Lung Injury and Acute Respiratory Distress Syndrome After Cardiac Surgery

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As many as 20% of patients undergoing cardiac surgery will have acute respiratory distress syndrome during the perioperative period, with a mortality as high as 80%. If patients at risk can be identified, preventative measures can be taken and may improve outcomes. Care for patients with acute respiratory distress syndrome is supportive, with low tidal volume ventilation being the mainstay of therapy. Careful fluid management, minimization of blood product transfusion, appropriate nutrition, and early physical rehabilitation may improve outcomes. In cases of refractory hypoxemia, rescue therapies such as recruitment maneuvers, high-frequency oscillatory ventilation, and extracorporeal membrane oxygenation may preserve life.

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REVIEW

The acute respiratory distress syndrome (ARDS) is a devastating syndrome of acute hypoxemic respiratory failure and bilateral pulmonary infiltrates [1–3]. The recently published 2012 Berlin Definition of ARDS [3] describes ARDS as hypoxemia, occurring within 1 week of a known clinical insult or new or worsening respiratory symptoms, associated with bilateral opacities on chest imaging not fully explained by pleural effusions, atelectasis, or nodules, and not fully explained by cardiac failure or fluid overload. Formerly described as a subset of acute lung injury (ALI), with ALI describing patients with a ratio of PaO_2 to fraction of inspired oxygen (FiO_2) equal to or less than 300, and ARDS reserved for patients with PaO_2:FiO_2 equal to or less than 200, ARDS is now divided into three categories: mild ARDS (200 mm Hg $<$ PaO_2:FiO_2 $\leq$300 mm Hg with PEEP [positive end-expiratory pressure] or continuous positive airway pressure $\geq$5 cm H_2O); moderate ARDS (100 mm Hg $<$ PaO_2:FiO_2 $\leq$200 mm Hg with PEEP $\geq$5 cm H_2O); and severe ARDS (PaO_2:FiO_2 $\leq$100 mm Hg with PEEP $\geq$5 cm H_2O).

Cardiac surgery is a known risk factor for ARDS; of the more than 300,000 patients who undergo cardiac surgery every year in the United States, as many as 20% will have ARDS [4–9]. The mortality associated with ARDS approaches 40% in the general population, but among post–cardiac surgery patients, mortality may be as high as 80% [10, 11]. Survivors may have increased intensive care unit (ICU) and hospital length of stay, as well as substantial long-term physical and psychological morbidity [12]. An understanding of ARDS risk factors and the principles of its management may help both to prevent ARDS after cardiac surgery and to improve patient outcomes after ARDS has occurred.

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Risk Factors and Specific Etiologies

Many of the techniques and sequelae of cardiac surgery increase the risk of ARDS. Cardiopulmonary bypass (CPB), which induces a systemic inflammatory state, and pulmonary ischemia-reperfusion (IR) injury have both been associated with ARDS. The use of allogenic blood products exposes patients to the risk of transfusion-related acute lung injury (TRALI). Pharmaceuticals such as amiodarone have the capacity to induce drug-related ALI. Finally, all patients undergoing cardiac surgery are intubated, sedated, and mechanically ventilated, exposing them to the risks of aspiration, ventilator-associated pneumonia, and ventilator-induced lung injury.

Surgical Procedure Performed

Type of surgery greatly influences the risk of developing ARDS. Among all patients undergoing cardiac surgery, the risk of ARDS may be as high as 10%, but that risk is increased to nearly 17% among patients undergoing aortic surgery [8]. Longer bypass times, the use of hypothermic circulatory arrest, and requirement for more blood products may all play roles in increasing risk. Emergent repair of aortic catastrophe carries an even higher risk of respiratory failure—nearly 50% (13). High rates of respiratory failure (more than 20%) have also been reported after left ventricular assist device placement [14], although not all of these failures may be due to ARDS. Postoperative respiratory failure is associated with higher 1-year mortality among ventricular assist device recipients [14].

Cardiopulmonary Bypass

Although the development of CPB made open heart surgery possible, saving hundreds of thousands of lives, the circulation of blood through an artificial extracorporeal circuit can incite systemic and pulmonary injury. During CPB, bronchial artery flow is maintained, but

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Abbreviations and Acronyms

ALI = acute lung injury
ARDS = acute respiratory distress syndrome
CPB = cardiopulmonary bypass
ECMO = extracorporeal membrane oxygenation
FiO_2 = fraction of inspired oxygen
ICU = intensive care unit
IR = ischemia-reperfusion
PBW = predicted body weight
PEEP = positive end-expiratory pressure
PGD = primary graft dysfunction
TRALI = transfusion-related acute lung injury
VAP = ventilator-associated pneumonia
V_T = tidal volume

pulmonary arterial flow is markedly decreased. Concurrently, ventilation of the lungs is typically stopped to improve surgical exposure and field stability. The absence of ventilation in combination with reduced blood flow to the lungs may increase susceptibility to pulmonary injury. Cardiopulmonary bypass also initiates a profound systemic inflammatory cascade that can lead to pulmonary injury. As many as 60% of patients have increased pulmonary vascular permeability during CPB [15]. Polymorphisms in the interleukin-6 and interleukin-18 genes may predispose toward ALI after CPB [16, 17]. Ameliorating the injurious effects of CPB is an area of active investigation [18].

Ischemia-Reperfusion

Transient ischemia and subsequent reperfusion of the lungs can result in the production of injurious reactive oxygen species [19, 20]. Some degree of pulmonary IR injury predictably occurs during and after CPB and during resuscitation from shock. Longer periods of pulmonary ischemia and subsequent IR injury occur during procedures such as pulmonary endarterectomy, hypothermic circulatory arrest, and lung transplantation. Extrapulmonary IR can also contribute to lung injury: in aortic procedures, hepatosplanchnic IR releases inflammatory mediators that contribute to the increase in pulmonary vascular permeability [21].

Pulmonary Endarterectomy

Pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension can dramatically improve functional status. However, these patients are uniquely susceptible to reperfusion-induced high-permeability pulmonary edema, resulting in profound shunt physiology and severe hypoxemia. Limited to portions of the lung from which proximal vascular obstruction has been removed, this generally occurs in the first 72 hours postoperatively. The management of patients after pulmonary endarterectomy has recently been reviewed [22].

Lung Transplantation

Of the approximately 2,700 patients in the United States who undergo lung transplantation each year [23], 10% to 25% will experience primary graft dysfunction (PGD). Primary graft dysfunction is a form of ARDS that occurs in the first 72 hours after lung transplantation and confers a significant increase in mortality [24]. Primary graft dysfunction is multifactorial in etiology; IR injury to the pulmonary endothelium and physiologic changes associated with donor brain death are thought to be of primary importance [24]. Obesity is a risk factor for PGD, as is the use of CPB, ventilator-induced lung injury, and large volume transfusion of blood products [24, 25]. Importantly, although PGD typically improves within 3 to 5 days if the patient survives, the occurrence of PGD increases the risk of bronchiolitis obliterans syndrome and allograft failure [26]. Prevention of this entity is essential to the long-term survival of lung transplant recipients.

Transfusion-Related Acute Lung Injury

Cardiac surgical patients frequently require blood product support for anemia, thrombocytopenia, or coagulopathy. All transfusions carry the risk of TRALI, the leading cause of transfusion-related morbidity and mortality. Transfusion-related acute lung injury has been linked to longer ventilator times and increased ICU length of stay [27, 28]. Defined as the acute onset of hypoxia and bilateral pulmonary infiltrates within 6 hours of a transfusion, TRALI can present with tachypnea, cyanosis, dyspnea, and fever [29]. Mortality ranges from 5% to 25%. Cardiac surgery has been identified as an independent risk factor for TRALI [28]. The incidence of TRALI has been reported to be 2.5% among cardiac surgical patients [27]; that is probably an underestimate [30]. TRALI is likely immune-mediated, as donor-related antileukocyte antibodies or antibody-producing donor leukocytes trigger neutrophil activation with resultant pulmonary endothelial damage and high-permeability edema [27, 31]. Transfusion of plasma-rich products such as fresh frozen plasma and platelets, especially from multiparous female donors, carries a higher risk of TRALI [27, 30, 32]. Transfusion of red cells is not harmless, and increases pulmonary permeability in a dose-dependent fashion [33, 34]. In addition, TRALI may be more likely in the presence of other ALI risk factors (30). Transfusion can also lead to transfusion-associated circulatory overload, which also develops acutely but responds rapidly to diuresis [29]. Transfusion-associated circulatory overload and TRALI can coexist, leading to mixed hydrostatic and permeability edema. Even in the absence of TRALI or transfusion-associated circulatory overload, transfusion increases pulmonary complications after cardiac surgery [35]. A restrictive transfusion strategy, targeting a hemoglobin of 7 to 8 mg/dL rather than 10 to 12 mg/dL, may help avoid the complications of transfusions. Although the incidence of lung injury was not a specific endpoint, the safety of a restrictive transfusion strategy after cardiac surgery was shown in a 500-patient randomized controlled trial [36].