Pulmonary Complications of Cardiac Surgery

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Abstract
Cardiothoracic surgery posits an arrangement of large, significant hemodynamic, and physiologic alterations upon the human body, which predisposes a patient to develop pathology. The care of these patients in the postoperative realm requires an astute physician with deep understanding of the cardiopulmonary system, who is able to address subtle developing problems promptly, before the patient suffers further sequelae. In this review, we describe the presentation and management of an assortment of important complications which occur in the pulmonary system. In addition, we aim to shed better light upon how the physiology of a patient responds to the condition of cardiothoracic surgery.

Keywords Cardiothoracic surgery · Postoperative complications · Complications · Cardiothoracic intensive care unit · Acute respiratory failure · Critical care

Introduction

Cardiac surgery is a high-risk field requiring specialized teams to manage patients in the perioperative and postoperative environment. The pulmonary system, exquisitely related in both spatial proximity and synergistic function, requires close attention and support during cardiac surgery's acute stress. Pulmonary complications are common in patients who undergo cardiac surgery with outcomes such as pneumonia, pulmonary embolism, ventilation longer than 24 h, and pleural effusions necessitating drainage being reportable to the Society of Thoracic Surgeons [1]. Pulmonary complications after cardiac surgery result in prolonged hospital stay and increase in healthcare cost [2]. Patients prone to complications tend to have limited homeostatic reserve associated with chronic heart failure, pulmonary illness, multiple comorbidities, older age, or have completed more invasive and longer duration surgeries [3, 4]. As the field continues to advance medical acumen, we seek to protect the pulmonary system better.

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Cardiopulmonary Bypass

Cardiac surgery commonly uses cardiopulmonary bypass (CPB), which provides advanced physiologic support with an extracorporeal circulatory device. Depending on the type of cardiac surgery, the lungs experience up to several hours of relative ischemia during bypass. Under normal physiology, blood is delivered to the lungs by both pulmonary and bronchial arterial systems which share collateral circulation. During bypass, perfusion is solely provided to the bronchial system, placing the lungs in a relative state of ischemia. Upon cessation of bypass, reperfusion of the lungs occurs after reinstatement of pulmonary arterial flow. In addition, bronchial arterial flow on bypass paradoxically decreases, contributing to worsening low flow ischemia, which normalizes after pulmonary arterial clamping ends [5]. This environment generates ischemia–reperfusion injury with a pro-inflammatory/proapoptotic state, characterized by reduced microvascular permeability, increased arteriolar resistance with pulmonary hypertension, and pulmonary edema with impaired gas exchange. These physiological changes generate an overall predisposition to develop pulmonary complications [6].

Several changes in intraoperative care have been studied aiming to alleviate pulmonary ischemia/reperfusion. Bronchial arterial flow during bypass is continuous. Adding pulsatile flow to the extracorporeal output did not improve pulmonary outcomes, but parallel continuous pulmonary

arterial cold perfusate infusion attenuated pulmonary ischemia–reperfusion injury [7, 8]. This may preferentially benefit patients with pulmonary conditions like COPD [9], but this practice is not standard of care and would require further study.

Ischemia–reperfusion injury affects the intravascular compartment adjacent to pulmonary microcirculation, causing no-reflow phenomenon. No reflow was initially coined in coronary vasculature during atheroembolism. With diminished flow and concurrent ischemia to local endothelial and interstitial tissue, cells of the vessel wall swell and protrude into the lumen, obstructing flow [10]. Activated neutrophils and platelets also likely trap red blood cells to obstruct microcirculation, causing persistent vascular insufficiency after reperfusion [3, 4].

Other strategies to limit lung injury during CPB are being studied and remain active areas of research. Some suggested strategies include introducing prophylactic steroids to reduce the inflammatory cascade associated with CPB [11], biocompatible circuits to mimic endothelial surface [12], and leukocyte filters to preferentially remove activated leukocytes [13].

Coagulopathy and Thromboembolism

Continuous heparin infusion is maintained during CPB, with activated clotting time (ACT) kept within therapeutic range to offset thrombosis within the extracorporeal circuit. A primary reason for using heparin is that it is rapidly reversed with protamine sulfate, an alkaline polypeptide which reacts with the acidic heparin to generate neutral inert salt. On occasion, protamine-heparin complexes can induce non-immunogenic anaphylaxis (anaphylactoid reactions, with classic complement activation and degranulation of mast cells), which is less severe with lower protamine dose and slower infusion rate [14]. Series report this complication in 0.06–10.7% of patients, with clinically significant pulmonary reactions to protamine, including wheezing/bronchospasm, pulmonary hypertension, and noncardiogenic pulmonary edema, with worsening mortality [15]. This protamine reaction likely exists on a spectrum. It more commonly presents subclinically with small decreases in systemic arterial pressure and increased pulmonary artery pressure noted by the operative team after use. These minor reactions, even when isolated and adjusted for preoperative and intraoperative risk factors, were associated with increased inpatient mortality [16]. Management of the protamine reaction is supportive, although patients with severe anaphylaxis are sometimes re-heparinized and temporarily placed back on CPB [17].

Managing multifactorial coagulopathy is a large component of bypass care during cardiac surgery, and venous thromboembolic disease associated with the venous access cannula (and embolization into the pulmonary circulation) is a rare, catastrophic complication during cardiac surgery. The circulation during cardiac surgery is in a focally static state with endothelial injury, fulfilling Virchow's Triad. Williams et al. [18] compiled 48 cases of acute intracardiac thrombosis and pulmonary embolism after CPB. Common features among these cases included congestive heart failure (50%), platelet transfusion (37.5%), CPB duration > 3 h (37.5%), and aortic injury (27.1%). Thrombolytic therapy was only used in 5 out of 48 cases but efficacy was unclear, given frequent use of the antifibrinolytic protamine sulfate therapy (77.1% of cases). Intracardiac thrombosis with pulmonary embolism can present with profound refractory hypotension and biventricular failure during or after separation from bypass. One case presented with cardiac arrest after protamine administration. 64.6% of cases were diagnosed with transesophageal echocardiography. Treatment has typically been to reestablish CPB (54.2%) and perform thrombectomy (31.3%). This generally required additional mechanical support devices, culminating in an 85.4% mortality rate.

Transfusion-associated Lung Injury

Cardiac surgery is invasive and frequently requires therapeutic anticoagulation during CPB, which commonly requires allogeneic blood transfusion [19]. An estimated 10–15% of the collective blood donor supply is utilized during cardiac surgery. With restrictive transfusion strategy, over 50% of the patients receive perioperative transfusion [20, 21]. While the chance of clinically significant microbial contamination is equal to being struck by lightning, transfusion-related acute lung injury (TRALI) is the primary adverse event and most common cause of death from blood transfusion worldwide [22]. TRALI is defined as acute onset of hypoxia and bilateral pulmonary infiltrates after allogeneic blood transfusion that is difficult to distinguish from alternative causes of acute lung injury. The condition is more prominent in cardiac surgery patients than in other transfused groups in the inpatient setting [23]. This condition, mediated by donor antibodies directed against host leukocytes, is thought to unfold in a "two hit" manner. The first hit involves systemic inflammatory activation in the host, activating endothelial cells within the lung to induce neutrophil sequestration. The second hit involves preformed donor alloantibodies reacting with these neutrophils to induce an inflammatory cascade that injures the pulmonary interface [23, 24]. CPB is associated with neutrophil activation and inflammatory response, which may prime the environment for TRALI to occur [25]. Treatment is discontinuation of the inciting transfusion and supportive care. Reduction in the

frequency and amount of blood products transfused is beneficial, but even small sub 10–20 cc volumes of plasma have been shown to induce TRALI [23]. Use of a restrictive transfusion threshold for moderate- to high-risk cardiac surgery patients, even when controlled for chronic pulmonary disease, shows equivalent cardiac outcomes while allowing us to transfuse less patients and avoid this complication [21] (Table 1).

Postoperative Pulmonary Complications

Atelectasis

Atelectasis is a common cause of hypoxemia and impaired gas exchange after cardiac surgery. Atelectasis is seen in 30–72% of postoperative chest radiographs after cardiac surgery and is a major contributor to the postoperative respiratory dysfunction [26, 27]. Nearly all patients with general anesthesia develop atelectasis while spontaneously breathing and after muscle paralytics are administered, regardless of the use of intravenous or inhalational anesthetics [40]. In an animal study, cardiopulmonary bypass produced large atelectasis with a corresponding increase in intrapulmonary shunt and decrease in PaO_2 [41]. In the same study, animals who had sternotomy without CPB only had minor atelectasis in comparison. In another study using computed tomography (CT) scans to assess the degree of atelectasis in patients who underwent CABG and MVR, the area of atelectasis was considerably larger than previously seen if the patient underwent additional abdominal and lower extremity surgery on the first day after operation [42]. The amount of atelectasis and shunt was similar in patients who had undergone MVR or CABG open surgeries [42]. Other postoperative factors worsening atelectasis include diaphragmatic dysfunction due to phrenic nerve injury, inadequate pain control, and immobilization. Treatment of atelectasis includes frequent chest physiotherapy, incentive spirometry, encouraging

pulmonary hygiene, as well as noninvasive ventilation and high-flow nasal cannula [43, 44].

Pleural Effusions

Postoperative pleural effusions in cardiac surgery can have a broad range of etiologies and should be approached with care and heightened attention. Thorough clinical history and pleural fluid analysis is often required to delineate the origin. Timing is a key component of an effusion's etiology. Early effusions (the initial 15 postoperative days) are typically hemorrhagic, neutrophil predominant, and associated with operative trauma. Later effusions tend to be lymphocyte predominant and autoimmune in etiology [45]. After CABG, effusions are associated with low BMI, female gender, history of atrial fibrillation, history of heart failure, concurrent valve replacement, and history of anticoagulation [45]. Postoperative pleural effusion is the second most common cause of readmission in a CABG patient (22.5% of patients), and the need for thoracentesis is a poor prognostic sign [45, 46]. A benign, self-resolving pleural effusion can often present after harvesting the left internal thoracic artery [47], but harvesting of the internal mammary artery does not share the same association [45]. Pleural effusions after cardiac surgery also often represent a limited or complete presentation of postpericardiotomy syndrome.

Postpericardiotomy syndrome is a spectrum of pathology following cardiac surgery in approximately 15% of cases [47]. While traditionally defined as pericarditis following cardiac surgery, it has evolved to define a (likely) autoimmune response to both pleural and pericardial interfaces after direct damage or entry of blood into the pericardium [45]. In fact, isolated intraoperative pleural incision predicts development of this complication, with hazard ratio of 4.31 on one series [48]. The clinical presentation usually includes 2 of the following: fever without an infectious source, pleuritic chest pain, new pleural effusion, pericardial friction rub, or persistent pericardial effusion several weeks after surgery. Over 80% of postcardiotomy syndrome cases have pleural involvement and development of effusion [48, 49], and a late atypical presentation can be with an isolated pleural effusion [49]. The pleural fluid is typically exudative, 75% showing > 10,000 erythrocytes and lymphocytes > 50% [50]. The syndrome was also shown to produce similar clinical presentation and fluid qualities, regardless of whether a patient was post-cardiac surgery or post-pacemaker placement [50]. Postcardiotomy syndrome-related effusions have strong predilection for the left hemithorax; 83% are left-side predominant, 67% are unilateral (> 95% unilateral and left sided), and 38% of the effusions are noted to fill greater than ½ of the affected hemithorax [50, 51]. Treatment of the syndrome is typically with NSAIDs and colchicine, and therapeutic thoracentesis should be promptly offered to those

Table 1 Pulmonary complications associated with cardiac surgery

Complication	% Incidence	References
Atelectasis	30–72	[26, 27]
Pleural effusion	24–63	[26, 28]
Phrenic nerve injury	10–21	[29, 30]
Pneumonia	2–20	[31, 32]
Prolonged mechanical ventilation > 48 h	2–6	[33–35]
Acute respiratory distress syndrome (ARDS)	0.4–2	[36–39]

with moderate and large effusions. Therapeutic thoracentesis significantly affects physical recovery rate through 30 days mean walking distance, which is associated with reduced postoperative cardiovascular events [52–54].

As discussed earlier, cardiac surgery is commonly associated with postoperative blood loss, often collected in the pericardial and pleural systems. Acute-retained blood manifests with hemothorax and gross blood drainage through thoracostomy tube, which is prone to coagulate within the chest cavity or the chest tube lumen and make the situation less amenable to nonoperative drainage. Subacute-retained blood presents as pleural effusion, with drainage appearing more as liquefied blood-containing pleural fluid than frank blood. Chronically retained blood can manifest with fibrothorax, an outcome of prolonged inflammatory states of the involved serous membranes, which eventually deposit dense adhesive fibrotic tissue [55, 56]. This continuum of complications is called retained blood syndrome, which negatively impacts hospital and 30-day mortality in CABG patients, prolongs ICU stay, prolongs the duration of mechanical ventilation, and increases the incidence of stroke (particularly when intervention is required) [55, 57, 58]. Risk factors for postoperative bleeding in cardiac surgery patients include advanced age, low body weight, nonelective surgery, CPB time over 150 min, high complexity of procedure, perioperative use of antiplatelet agents, and use of over 5 bypass grafts [58]. Incidence has been estimated to be 13.8–22.7% [59]. Concurrently with pleural effusions and retained blood products, there should always be concern for pulmonary infection, discussed next.

Phrenic Nerve Injury and Diaphragmatic Dysfunction

The left and right phrenic nerves originate from C3, C4, and C5 within the cervical spine, moving caudally within the thorax alongside the great vessels (particularly the subclavian arteries) and pericardium bilaterally. Eventually these nerves pierce the two diaphragmatic domes, relaying sensory and motor innervation. In addition, these nerves receive sensory innervation from the pericardium and the mediastinal portion of the parietal pleura. The phrenic nerves are key components to maintain successful independent respiratory function. Surgical injury typically causes complete unilateral suspension of diaphragmatic function, commonly while the surgeon dissects near the internal thoracic artery [60]. In addition, prior studies have shown that phrenic nerve injury is associated with cold-induced injury during myocardial protection strategies [61, 62].

The incidence of phrenic nerve injury is unclear, with studies citing between 10 and 73%, likely owing to the sensitivity of diagnostic testing [1]. Diaphragmatic dysfunction generates paradoxical diaphragmatic movement or grossly reduced diaphragmatic excursion, which can be visualized through liver and splenic windows with bedside ultrasonography. Diaphragmatic atrophy is also noted with prolonged paralysis, depicted as a diaphragmatic thickness below 0.2 cm at end expiration. Other ultrasound modalities used include diaphragmatic thickening and diaphragmatic excursion fraction to assess function [63]. Management of diaphragmatic dysfunction typically requires supportive care, while addressing potential differential causes. Many patients fully recover the nerve function over time [61]. Debilitating cases of diaphragmatic paralysis with paradoxical diaphragmatic motion have been treated with early tracheostomy as it is felt to lessen the severity of pulmonary complications [61].

Pneumonia

Healthcare-associated infection is one of the leading causes of non-cardiac morbidity after cardiac surgery, with pneumonia being the most common, costly, and resource-intensive infectious complication [31, 64]. 2.4–20% of patients develop pneumonia after cardiac surgery, 33% of which occur after discharge [31, 32]. Ventilator-associated pneumonia also becomes problematic in postoperative patients experiencing prolonged mechanical ventilation, complicating 35.2% of patients who remain intubated for over 48 h [64].

In a prospective cohort trial observed 5158 patients in 10 centers, Ailawadi et al. worked to categorize postoperative pneumonia and clinical outcome [31]. Risk factors isolated included known COPD, older age, current steroid use, low hemoglobin level perioperatively, longer duration of surgery, and the involvement of LVAD insertion or heart transplant. Measures found which may protect against development of this complication include perioperative use of second-generation cephalosporins, under 24 h on the ventilator, avoiding the use of a nasogastric tube perioperatively, restrictive transfusion of packed RBCs, and use of few platelet transfusions. Most common isolated organisms, in order of frequency, included pseudomonas, klebsiella, then enterobacter cloacae. Finally, postoperative pneumonia showed a ninefold increase in mortality and 2 weeks increase in hospital length of stay [31]. Chlorhexidine oral care has also been shown to reduce ventilator-associated pneumonia in postoperative patients, also beneficial when administered to preoperative patients as well [65].

In addition to preventative therapies, it is important to have standardized postoperative care to promote aggressive pulmonary toilet and mobilization. Postoperative pneumonia is reduced when the head of bed is kept elevated. The patient should be given ample motivation to leave the bed for the chair (particularly during mealtime) and to ambulate (even in the post-anesthesia care unit). Patients should

be encouraged to perform frequent deep breathing and use incentive spirometry [66]. Patient education throughout the process is key, allowing the patient and his/her loved ones to become actively involved in their recovery.

Acute Respiratory Distress Syndrome

The most significant postoperative pulmonary complication is acute respiratory distress syndrome (ARDS), which is predominantly proinflammatory injury to the alveolar interface, characterized by a constellation of diffuse endothelial injury, severe hypoxia, and pulmonary edema not predominantly of cardiogenic origin [67]. Preoperative risk factors for ALI/ARDS development include age > 60, history of COPD, current or recent smoking, history of previous heart surgery, NYHA III/IV congestive heart failure, liver cirrhosis, and multiple recent transfusions. Operative risk factors include low cardiac output syndrome, more than 3 U of packed RBCs (or massive transfusion), isolated valve surgery, and development of postoperative pneumonia [68, 69]. There is a multifactorial pathogenesis to this condition that overwhelms homeostasis in the pulmonary microcirculation. In addition to the previous conditions described thus far, which place injurious stress on the alveolar interface, additional stressors can include reduced respiratory function due to general anesthesia (causing impairment of vital and functional residual capacities) or other surgical factors (sternotomy, pleural dissection due to internal mammary utilization, CPB, and ischemia–reperfusion injury) [67]. Although there is paucity of information on optimal perioperative mechanical ventilation in these patients, recent data show an improved complication profile with intraoperative lung protective ventilation. This bundle emphasized keeping tidal volume below 8 ml/kg ideal body weight, PEEP greater or equal to 5 cm H_2O, and actively aiming to keep modified driving pressure (a surrogate for lung compliance, defined as peak inspiratory pressure minus PEEP) at a value lower than 16 cm H_2O [70, 71]. Open lung strategies during CPB, defined as the provision of low tidal volumes and high PEEP (typically 8), along with frequent use of recruitment maneuvers, did not improve postoperative pulmonary outcomes [72, 73]. CPB time, restrictive transfusion, careful sternotomy with preservation of pleural integrity, and fluid restriction have been other potentially helpful preventative interventions described [74].

Pneumothorax

Mediastinal and pleural drains are routinely inserted following cardiac surgery to evacuate the postoperative bleeding, fluids, and air from the mediastinum or pleural cavities. These drains are usually removed when fluid output is minimal, accompanied by stable cardiac and respiratory status. Recurrent pneumothorax with tension physiology following discontinuation of a thoracic cavity drain is a most significant and life-threatening complication. It occurs due to a one way communication between lung parenchyma and the pleural cavity leading to air entrapment in the pleural cavity. A large retrospective study looking at 8900 patients undergoing various cardiac surgical procedures showed that an overall incidence of recurrent pneumothorax after chest tube discontinuation to be approximately 1.4% [75]. Patients should be clinically monitored closely for development of respiratory difficulty following chest tube removal. Chest X-ray and/or bedside ultrasound are useful modalities to look for a pneumothorax.

Pulmonary Artery Catheter

While routine use of the pulmonary artery catheter became less prevalent over the previous decades, it still holds a central role in the postoperative care of cardiac surgery patients. Most of these catheters are placed in the operating room and remain in place to guide therapy during early recovery. Complications involved with the pulmonary artery catheter are rare, but tend to be devastating. The most feared complication is rupture of the pulmonary artery, which can occur during or following catheter insertion. One series describes the incidence of pulmonary artery rupture at 0.031%. It presents with hemoptysis, acute pulmonary hypertension in 50% of patients, and carries a mortality rate of 70% [76]. Ruptures with massive hemoptysis or signs of developing hemothorax typically require emergent thoracotomy. Delayed hemoptysis following pulmonary artery catheter placement can be associated with catheter-associated pulmonary artery pseudoaneurysm, which start as a collection of blood between the tunica media and adventitia and progressively expands before rupturing [77]. Treatment includes vessel ligation, wedge resection, lobectomy, embolization, stenting, and watchful waiting [77]. Other complications to watch for carefully include pulmonary infarction (when the balloon of the catheter is inflated for a prolonged amount of time or the uninflated catheter tip migrates into distal branches of the pulmonary artery) and pulmonary embolism (when the catheter presents a foreign body nidus for inflammation and infection, accompanied by thrombosis) [78].

Conclusion

As the lungs are closely interdependent with the heart, adequate pulmonary support and monitoring are paramount in the care of a post-cardiac surgery patient. It is important that the cardiothoracic intensivist remains vigilant with regard to the unique pulmonary challenges faced in the cardiac surgery patient. Unique stresses are posed, associated with

cardiopulmonary bypass (along with the coagulopathy it generates), operative intervention in close proximity to the pleural surfaces and vasculature, frequent need for continued postoperative intubation, and the routine use of pulmonary artery catheterization. As surgical techniques advance to become more amenable with human physiology, postoperative care will evolve concurrently. It will be important for that evolution to address these complications and find unique and novel modalities of care to prevent them.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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