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Pulmonary complications of cardiopulmonary bypass

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Pulmonary complications after the use of extracorporeal circulation are common, and they range from transient hypoxemia with altered gas exchange to acute respiratory distress syndrome (ARDS), with variable severity. Similar to other end-organ dysfunction after cardiac surgery with extracorporeal circulation, pulmonary complications are attributed to the inflammatory response, ischemia–reperfusion injury, and reactive oxygen species liberated as a result of cardiopulmonary bypass. Several factors common in cardiac surgery with extracorporeal circulation may worsen the risk of pulmonary complications including atelectasis, transfusion requirement, older age, heart failure, emergency surgery, and prolonged duration of bypass. There is no magic bullet to prevent or treat pulmonary complications, but supportive care with protective ventilation is important. Targets for the prevention of pulmonary complications include mechanical, surgical, and anesthetic interventions that aim to reduce the contact activation, systemic inflammatory response, leukocyte sequestration, and hemodilution associated with extracorporeal circulation.

Introduction

Postoperative pulmonary complications after cardiac surgery with cardiopulmonary bypass (CPB) are common, and hypoxemia after bypass may be related to cardiac failure or pulmonary failure, or a

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combination of both [1–4]. This review focuses on hypoxemia after CPB, and it defines the etiologies, risk factors, and some prevention strategies for pulmonary complications. Historically, lung injury associated with CPB was thought to be due to antiquated bubble oxygenation and pump circuitry. With the advent of membrane oxygenation and improvement in technological advancements for the use of extracorporeal circulation, the incidence of lung injury should have declined.

Altered postoperative pulmonary mechanics and impaired gas exchange contribute to pulmonary complications after the use of extracorporeal circulation. Manifestations range from hypoxemia and atelectasis to acute lung injury (ALI), respiratory failure, and acute respiratory distress syndrome (ARDS), described originally in 1994 with the publication of the American–European Consensus Conference [5]. In 2012, as a result of the need to describe changes based on ventilator settings, the ARDS Definition Task Force convened and proposed the Berlin Definition for ARDS. This defines ARDS based on three severities and several other ancillary variables [6] (see Table 1).

Surgical factors, including hemidiaphragmatic paresis leading to atelectasis, pain from sternal wound and surgical drains, and residual pleural effusions, contribute to some of the additional pulmonary risks after CPB and cardiac surgery. Atelectasis, shunt, alterations in the chest wall and lung mechanics, changes in the capillary bed permeability, and in the lung tissue itself participate in the risk of lung dysfunction. Most importantly, inflammation related to the use of extracorporeal circulation is postulated to be responsible for many of the other gas exchange issues and eventual ARDS. While postoperative pulmonary complications after cardiac surgery leading to hypoxemia are thought to be common, on the order of 5–7% in some studies, lung injury and ARDS are more rare complications [7–11]. Weiss et al. performed a study on post-CPB hypoxemia, and they found that 1.3% of patients had transient reduction in PaO_2/FiO_2 ratio, but these patients had prompt recovery and were extubated within 12 h after surgery [12]. ARDS is thought to occur in as many as 2–3% of patients who underwent cardiac surgery post operatively, but it carries a very poor prognosis with mortality in the 15–50% range [3,4,13,14].

Etiology

Lung ischemia

During the course of CPB, the lungs are excluded from the systemic circulation as blood is diverted from the right side of the heart to the venous reservoir, through the membrane oxygenator, and finally oxygenated blood is returned to the aorta and systemic circulation. Metabolic demands of the lungs, excluded from the systemic circulation for the duration of the CPB period, are dependent on the blood flow from the bronchial arteries. The bronchial arteries supply about 3–5% of the pulmonary blood flow in normal physiologic conditions, but upon experimental conditions of CPB in pigs, this flow may decrease as much as 10-fold [15–17]. Thus, there is some period of ischemia to the pulmonary bed, which is followed by reperfusion after CPB. This ischemia–reperfusion is thought to aggravate the inflammatory response initiated by CPB in general. During CPB, ATP in the lungs is reduced [18], and lactate in the pulmonary blood is increased even to 6 h after the use of CPB [19]. In addition to the effects of pulmonary ischemia during CPB with reperfusion and reoxygenation, oxygen-free radicals are generated, and they contribute to this process of lung injury [20]. Oxygen-free radicals augment inflammation and activate neutrophils, macrophages, and endothelial cells [1,21]. Pulmonary

Table 1
Updated Berlin Definition for acute respiratory distress syndrome.

Oxygenation defect	Mild: 200 mm Hg < PaO_2/FIO_2 ≤300 mm Hg with PEEP or CPAP ≥5 cm H_2O Moderate: 100 mm Hg < PaO_2/FIO_2 ≤200 mm Hg with PEEP ≥5 cm H_2O Severe: PaO_2/FIO_2 ≤100 mm Hg with PEEP ≥5 cm H_2O
Timing	Occurs within 7 days of known clinical insult, new or worsening respiratory symptoms
Imaging	Bilateral pulmonary opacities, not otherwise explained by pleural effusions, lobar/lung collapse, or pulmonary nodules
Characteristics of pulmonary edema	Noncardiogenic, nonoverload. Echocardiography to exclude hydrostatic edema with no risk factors

ischemia–reperfusion injury causes an increase in microvascular permeability, increased pulmonary vascular resistance, pulmonary edema, impairment in oxygenation, and pulmonary hypertension [22].

Inflammatory response

The inflammatory reaction related to CPB has been hypothesized to contribute to lung injury and postoperative pulmonary dysfunction. A review of the inflammatory response related to extracorporeal circulation is the sole topic of a chapter by Zarbock et al. in this issue of Best Practice and Research Clinical Anaesthesiology. The systemic inflammatory response syndrome (SIRS) initiates this process with important contributions from pro-inflammatory and anti-inflammatory cytokines, the complement system, and neutrophils [23–25].

Complement activation in combination with an imbalance of pro-inflammatory and anti-inflammatory cytokines affects the magnitude of the SIRS response. Complement activation involves approximately 20 proteins, activated in a sequence by classic and alternative pathways. The alternative pathway is activated by the exposure of patient blood to extracorporeal ("foreign material") circuitry, which leads to the formation of C3a and C5a. The classic pathway is activated after heparin reversal with protamine, and it causes an increase in C4a and subsequent C3a levels [23]. Endotoxin release in the systemic circulation may activate both the alternative and classic complement pathways, and it augments/amplifies the inflammatory response by increasing other pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), procalcitonin, and interleukins (ILs) IL-1, IL-2, IL-6, and IL-8 [26–29]. This amplification leads to endothelial cell swelling, plasma and protein extravasation into the interstitium, the release of enzymes, and the congestion of the alveolar air sacs with plasma, red blood cells, and other debris [26].

The lungs are especially vulnerable to the inflammatory effects ascribed to the use of CPB and extracorporeal circulation. Apostolakis et al. described three reasons the lungs seem to be so vulnerable to injury [30]. The inflammatory process and ischemia affect endothelial cells of the lungs, the lungs receive the full cardiac output with each ventricular systole, and the neutrophils that become entrapped in the lung vasculature lead to congestion in the lung bed. These neutrophils become aggregated via thromboxane A2, and they have been shown to be at their peak 2–4 h after CPB is weaned [31,32]. Activated leukocytes increase capillary permeability and cause accumulation of fluid in the interstitial space and increase in the extravascular lung water [18]. This edema causes worsening of gas exchange and mechanics of the chest wall and lungs. Edema, in addition to constrictive mediators, leads to obstructive process in the airways, which serves to worsen bronchospasm and atelectasis [33].

Relating the inflammatory response with the use of high concentration of oxygen and high PaO_2 levels, Fujii et al. evaluated the effect of hyperoxia versus normoxia in the rat model of CPB, and they found increased pro-inflammatory cytokines such as TNF-α, IL-6, and IL-10, and biochemical markers such as lactate dehydrogenase, alanine transaminase (ALT), and aspartate aminotransferase (AST) in the hyperoxia group (PaO_2 >400 mm Hg). There was also suppression in the increase of anti-inflammatory cytokines in the hyperoxia group as compared to the normoxia group. The wet–dry weight of the rat lungs was increased in the hyperoxia group, thus indicating an increase in the extravascular lung water and edema [34]. In human patients, high oxygen concentrations have been studied during CPB, and these were found to exacerbate lung injury. Pizov et al. divided 30 patients undergoing coronary artery bypass graft (CABG) surgery with CPB into high oxygen (FiO_2 1.0) and low oxygen (FiO_2 0.5) groups. Both groups experienced a decrease in oxygenation in the early period following CPB, but patients treated with FiO_2 1.0 throughout surgery had a significant delay in the recovery of oxygenation, and they had significantly higher levels of TNF-α in the bronchoalveolar lavage fluid [35].

Atelectasis

Atelectasis occurs commonly after cardiac surgery with CPB, and it can contribute not only to hypoxemia but also to other postoperative risks such as the development of pneumonia. In a radiologic-computed tomography study by Rodrigues et al., there was a 31% reduction in pulmonary gas volume but a 19% increase in tissue volume in patients after CABG with CPB. Nonaerated spaces

increased significantly from 3% to 27%, poorly aerated spaces increased from 24% to 27%, and normally aerated spaces decreased significantly from 72% to 46%, preoperatively and post operatively [36]. Hutschala et al. found that perioperative atelectasis significantly impairs antibiotic penetration in patients undergoing coronary artery bypass surgery using CPB as compared to those having off-pump coronary artery bypass surgery (OPCAB) [37].

Transfusion

Transfusion as a contributor to pulmonary dysfunction is difficult to cover comprehensively within a review such as this. Transfusion results in complications such as transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO), and it contributes to immune and inflammatory complications. Even if transfusion does not lead to TRALI, it increases the risk of post-operative pulmonary complications. In a prospective multicenter cohort study, patients who received transfusion during cardiac surgery with CPB had significantly greater increase in pulmonary capillary permeability than those not transfused. The amount of packed red blood cell transfusion, not fresh-frozen plasma or platelets, was associated with this increase in the pulmonary leak index [38]. In a study of nearly 12,000 patients undergoing CABG surgery, the transfusion of red blood cells was associated with a significantly increased risk of prolonged ventilatory support, among other post-operative morbidities [39]. Additionally, the use of "older" blood as compared to "newer" blood appears to be significantly associated with higher complications including intubation beyond 3 days post operatively from cardiac surgery [40].

TRALI is characterized by the onset of acute respiratory distress, hypoxemia as evidenced by PaO_2/FiO_2 ratio <300, bilateral infiltrates on chest X-ray, fever, and hypotension, temporally related to transfusion within 6 h of symptoms. These criteria make it difficult to diagnose TRALI in patients who underwent postoperative cardiac surgery. Patients are often hypothermic, intubated, and sedated after bypass, and they receive blood products in the intraoperative and postoperative phases of cardiac surgery procedures. Koch et al. evaluated >16,000 patients undergoing cardiac surgery, and they found that patients receiving packed red blood cells and/or fresh-frozen plasma had significantly more risk-adjusted respiratory complications including respiratory distress, respiratory failure, longer intubation times, ARDS, and requirement for reintubation [41].

Patient risk factors

Despite all of pathophysiological changes associated with extracorporeal circulation and the lungs, most patients do not develop lung injury and ARDS after bypass. Thus, aside from the inflammatory response, lung ischemia and reperfusion, and oxygen-free radicals, there must be a patient component. Response to the inflammatory changes of CPB may be variable among patients. Recently, gene polymorphisms have been shown to be associated with elevated levels of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-8, all of which are significantly associated with postoperative pulmonary dysfunction and prolonged intubation [42–44].

Risk factors for hypoxemia in previous studies included advanced age, obesity, reduced cardiac function, previous myocardial infarction (MI), the emergency nature of surgery, baseline chest X-ray with alveolar edema, a high creatinine level, prolonged CPB time, a decreased baseline P/F ratio, the need for dopamine after CPB, an increased Hgb or protein content, persistent hypothermia, and the need for reexploration [12]. Ji et al. found independent patient risk factors for postoperative pulmonary complications after cardiac surgery with CPB to include age >65 years, preoperative congestive heart failure, low preoperative oxygenation (PaO_2), prolonged CPB, intraoperative phrenic nerve injury, and postoperative acute kidney injury [2]. In a study of >5000 patients who underwent cardiac surgery, Cislaghi et al. similarly found age >65 years, chronic renal failure, chronic obstructive pulmonary disease (COPD), repeat surgery, emergency surgery, New York Heart Association (NYHA) Class 2 or greater heart failure symptoms, left ventricular ejection fraction $\leq$30%, red blood cell or fresh-frozen plasma transfusion more than four units, and CPB time >77 min to predict mechanical ventilation time beyond 12 h [45]. By contrast, patients who were extubated early had shorter intensive care unit (ICU) and hospital stays. A more recent study found that the body mass index (BMI) >30 was an

independent risk factor for postoperative hypoxia defined as PaO_2/FiO_2 ratio <200 at arrival in the ICU [46].

Allou et al. developed a preoperative risk score for the development of postoperative pneumonia in patients undergoing cardiac surgery. Upon multivariate analysis of 5582 patients, four risk factors were found to be significantly associated with postoperative pneumonia: advanced age >70 years, COPD, preoperative left ventricular ejection fraction <60%, and the interaction between the transfusion of red blood cells and the duration of CPB. In their study, Allou et al. found postoperative pneumonia to be a frequent complication after cardiac surgery with high mortality (>40%) [47].

Prevention

As the end point "lung injury" after cardiac surgery utilizing CPB is a result of a multifactorial process, efforts to ameliorate lung injury must address these factors in a multimodal approach. The following section highlights some selected options (see Table 2). Although some studies were able to demonstrate a beneficial effect either on a cellular or on a short-term clinical level, most studies failed to show a long-term benefit. It must be kept in mind that these end points are influenced by a number of factors, and therefore they rarely reflect only pulmonary function.

Mechanical factors

The CPB circuit

The artificial surface of the CPB circuit acts as a contact-activating agent leading to an SIR [48]. The reduction in the surface area to improve inflammation has been achieved by the introduction of smaller, newer oxygenators with smaller reservoirs, and arterial–venous loops. The development of a

Table 2
Prevention strategies for postoperative pulmonary complications.

	Options	Proposed mechanisms
Mechanical factors	Miniaturized CPB circuit	Decrease contact activation, decreased hemodilution
	Coated CPB circuit (heparin, PMEA)	Decrease contact activation
	Leukocyte filtration	Remove activated leukocytes, especially for longer CPB duration
	Retrograde autologous priming (RAP)	Decrease hemodilution
	Ultrafiltration (modified, zero-balance)	Hemoconcentration, filtration of mediators
	Normoxia on CPB	Reduce reperfusion injury with free oxygen radicals
Surgical technique	Avoid CPB if possible	
	Reduce the duration of time on CPB	Reduction in time available for inflammation/ischemic injury to lungs
	Cardioprotection with cardioplegia	Prevent ischemia–reperfusion injury
	Minimize cardiotomy suction	Decrease blood–air contact; decrease activation of inflammatory response
	Transfusion-sparing techniques	Decrease inflammation/immune responses to transfusion
	Partial lung perfusion	Decrease ischemia to lungs, more complicated surgical procedure
Anesthesia factors	Intermittent ventilation	Prevent atelectasis
	Recruitment maneuver	Reduce atelectasis, improve respiratory mechanics, reduce volutrauma
	Low tidal volume ventilation	Prevent shear stress, various types of trauma to lungs: volutrauma, barotraumas, and atelectatrauma
	Volatile anesthesia-based	
Medications	Steroids	Modulate immune response, potential negative impact on glucose control and wound healing
	Neutrophil elastase inhibitors	Inhibit neutrophil elastase and reduce leukocyte sequestration in the lungs
	Hypertonic saline	Decrease extravascular lung water, improve oxygenation
	Aprotonin	Decrease extravascular lung water, improve oxygenation, and reduce neutrophil sequestration

miniaturized, closed-volume circuit system is the latest emergence in this effort. The miniaturized CPB circuit reduces priming volume, the degree of hemodilution and its negative effects on organ perfusion, and reduces transfusion requirements [49–52]. The miniaturized circuit eliminates the venous cardiotomy suction reservoir, thereby decreasing the blood–air interface and stasis in the reservoir. All salvaged blood is cell-saved and washed before reinfusion, reducing inflammation and dilution of coagulation factors. This system is more complex than the standard CPB system, and it requires communication between a surgeon, a perfusionist, and an anesthesiologist. While it is not suitable for all types of surgeries, it has been shown to be beneficial in complex procedures requiring longer perfusion times [50].

Another approach in reducing the blood-circuit surface is by biocompatible coating, which mimics the endothelial surface and thereby reduces the activation of the inflammatory system. Newer generation materials are coated with heparin [53,54] or other biocompatible materials [55–57]. Beneficial effects of reduced cellular immune response (platelets, leukocytes, and endothelial cells) as well as diminished release of inflammatory markers (IL-6, IL-8, E-selectin, lactoferin, myeloperoxidase, integrin, selectin, platelet β-thromboglobulin, and oxygen-free radicals) have been observed in multiple studies [58–61]. Positive clinical effects on postoperative lung compliance, pulmonary shunt fraction, pulmonary vascular resistance index, and PaO_2/FiO_2 ratio as well as reduced pulmonary capillary endothelial cell activation after CPB by using heparin-coated circuits have been observed. However, this did not influence the intubation time or the length of ICU stay in most studies [58,62–64].

Beneficial effects on clinical outcomes were observed especially in procedures requiring long cross-clamp times [54,65].

Leukocyte filtration

Activated leukocytes and oxygen-free radicals have been implicated in the pathogenesis of lung injury associated with CPB. Some experimental studies demonstrated a substantial reduction in pulmonary injury after leukocyte depletion [66], but the results of clinical studies have been mixed [67–70]. Various positions of the filter within the CPB circuit as well as strategic timing and temperature of the filtration have been studied. Warren et al. summarized the current literature for leukocyte filtration in their review [71]. The observed improvements in the early postoperative lung function in patients receiving systemic leukodepletion did not lead to a reduced hospital stay or to a decreased mortality. There is substantial evidence that cardioplegic leukocyte filtration attenuates the reperfusion injury at a cellular level, but this has not translated into clinical improvements.

Ultrafiltration

Upon institution of CPB, there is mixing of the patient's blood with the acellular CPB prime that leads to hemodilution. Hemodilution may be helpful to facilitate tissue perfusion, yet hematocrit levels below 23% have been associated with increased interstitial edema and dysfunction of end organs such as brain, heart, and lungs [72]. Ultrafiltration during CPB removes fluid volume from the pump prime, thus increasing hematocrit and colloid osmotic pressure. The combined effect of the reduced total body water and the increased intravascular colloid osmotic pressure reduces postoperative total body water and edema. Indeed, beneficial effects on the postoperative lung function have been demonstrated in numerous experimental and clinical studies [73–76]. Furthermore, the ability of ultrafiltration to remove inflammatory substances from the circulation is a focus of interest. Most inflammatory mediators have a molecular weight that is below the membrane pore size of commonly used ultrafilters, which should allow them to be freely filtered [77,78]. A number of variants of the conventional ultrafiltration have been developed and applied in the pediatric population where positive effects on the total body water content [79] and edema formation, improved pulmonary function [73,75], reduced inflammatory response, decreased coagulopathy [80,81], and blood transfusion requirements [82] have been demonstrated. Ziyaeifard et al. summarized the current literature in a review article [83]. Retrograde autologous priming (RAP) of the CPB circuit prior to the institution of CPB helps to remove some of the crystalloid prime fluid by allowing priming of the circuit with some of the patient's own circulating blood after cannulae have been inserted for bypass. A study by Hwang et al. showed that

patients who underwent RAP prior to bypass had significantly higher hematocrit as well as cerebral oxygenation saturation levels during the bypass period [84].

Surgical technique

While this issue of Best Practice is a review of extracorporeal circulation and its effects and outcomes, the avoidance of CPB when possible may be one of the only options for the amelioration of ARDS and lung injury [85]. A meta-analysis of studies evaluating effects of cardiac surgery with CPB versus OPCAB on various postoperative complications for patients with a reduced left ventricular function (preoperative ejection fraction <40%) revealed significant reduction in intubation time in the ICU but comparable postoperative pulmonary complication rates between the groups [86]. However, this is only possible in CABG surgery and not applicable to most valve procedures. Therefore, maintaining the duration of CPB as short as possible is a key factor in the prevention of ALI [87].

During surgery, ensuring excellent cardioprotection during aortic cross-clamp time is a mainstay in protecting the lung from the release of mediators during reperfusion. The type (crystalloid, blood, cold, and warm) and route (antegrade, retrograde, or both) of administered cardioplegia seem to play a role in cytokine release [88]. Partial-lung and full-lung perfusion techniques during CPB include partial continuous low-flow perfusion, intermittent perfusion with a protective solution (pneumoplegia), and biventricular CPB [89–93]. The so-called Drew–Anderson technique uses the patient's own lungs in a biventricular CPB as an oxygenator, excluding the artificial oxygenator as an inflammatory stimulator from the CPB circuit [94]. Although some favorable results have been demonstrated, this technique has not made it into clinical routine [95–97]. A review by Suzuki summarizes the current knowledge on this topic [98].

Anesthetic management

Ventilation

Blood flow to the lungs during total CPB is limited to the bronchial artery flow, and ischemic pulmonary injury causes the bronchial flow to become insufficient to meet the metabolic demands [16]. The concept of ventilating the lungs during CPB is mainly to prevent atelectasis. Oxygenation will only occur through passive diffusion as the pulmonary vasculature is excluded during CPB. Various regimens of ventilatory settings (i.e., intermittent, continuous, CPAP, low tidal volume, and positive end-expiratory pressure (PEEP)) have been studied, during and after separation from CPB, with mixed results in regard to inflammatory markers as well as to clinical outcomes [99–101]. Ventilation during CPB might not always be feasible as the inflated lung could interfere with surgical exposure. Apnea not only promotes atelectasis but also promotes the activation of enzymes in the pulmonary circulation that may lead to postoperative lung dysfunction [102]. A small study of patients who underwent valve surgery found that patients managed with beating heart, on CPB, with low tidal volume ventilation throughout had lower levels of inflammatory and oxidative stress markers such as malondialdehyde, lactic acid, and myeloperoxidase [103]. Vital capacity maneuvers one to three times with a pressure of 35–40 cm H_2O at the end of the CPB period improves oxygenation in the early postoperative period, but there are no sustainable effects on oxygenation or lung function once into the ICU [104].

Choice of anesthesia

Balanced anesthesia including a volatile agent plus opiate is a common choice for the maintenance of anesthesia during cardiac surgery and CPB. Total intravenous anesthesia (TIVA) versus balanced anesthesia has been studied by a variety of authors, and it has not been found to significantly reduce the pro-inflammatory cytokine milieu [105,106]. While the myocardium may be a source of pro-inflammatory cytokines during surgery with CPB, the lungs are often the consumers of those cytokines [107,108]. Some studies have demonstrated benefit in the reduction of pro-inflammatory cytokines as well as reduction in the pulmonary sequestration of cytokines with the use of volatile anesthetic agents such as sevoflurane [109,110].

Steroids

There have been several large trials in patients undergoing cardiac surgery to evaluate the impact of steroids on the inflammatory response and many other outcomes after the use of extracorporeal circulation. Study results including small studies [111], Cochrane review [112], and large, multicenter international trials [113,114] have yielded mixed results; thus, steroids are not currently indicated to reduce pulmonary complications.

Alternative treatments

As neutrophil and leukocyte activation and sequestration in the lungs contribute to postoperative pulmonary dysfunction, one potential target for prevention is white blood cells. Neutrophil elastase inhibitors such as sivelestat and ulinastatin have been used to competitively inhibit neutrophil elastase activity and improved respiratory and oxygenation indices, as well as shorter time to extubation [115,116]. A small study by Lomivorotov et al. randomized patients to receive hypertonic saline infusion (7.2% NaCl/hydroxylethyl starch) versus 0.9% NaCl infusion, and they found decreases in extravascular lung-water index measurements and improvements in arterial oxygenation in the early time period after weaning from CPB in the hypertonic saline group [117]. While it is currently not available in the United States, aprotinin, a serine protease inhibitor used for hemostasis and for the prevention of fibrinolysis in cardiac surgery, has been shown to have a variety of positive effects on multiple organ systems, including the lungs. Aprotinin use has been associated with a reduction in the ventilation time and pulmonary complications as well as decreased extravascular lung water and improvement in oxygenation indices [118,119].

Conclusion

Postoperative pulmonary complications after cardiac surgery with extracorporeal circulation are common, and they range from transient hypoxemia to the more severe ALI and ARDS, which are difficult to treat. There are multiple etiologies and patient risk factors, but the inflammatory response associated with extracorporeal circulation and CPB is thought to play a major role in lung injury and pulmonary complications after cardiac surgery. The prevention techniques reviewed here aim to modulate the inflammatory immune response as well as the coagulation system. It is important to remember that pulmonary complications after extracorporeal circulation have a multifactorial component; thus, prevention and treatment must be directed toward multiple targets.

Practice points

- Pulmonary complications including hypoxemia, pneumonia, ALI, and ARDS continue to occur with frequency, and they are associated with significant morbidity and mortality risks after cardiac surgery utilizing extracorporeal circulation despite advances in technology.
- Much of the risk associated with the use of CPB for ALI and ARDS is postulated to occur due to inflammation, ischemia, and reperfusion of the lung bed that occurs during the bypass period.
- Atelectasis occurs commonly during general anesthesia, and it is worsened with the use of extracorporeal membrane oxygenation. Atelectasis worsens hypoxemia and increases the risk of pneumonia. Lung recruitment maneuvers are important to reduce atelectasis.
- Transfusion increases risks of pulmonary complications through increased inflammation, TRALI, and TACO. Avoid transfusion if possible, and utilize "newer blood" as compared to "older blood" to ameliorate inflammatory reaction.
- Optimize and treat aggressively conditions such as heart failure and COPD that impair gas exchange and predict pulmonary complications in the postoperative period.
- Consider mechanical, surgical, and anesthetic techniques to ameliorate lung injury such as shortest CPB as possible, coated circuits, hemoconcentration, volatile anesthesia, and ventilatory recruitment maneuvers.

Research agenda

- Many of the studies are small and underpowered to detect differences in the severe pulmonary complications after extracorporeal circulation. Large studies are needed to evaluate the effect of interventions on the more rare, but severe pulmonary complications such as ALI and ARDS.
- Interventions to reduce inflammation and transfusion risk should be sought, as these seem to be major complicating risk factors for pulmonary complications.
- Alternative ventilation and perfusion techniques for the lungs during CPB have shown variable results; thus, larger trials should aim to define which of these strategies are helpful to reduce pulmonary complications post operatively.

Conflict of interest

The authors do not have any conflict of interest.

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