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Review Article

Protective Invasive Ventilation in Cardiac Surgery: A Systematic Review With a Focus on Acute Lung Injury in Adult Cardiac Surgical Patients

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PROSPECTIVE STUDIES and meta-analyses have demonstrated that early application of and adherence to "low tidal volume-protective" ventilation (6-8 mL/kg predicted body weight) improves mortality and other clinically important outcomes in patients with acute respiratory distress syndrome (ARDS).[1–6] "High tidal volume" ventilation (> 8 mL/kg predicted body weight) has been associated with ventilator-induced lung injury (VILI) in mechanically ventilated patients with healthy lungs.[7] "Protection," however, is not a binary state, and the relationship between volume and outcome is unlikely to be linear—"low tidal volume" lung ventilation in "healthy" lungs could potentially trigger subclinical VILI, as evidenced by gene expression and inflammatory markers.[8]

Data obtained from observational studies and randomized controlled trials investigating the effect of different intraoperative ventilation strategies on pulmonary morbidity in "noncardiac" surgery suggest that low tidal volume (6-8 mL/kg predicted body weight) in conjunction with positive end-expiratory pressure (PEEP) and alveolar recruitment maneuvers reduces postoperative pulmonary complications and leads to improved respiratory mechanics.[9–12] A meta-analysis of 15 randomized controlled trials (n = 2,121) undertaken in different surgical settings (general, thoracic, and cardiac) examined the individual association between tidal volume and postoperative pulmonary complications and showed that low tidal volume (≤ 8 mL/kg predicted body weight) was protective against pulmonary dysfunction.[13]

Cardiac surgery causes substantial perioperative pulmonary morbidity, leading to prolonged length of stay and increased costs in hospital care. The need for a ventilatory strategy that potentially could reduce the risk of postoperative pulmonary dysfunction, including lung injury in cardiac surgery, has received increased attention in recent years.[14–16]

The aim of this systematic review and narrative synthesis was to summarize the evidence pertaining to perioperative mechanical ventilation strategies in cardiac surgical patients and their effect on clinically important outcomes, in particular postoperative pulmonary dysfunction. The authors examined the current state of knowledge of the mechanisms of lung injury in cardiac surgery with cardiopulmonary bypass,

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identified gaps, and evaluated the evidence relating to the role of different ventilatory approaches. The authors built on previous reviews and expanded them using a more stringent approach and methodology.[17,18]

Mechanisms of Pulmonary Dysfunction and Lung Injury in Cardiac Surgery

Postoperative Pulmonary Complications: Definitions and Clinical Features

Clinical manifestations of postoperative pulmonary dysfunction include atelectasis, pleural effusions, lower respiratory tract infection, symptomatic or asymptomatic hypoxemia, and ARDS. The cumulative reported incidence of postoperative pulmonary complications in cardiac surgery with cardiopulmonary bypass varies from 10% to 25%[15,19,20]; however, there is no consensual definition for postoperative pulmonary complications in the context of cardiac or noncardiac surgery, and in most recent studies they are considered as a composite outcome measure. In 2015, a joint task force of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology published guidelines for perioperative clinical outcomes definitions. The task force defined respiratory infection, respiratory failure, atelectasis, pneumothorax, pleural effusion, bronchospasm, and aspiration pneumonitis as the "composite outcome measures" and considered pneumonia, ARDS, and pulmonary embolism to be individual adverse outcomes.[21,22] The majority of studies examining preoperative pulmonary risk used a combination of respiratory failure and pneumonia to define postoperative pulmonary complications.[22,23] In a recent, large randomized controlled trial that enrolled hypoxemic cardiac surgical patients and investigated the effect of postoperative intensive alveolar recruitment maneuvers on severity of pulmonary complications, the authors used a modified severity score and graded complications on a scale from 0 (no complication) to 5 (death before hospital discharge). Each grade included combinations of the aforementioned conditions; physiologic parameters (pyrexia, hypoxemia, hypercapnia); and level and duration of respiratory support.[24]

Lung Injury in Cardiac Surgery: Risk Factors, Pathogenesis, and Mechanisms

The incidence of perioperative "Berlin" ARDS in cardiac surgery is unknown.[25] Using the American-European Consensus Conference ARDS definition,[26] previous studies reported an ARDS incidence of 0.6% to 20% after cardiac surgery that was associated with high mortality (up to 80%).[27–33] In up to 43% of postcardiac surgery patients who require readmission to the intensive care unit (ICU), the reason for ICU readmission is pulmonary dysfunction.[34,35]

The pathogenesis of pulmonary complications and dysfunction after cardiac surgery is multifactorial and involves anesthesia-related factors (reduction in vital and/or functional residual capacity leading to impaired respiratory mechanics); surgical factors (sternotomy, internal mammary artery retrieval necessitating pleural dissection, extracorporeal circuit, ischemia-reperfusion); and patient-related factors (preexisting lung disease, obesity, heavy smoking history).[14,15,36–41]

In particular, risk factors associated with the development of perioperative lung injury include impaired left ventricular function (left ventricular ejection fraction $< 40\%$), chronic obstructive pulmonary disease, hypertension, combined cardiac procedures, previous cardiac surgery, complex cardiac surgery, and packed red cell transfusions.[30,32,33,42] Recent evidence suggests that in isolated valvular heart surgery, age, liver cirrhosis, massive transfusions, and tricuspid valve replacement are independent risk factors for ARDS.[43]

The main determinants of acute lung injury in cardiac surgery are cardiopulmonary bypass, blood product transfusion, and injurious mechanical ventilation. The pathophysiology of lung injury after cardiopulmonary bypass is not fully understood. Complement-mediated leukocyte activation leading to damage of the endothelium and extravasation of neutrophils, bacterial endotoxin translocation in low cardiac output states, and interleukin (IL)-18 and IL-6 gene polymorphism all have been associated with the susceptibility of developing lung injury due to cardiopulmonary bypass.[44–50] Transfusion-related lung injury (defined as acute onset hypoxemia and bilateral pulmonary infiltrates during or within 6 hours of blood product transfusion) has a prevalence of approximately 2.4% in cardiac surgery; possible mechanisms implicated in its pathogenesis include bioactive lipids and/or antibodies accumulated during blood storage and the presence of inflammatory condition in the host causing neutrophil activation and systemic and pulmonary inflammation.[51]

The development of VILI can be triggered by the following potentially "damaging' factors":[52–54] (1) high tidal volume causing alveolar overdistension (volutrauma); (2) cyclic alveolar expansion and collapse during the respiratory cycle, which creates shear forces that distend adjacent alveoli causing injury (atelectrauma); (3) conversion of surfactant molecules into inactive surfactant[52–54]; and (4) lung stress, measured as transpulmonary pressure (alveolar pressure minus pleural pressure) and strain (tidal volume normalized to the functional residual capacity).[55,56] The proportional relationship between stress and strain (Stress $=$ k $\times$ Strain, where k is the lung-specific elastance) shows that pressure and volume as causes of VILI (barotrauma and volutrauma, respectively) are strictly linked.[56] The aforementioned factors can cause "mechanical destruction" of the extracellular matrix and microfractures of weak polymers (hyaluronan) embedded in the matrix, leading to activation of a local and systemic inflammatory reaction (biotrauma) (Fig 1).[56–58]

"Nonventilatory" measures that potentially could reduce the risk of lung injury—although the evidence base is weak—are outlined in Table 1.[17,39,44,58–67] The main focus of the current systematic review was to rate the certainty in evidence relating to perioperative ventilatory strategies.

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