of TDM in guiding fluid management in patients undergoing lung resection surgery.

EVLW was shown to be an independent predictor of survival in critically ill patients [66]. Its application in thoracic surgery as an early monitor of ALI was performed in a prospective observational study and showed no change from baseline in patients who had PLV during OLV together with a non-GDT, normovolemic fluid regimen [54]. The concern about the accuracy of single thermodilution measurement to estimate EVLW after lung resection was validated against double dye technique and found to be well correlated for up to 12 h [67].

Another approach to GDT is monitoring dynamic variables including stroke volume variation (SVV) and pulse pressure variation (PPV). These variables integrate the function of preload, respiratory variation, and conventional hemodynamics (blood pressure) in a dynamic form to assess fluid responsiveness. This approach was shown to be superior to conventional monitoring in major abdominal surgery in respect to hemodynamic stability, complication rate, and hospital stay [68]. Two factors influence the use of these dynamic variables in thoracic surgery. First, its accuracy depends on the tidal volume given. In a recent study in cardiac surgery patients, tidal volume more than 7 ml/kg was found to be the most predictive of fluid responsiveness compared to lower tidal volumes [69]. This will be hard to achieve in the era of PLV. Second, the benefit of dynamic variables in open chest surgeries tends to be controversial [70,71]. Encouragingly, a randomized controlled study on patients undergoing thoracotomy with OLV found that PPV was more predictive of fluid responsiveness in the group who received PLV with tidal volume less than 6ml/kg compared to the group who received conventional therapy without PLV [72]. Recently, Haas et al. [73] showed that GDT utilizing SVV did not result in an increase in EVLW in patients undergoing thoracotomy for lung resection and esophagectomy with OLV under PLV.

**CHOICE OF FLUIDS: CRYSTALLOIDS AND COLLOID SOLUTIONS**

The debate on optimal perioperative fluid management in thoracic surgical patients is not complete without questioning the type of fluid used for maintenance as well as resuscitative purposes. However, the two main types of available fluids, crystalloid and colloids, have been considered as two different and opposing strategies employed to achieve this goal. The debate revolves around the issue of edema formation, including pulmonary edema, in situations in which large amounts of crystalloids are used versus the possibility of colloid-induced kidney dysfunction or coagulopathy in situations in which colloids are used as the main fluid regimen.

Colloids have also been classified based on their oncotic properties as hyperoncotic, and hyponcotic. The value of hyperoncotic colloids is that they are rapid plasma expanders, by their virtue of increasing the intravascular oncotic pressure and thus determining shifting of extravascular fluids into the bloodstream. As such, many researchers have
considered hyperoncotic colloids as potentially having beneficial effects in patients with ARDS/ALI, by promoting the shift of lung water into the vascular compartment. In anesthetized animal models ventilated with high tidal volumes, infusion of hydroxyethyl starch (HES) solutions resulted in a decrease in the incidence of VILI and pulmonary edema as compared to infusion of crystalloid solutions [74,75]. In a surgical population, Verheij et al. [76] compared the pulmonary effects of volume loading with 0.9% sodium chloride, gelatin 4%, HES 6%, or albumin 5% and found that HES decreased the pulmonary capillary permeability. Similar effects were demonstrated in a study on patients with early ARDS who were resuscitated with HES and were found to have a rapid improvement of their hemodynamics at no cost to the overall lung mechanics [74]. However, other studies on surgical patients with ALI/ARDS have not suggested any pulmonary beneficial effects when using colloids versus crystalloids [77]. Similarly, in patients with ALI after cardiac or major vascular surgery, loading with colloids or crystalloids had no impact on pulmonary mechanics, provided that fluid overload was prevented. More importantly, the recent Cochrane systematic review failed to prove any outcome benefit when fluid resuscitation was performed with colloids versus crystalloids [78**]. However, it is important to underline that most of the randomized controlled trials included in the systematic review were performed on patients with sepsis or following non-thoracic surgeries, which limits the overall value for the thoracic anesthesiologist. In summary, colloid infusions appear to have a modest benefit on pulmonary mechanics but no overall survival benefit.

In this setting, the perioperative clinician is left with the question of the impact of colloids on kidney function. It has been suggested that hyperoncotic colloid use induces a hyperoncotic renal injury [79]. This syndrome usually occurs when the high plasma oncotic pressure offsets the hydraulic pressure of glomerular filtration and thus suppresses urinary output [80]. Another possible mechanism of colloid nephrotoxicity is the occurrence of kidney lesions such as osmotic nephrosis [81]. In a prospective cohort study, Schortgen et al. [82] found that resuscitation with hyperoncotic colloids was associated with a significantly higher rate of adverse renal events. These findings are in line with those of the VISEP trial. The study identified that HES therapy was associated with higher rates of AKI and requirement of renal replacement therapy as compared to Ringer’s lactate [83]. However, it must be emphasized that, in the above studies, large amounts of colloids were used (up to 34 ml/kg), thus potentially not providing enough free water at the glomerular level and potentiating the development of hyperoncotic syndrome. Similarly to the VISEP trial, another randomized, blinded trial, which included 798 ICU patients with severe sepsis, identified that fluid resuscitation with HES 130/0.42 is associated with a higher mortality at 90 days and an increased risk of requiring renal replacement therapy [84]. In the recently published CHEST trial (The Crystalloid versus Hydroxyethyl Starch Trial) which included 7000 ICU patients randomized 1:1 to receive either 6% HES 130/0.4 or 0.9% sodium chloride, the investigators did not find any difference in 90-day mortality among the two groups but identified that the patients resuscitated with HES had a higher rate of renal replacement therapy [85]. Ishikawa et al. [10*] in their retrospective study in patients after lung surgery suggested a possible association between HES use and development of AKI. Few patients received HES in the study and, thus, this association should be regarded with caution.

In contrast to these studies, Sakr et al. [86] demonstrated in a large multicenter observational study performed on critically ill patients that administration of HES had no impact on the renal function or the need for renal replacement therapy. However, in this study, the median use of HES was only 500 ml/day with a total maximal volume of 1000 ml over 2 days. Mahmood et al. [87] demonstrated that volume expansion with 6% HES in combination with crystalloid, during openrepair of abdominal aortic aneurysm, had improved renal function and reduced renal injury as compared to volume expansion with 4% gelatin. Taking this approach further, Godet et al. [88] evaluated the impact on renal function of 6% HES 130/0.4 in comparison to 3% gelatin in patients with baseline renal dysfunction undergoing open repair of abdominal aortic aneurysm. They concluded that resuscitation with HES had no adverse effects on renal function even in patients with baseline renal injury. It is important to emphasize that in all the studies showing no harmful renal effects of the modern 6% HES 130/0.4 molecule, colloids were used in combination with crystalloids and in total volumes not higher than the maximal manufacturer recommended dose of 20 ml/kg per day.

In conclusion, few studies address the issue of optimal fluid selection to be used in patients undergoing lung resection surgery. As such, most of the data are extrapolated from studies performed on septic, critically ill patients in ICUs or from patients undergoing cardiovascular surgeries. Evidence against reasonable use of the modern 6% HES 130/0.4, in a volume within the accepted limits, remains inconclusive. As such, it appears that HES is best used in combination with crystalloids, as part of a multimodal fluid resuscitation.
CONCLUSION

The current evidence shows strong support for PLV to reduce the incidence of ALI. In contrast, the widely used restrictive fluid therapy in lung resection surgery has limited supporting evidence and may pose risks on organ perfusion. Recent data suggest a significant incidence of kidney dysfunction after thoracic surgery. Alternative fluid strategies using euvoemia protocols or GDT as well as the use of colloidal solutions are being explored as opportunities to reduce the high morbidity following lung resection surgery.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

● of special interest

★ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 100).


A retrospective analysis of 1,345 patients who underwent lung resection surgery. AKI was defined according to RIFLE criteria. The incidence of AKI was 6.8% and that was associated with more frequent admission to the ICU, higher incidence of cardiopulmonary complication, and higher mortality rate.


Fluid management in thoracic surgery Assaad et al.


61. Perel P, Roberts I. Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev 2012:CD000567. A randomized controlled study of 49 patients undergoing lung resection surgery who were randomized into a PLV group or a conventional ventilation group. Both groups received fluid boluses and were monitored for PPV and cardiac output. PPV was more indicative of fluid responsiveness in the PLV group.


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