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Over the past two decades there has been a steady evolution in the practice of adult cardiac surgery with the introduction of "off-pump" surgery. However, respiratory complications remain a leading cause of postcardiac surgical morbidity and can prolong hospital stays and increase costs. The high incidence of pulmonary complications is in part due to the disruption of normal ventilatory function that is inherent to surgery in the thoracic region. Furthermore, patients undergoing such surgery often have underlying illnesses such as intrinsic lung disease (e.g., chronic obstructive pulmonary disease) and pulmonary dysfunction secondary to cardiac disease (e.g., congestive heart failure) that increase their susceptibility to postoperative respiratory problems. Given that many patients undergoing cardiac surgery are thus susceptiple to pulmonary complications, it is remarkable that more patients do not suffer from them during and after cardiac surgery. This is to a large degree because of advances in anesthetic, surgical and critical care that, for example, have reduced the physiological insults of surgery (e.g., better myocardial preservation techniques) and streamlined care in the immediate postoperative period (e.g., early extubation). Moreover, the development of minimally invasive surgery and nonbypass techniques are further evidence of the attempts at reducing the homeostatic disruptions of cardiac surgery. This review examines the available information on the incidences, consequences, and treatments of postcardiac surgery respiratory complications.

Over the past two decades a steady evolution has taken place in the practice of adult cardiac surgery. The introduction of percutaneous interventional cardiology procedures (balloon angioplasty and stents) has reduced the number of coronary artery bypass graft (CABG) operations.[1] This decrease has been somewhat offset by the aging of the population coupled with successful surgery on elderly patients, especially octogenarians.[2] Simultaneously, valve operations have increased, attributed to the increase in surgery performed on the elderly.[2] Along with these trends have been the introduction of new sugical techniques such as minimally invasive surgery, off-pump surgery, and the repair, rather than the replacement, of diseased valves.

Respiratory complications remain a leading cause of postcardiac surgical morbidity and can prolong hospital stays and increase costs (3). In a study that used an administrative database of 51,351 patients who underwent CABG from 1999–2002 in 76 hospitals in the United States, 0.78% had pneumonia, 4.86% had adult respiratory distress syndrome/pulmonary edema, and 2.96% had other respiratory complications.[1] The high incidence of pulmonary complications is in part due to the disruption of normal ventilatory function that is inherent to surgery in the thoracic region. Furthermore, the patients undergoing such surgery often have significant underlying illnesses that increase their susceptibility to postoperative respiratory problems. Among these underlying diseases are intrinsic lung disease (e.g., chronic obstructive pulmonary disease [COPD]) and pulmonary dysfunction secondary to cardiac disease (e.g., congestive heart failure).[4] Postoperative pulmonary failure occurs either as immediate failure, where the patient remains intubated upon leaving the operating room and then requires prolonged mechanical ventilation, or as delayed failure, where the patient is separated from mechanical ventilation in the immediate postoperative period but requires reinstitution at a later time.

This review initially examines the pathophysiologic changes to the respiratory system caused by cardiac surgery. It then focuses on a number of contemporary issues relating to the pulmonary consequences of the recent advances in cardiac surgery, among them:

1. Do the newer minimally invasive and noncardiopulmonary bypass (CPB) techniques reduce the incidence of pulmonary complications?
2. Are there fewer pulmonary complications with "fast-tracking" (extubation at the end of surgery or shortly thereafter)?
3. Is "postpump lung" still a major cause of postoperative morbidity in light of improved CPB techniques?

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4. Does postoperative pain management with thoracic epidural analgesia decrease postcardiac surgery pulmonary complications?
5. Do the older members (> 80 year old) of the cardiac surgical population have a greater incidence of pulmonary complications?

Pulmonary Pathophysiology

The very nature of traditional cardiac surgery—median sternotomy, CPB, depressed cardiac function, and manipulation of the thoracic contents—alters pulmonary and cardiac mechanics. Therefore, the pulmonary problems after such surgery include those secondary to cardiac dysfunction (pulmonary edema and congestive heart failure), those that are due to intrinsic pulmonary problems (e.g., atelectasis and pneumonia) and those resulting from CPB (postpump lung syndrome—acute respiratory distress syndrome). Clinical manifestations of postcardiac surgery pulmonary dysfunction span the spectrum from fever and productive cough to respiratory failure requiring prolonged mechanical ventilation. In three autopsy series, 5% to 8% of deaths after cardiac surgery were attributed to respiratory causes (e.g., pulmonary embolism, ARDS).[5-7] Recent studies have also linked genetic features, such polymorphisms of the tumor necrosis factor (TNF) locus and of the promoter of the interleukin (IL)-6 gene, to increased risks of postoperative pulmonary dysfunction.[8,9]

The major cause of poor pulmonary outcome after cardiac surgery is cardiac dysfunction.[10] This finding is not unexpected, because low cardiac output states directly and indirectly contribute to pulmonary dysfunction. Low cardiac output increases pulmonary capillary pressure and lung water, leading to problems ranging from mild congestive heart failure to overt cardiogenic pulmonary edema. Furthermore, a low cardiac output state leads to fatigue, which in turn results in weak coughing, reduced mobility, and lack of deep breathing. These conditions may exacerbate atelectasis and increase the propensity for pneumonia.

Lung Mechanics—Median Sternotomy with Cardiopulmonary Bypass

Cardiac surgery through a median sternotomy using CPB markedly affects pulmonary mechanics. After surgery there are decreases in forced vital capacity (FVC), expiratory volume in the first second of forced expiration (FEV_1), forced expiratory flow at 50% of vital capacity (FEF_{50}), 75% of vital capacity (FEF_{75}), peak expiratory flow rate (PEFR), and maximum voluntary ventilation (MVV). The VC and FEV_1 may decrease more than 50% from preoperative values.[11] Changes persist for more than 3.5 months after surgery and are attributed to reduced and uncoordinated rib cage expansion secondary to the median sternotomy, pain, and pleural effusions.[12-14]

When only saphenous vein grafts were used to bypass coronary arteries, functional residual capacity (FRC) and FEV_1 decreased less than when an internal mammary artery graft was also used.[15] Pleural changes on chest radiograph after internal mammary grafting were associated with greater decreases in pulmonary function than when no pleural changes were noted and when only saphenous veins were used.[16] These findings were ascribed to the extensive dissection of the interior portion of the anterior chest wall and the violation of the pleural cavity. As expected, there was a greater restrictive defect after bilateral than after unilateral mammary harvesting.[15]

Lung Mechanics—Median Sternotomy without Cardiopulmonary Bypass

The recent increase in off-pump surgery has provided an opportunity to examine the specific effects of CPB on lung mechanics. One could surmise that off-pump surgery causes fewer changes in pulmonary mechanics. In a study where both off-pump and on-pump CABG were performed through a median sternotomy, decreases in lung mechanics (FVC, FEV_1 and $FEF_{25/75}$) were similar in both groups during the first 6 postoperative days.[17] In addition, postoperative increases in the alveolar-arterial oxygen gradient and tissue elastance were similar in off-pump and on-pump patients.[18] The increases in tissue elastance were attributed to the development of atelectasis and positive fluid balance.[19,20] During the initial postoperative hours after both off-pump and on-pump surgery there were increases in the inspiratory resistance of the respiratory system attributed to the effects of sternotomy and surgery.[20]

Yet differences have been observed between on-pump and off-pump surgery. Patients who underwent on-pump surgery had significant increases in expiratory airway resistance that were

ascribed to inhomogeneous constriction of the peripheral airways.[19] The mechanism of this bronchoconstriction has not been determined but may be caused by the release of bronchoconstricting mediators during CPB. The increased airway resistance was not seen in on-pump patients treated with dopamine after bypass, presumably because of the bronchodilating β-adrenergic agonist effects of dopamine.[19] There appear to be relatively few differences in pulmonary mechanics between on-pump and off-pump cardiac surgery performed through a median sternotomy. This finding is ascribed to the major contributions of the median sternotomy itself and the manipulations of the thoracic contents, especially the lungs, during surgery.

Lung Mechanics—Ministernotomy

Median sternotomies have long been the classic incisions for cardiac surgery because of the excellent exposure they provide of the heart and great vessels. However, cardiac surgeons have long sought less extensive incisions to improve cosmetic results, decrease postoperative pain, and reduce pulmonary dysfunction, and thus have used partial sternotomies, also called ministernotomies, to bypass coronary arteries and replace aortic valves. No differences were seen in the time to extubation nor in the decreases in PaO_2, $PaCO_2$, FEV_1 and VC 4 and 10 days after aortic valve replacement and CABG surgery through a partial inferior midline sternotomy compared with a full sternotomy.[21-23] In one study, there were smaller decreases in FVC and FEV_1 and less pain after aortic valve replacement through partial superior sternotomies than after surgery through a median sternotomy.[24] In another study, there were smaller reductions in total lung capacity and maximum expiratory pressures, but not FEV_1, 5 days following aortic valve replacements performed through partial sternotomies compared with those performed through complete median sternotomies.[25] Patients who had partial sternotomies returned to baseline pulmonary function after a month, while after full median sternotomies it took 3 or more months to recover.[25]

Lung Mechanics—Thoracotomy

Limited thoracotomies are used in cardiac surgery for a number of reasons. For many years, limited anterolateral thoracotomies have been used for mitral valve surgery to provide better postoperative cosmesis.[26] More recently, the appeal of minimally invasive surgery has occasioned the use of alternative approaches such as limited anterior or posterior thoracotomies and video-assisted thoracoscopy. Experience with limited thoracotomies for lung surgery found less reduction in respiratory muscle strength and FVC than with standard thoracotomies.[27,28] Similar observations were made with off-pump minimally invasive CABG (MIDCAB) performed through anterior thoracotomies. The MIDCAB resulted in less impairment of VC and FEV_1 on postoperative days 3 and 5 than on-pump CABG performed through a median sternotomy.[29] Similarly, VC and FEV_1 was better preserved after off-pump MIDCAB performed through an anterior thoracotomy than after off-pump CABG performed through a median sternotomy.[30]

Oxygenation

Oxygenation can be impaired for a week or more after cardiac surgery with CPB. For example, after CABG with grafting of internal mammary arteries, decreases in PaO_2 (preoperative 78 ± 10 mmHg to 63 ± 9 mmHg) were observed on the second postoperative day.[13] Mechanisms include poor preoperative oxygenation; and intra- and postoperative leukocyte activation, atelectasis, and pulmonary fluid accumulation owing to cardiogenic or noncardiogenic pulmonary edema.[31,32] Regarding the former, Yamagishi et al[33] observed a negative correlation between $A\text{-}aDO_2$ and pulmonary capillary wedge pressure (PCWP) on the day after CABG surgery. Although studies have shown lower concentrations of inflammatory mediators following off-pump CABG, no differences were found in postoperative decreases in PaO_2, increases in $A\text{-}aO_2$ difference, or duration of mechanical ventilation.[18,34-38]

Respiratory Complications

The above pathophysiologic changes reflect the many different types of respiratory complications that occur during and after cardiac surgery. In a study of 2609 consecutive adult patients who underwent cardiac surgery with CPB, 7.5% had respiratory complications that led to either death (21%) or a hospital length-of-stay of more than

10 days in 64.3%. Only cardiac complications were more common (29%), but resulted in death (8%) or prolonged stay in only 29.4% of patients.[39] Moreover, 6-month mortality in patients requiring a prolonged postoperative intensive care unit (ICU) stay was higher in those with a combination of ventricular failure and respiratory failure (51%) than respiratory failure alone (36%).[40] These high morbidity and mortality rates make it important to prevent and treat pulmonary complications.

Atelectasis

Atelectasis and pleural effusions are the most frequently encountered clinical pulmonary abnormalities after cardiac surgery. In a large series, 63% of patients had atelectasis or pleural effusion, or both, on their postoperative chest radiographs.[41] The most frequently observed radiologic abnormality was left lower-lobe atelectasis. It occurred in 73% of patients after internal mammary artery grafting and in 54% when only vein grafts were used.[42] Among hemodynamically stable patients with seemingly normal chest radiography, but reduced oxygenation, computed tomographic (CT) scans of the chest revealed bilateral crescent-shaped densities in the dependent portions of the lungs consistent with atelectasis. Studies using multiple inert gas elimination techniques and CT scanning on the first postoperative day showed large areas of atelectasis in the posterior portions of the lungs without any clear correlation between atelectasis and the shunt fraction. The lack of correlation was more evident in CABG than mitral valve replacement patients and was attributed to mechanisms other than atelectasis, such as resistance to oxygen diffusion.[31,43] In studies in pigs, the extent of the atelectasis was greater in animals that underwent CPB than in those who only had sternotomies.[44] This finding was partially attributed to the lack of ventilation during CPB.

Atelectasis may be due to both intraoperative and postoperative etiologies. Intraoperative causes include the induction of general anesthesia, manual compression of the left lower lobe during maneuvers to expose the posterior surface of the heart, manual compression of the right lung during cannulation of the inferior vena cava, manual compression of the lung during internal mammary artery dissection, and apnea during cardiopulmonary bypass.[44,45] The harvesting of internal mammary arteries results in atelectasis, which is increased by the creation of a pleurotomy.[46] Despite greater pain and decrease in VC and FEV_1 with pleurotomy, as opposed to harvesting without pleurotomy, there was no evidence of adverse respiratory clinical outcome.[47] Interestingly, the incidence of postoperative respiratory complications was not greater when bilateral, as compared with unilateral, internal mammary grafting was used.[48]

Postoperative causes of atelectasis after cardiac surgery are many and include poor postoperative coughing, lack of deep inspirations, pleural effusions, gastric distention, and increased interstitial lung water. The increased respiratory rate and shallow breaths that often characterize the postoperative spontaneous respiratory pattern are due to both pain and mechanical/neural changes. This pattern contributes to the formation of atelectasis. Discriminant analysis showed an increase in the severity of atelectasis with a larger number of grafts, longer operative and bypass times, violation of the pleural space, placement of a right atrial drain, lack of a phrenic nerve insulating pad during surface myocardial cooling, and a lower body temperature during bypass.[49]

Minimally invasive surgery performed through minithoracotomies or via thoracoscopy requires one-lung ventilation using either double lumen endotracheal tubes or bronchial blockers.[50] The deflated state of the nonventilated left lung in such situations may contribute to the development of atelectasis in the lung. Atelectasis may be further exacerbated by the use of CO_2 insufflation during thoracoscopy and the inability to periodically inflate and suction the nonventilated lung during delicate and prolonged coronary artery or valve surgery.

Despite the high rate of radiographic atelectasis, the incidence of clinically significant pulmonary complications is relatively low[51,52] owing to early postoperative mobilization and effective pain control. Additionally, postcardiac surgery patients commonly receive intensive chest physiotherapy in the form of preoperative instruction in deep breathing and coughing exercises, positional therapy, chest wall percussion, and the use of incentive spirometry devices. The rational for these therapies is that they increase PaO_2 and the aerated area (by 5%) of the lung as seen on CT scans performed on the day after CABG surgery before and after 30 deep breaths performed both with and without the use of mechanical aids, such as blow-bottles.[53]

Yet, the low incidence and low morbidity of most cases of atelectasis was reflected by the inability of a randomized study to find any advantage of adding single-handed percussions to early mobilization and deep breathing exercises after valvular surgery.[51] Additionally, patients did not benefit from deep breathing exercises added to routine chest physical therapy after elective cardiac surgery.[54] These findings are reflected in the inability of systematic literature reviews of numerous clinical trials to prove that the routine, prophylactic application of physical therapy (defined as incentive spirometry, continuous positive airway pressure [CPAP], physical therapy and intermittent positive pressure breathing) is helpful.[55,56] However, there are some patients where the retention of secretions due to pain, weakness, dyspnea, or neurologic impairment, is very often the trigger for delayed postoperative pulmonary failure owing to atelectasis and pneumonia. It is in these patients where chest physiotherapy might be useful in mobilizing secretions and preventing atelectasis from progressing to pneumonia.

Other methods have been proposed to prevent and treat intra- and postoperative atelectasis with its associated reduction in PaO_2 and lung volumes. These include providing CPAP (5 cm H_2O) during and positive end expiratory pressure (PEEP) immediately after CPB.[57] Animal investigations hint at improved pulmonary lung function (PaO_2 and $AaDO_2$) following CPB when 5 cm H_2O of CPAP is provided during CPB.[58,59] This finding was confirmed in a study in patients who received 10 cm H_2O of CPAP during CPB.[60] However, despite these recent studies, it is still unclear whether to continue ventilation during bypass, provide CPAP, or simply not to ventilate.[61] Because atelectasis is almost always present immediately after surgery with CPB, it has been proposed that mechanical efforts be made to increase and maintain lung volumes.

Experiments in pigs demonstrated that a vital capacity maneuver (inflating the lungs for 15 seconds to 40 cm H_2O) performed before terminating CPB decreased post-CPB atelectasis. The decrease in atelectasis was greater when the pigs were ventilated with 40% O_2 instead of 100% O_2 presumably owing to less absorption atelectasis.[46] The reduction in atelectasis lasted for a least 6 hours post-CPB and was not further improved by vital capacity maneuvers repeated hourly.[62] Similarly, better oxygenation was observed in patients ventilated with 50% O_2, rather than 100% O_2 during the entire period of cardiac surgery.[63]

Performing a vital capacity maneuver before terminating CPB to reduce shunting appears to have some advantages, although, these effects are short lived.[64] Despite these short-lived effects, one study did show that a vital capacity maneuver before the termination of bypass reduced the time to extubation by approximately 3 hours.[65] Some have proposed performing a lung recruitment maneuver (two 20-second inflations to 45 cm H_2O) after ICU admission. To maintain the resultant improved end expiratory lung volumes and PaO_2, it is necessary that PEEP (~14 cm H_2O) be used until extubation.[66,67] Failure to place the patients on PEEP after the recruitment maneuver did not sustain the improved lung volumes or oxygenation. Furthermore, the uses of no PEEP or only 5 and 10 cm H_2O PEEP without a recruitment maneuver did not improve oxygenation, although the PEEP did improve lung volumes.[68]

Noninvasive ventilation with a nasal mask or facemask and either CPAP or bilevel ventilation (BiPAP) have been used in an attempt to improve postcardiac surgery pulmonary function. After median sternotomy, CPAP via face mask has been shown to improve FRC to preoperative levels, but the effect is short lived with FRC returning to pretreatment levels within 10 minutes of discontinuing treatment.[69] In another study, patients treated after extubation with conventional chest physiotherapy plus incentive spirometry and either CPAP (5 cm H_2O) or BiPAP (5/12 cm H_2O) had higher VC, FEV_1 and PAO_2 on the second postoperative day.[13] However, there were no differences in the length of ICU stay.

Another study showed that CPAP was more effortless and less painful than incentive spirometry and coughing with deep breathing exercises.[70] However, it was not more effective in reducing the degree of atelectasis or hypoxia.

There have been concerns about the cardiac effects of facemask CPAP, yet Masouye et al[71] found that CPAP did not significantly affect right ventricular function after cardiac surgery. It is still unclear whether noninvasive ventilatory treatment after extubation reduces the incidence of pneumonia or reduces the length-of-hospital stay.

Pleural Effusions

Many patients develop pleural effusions immediately after cardiac surgery.[72,73] When chest radiographs were used to identify effusions, the reported incidence after CABG was 40% to 50%.

Most of the effusions were left-sided, small (confined to the costophrenic angle), asymptomatic, and resolved spontaneously. The prevalence of pleural effusions is higher with CABG performed with internal mammary arteries rather than only saphenous vein grafts. In a small (30 patients) study where CT scanning, a much more sensitive diagnostic modality, was performed 2 and 7 days after CABG, a higher incidence of pleural effusions was found:[74] 48 hours after surgery 57% of patients had pleural effusions on the right side and 67% on the left side. By day 7 there had been a decrease on the right side to 23% and no change on the left side (63%).

These effusions have many causes, including postoperative bleeding, atelectasis, pneumonia, cardiogenic and noncardiogenic pulmonary edema, pleurotomy performed to harvest internal mammary artery grafts, damage from topical cardiac hypothermia, disruption of pleural lymphatic drainage by internal mammary artery harvesting, and leaking of fluid from the mediastinum.[75,76] Very rarely, pleural effusions have been caused by chylothoraces.[77] Pleural effusions occurring 2 to 3 weeks after surgery may be part of the postpericardiotomy syndrome, which occurs in 10% to 40% of patients after cardiac surgery. These effusions generally resolve within a few months of surgery and require no treatment.

A small group of postcardiac surgery patients (29 of 3707 [0.78%] CABG patients) develop large (occupying more that 25% of the hemithorax) pleural effusions.[73] These effusions tend to be unilateral and left-sided. Some are bloody, have a high eosinophil count, reach their maximum volume one month after surgery, and are thought to be caused by bleeding into the pleural space. Nonbloody effusions persist longer than bloody ones and are likely caused by etiologies other than bleeding. These large effusions are associated with dyspnea, but not chest pain or fever. Although most resolve within a year of surgery, some patients require treatment with thoracentesis or chest tubes.[72]

Pneumonia

The reported incidence of pneumonia after CABG and valvular surgery ranges from 2% to 22%.[51,78] This wide range is due to differences in study populations and in the definitions used to diagnose pneumonia.[79] These incidences are not surprising. Many patients undergoing cardiac surgery have either overt or covert COPD since cigarette smoking is a strong risk factor for coronary artery disease. Warner et al[80] found that patients who had stopped smoking for less than 2 months before CABG had a pulmonary complication rate almost 4 times that of patients who had stopped for more than 2 months (57.1% vs 14.5%). Patients who had stopped smoking for more than 6 months had complication rates (~11%), similar to those who had never smoked. Similarly, Ngaage et al[81] noted that postoperative complications were twice as common in smokers (29.5%) as nonsmokers (13.6%) and exsmokers (14.7%).

Besides preexisting conditions that predispose patients to postoperative pneumonia, postoperative conditions are also important. These include the frequent occurrence of atelectasis after cardiac surgery coupled with poor coughing owing to pain, increased lung water owing to cardiac failure, and advanced age. Postcardiac surgical neurologic and cognitive impairment may also contribute to the development of pneumonia by facilitating silent aspiration secondary to pharyngeal dysfunction.[82] Postoperative pneumonia causes a range of problems, from fever and productive cough to acute respiratory decompensation requiring prolonged mechanical ventilation. Diagnosing pneumonia with chest radiographs may be difficult after cardiac surgery because of concomitant atelectasis and pleural effusions. Therefore, it is important to have a high index of suspicion among patients with productive sputum and fever.

Prolonged postoperative intubation and mechanical ventilation may lead to ventilator-associated pneumonia (VAP), as can reintubation for reoperation, respiratory insufficiency, or cardiac failure.[83] VAP has an incidence of 9% to 21% among patients with respiratory failure.[84,85] The associated mortality can be as high as 75% because of the propensity for multiple organ dysfunction to develop.[86] In a prospective actuarial study, the risk of pneumonia in an ICU population increased by 1% with each day of mechanical ventilation.[87] In cardiac surgical patients, 8% had at least one episode of VAP, while 44% of those intubated more than 7 days developed VAP.[88]

Pneumonia is the most morbid and mortal infection that occurs after cardiac surgery.[89] In one series, pneumonia after CABG occurred on average 4 days after surgery and was associated with 27% mortality. Risks included a history of COPD, administration of H_2-receptor blocking agents,

and 2 or more days of postoperative mechanical ventilation.[90] In another study, COPD was not found to be a risk factor. However, reintubation, the presence of a nasogastric tube, transfusion of 4 units of blood products or more, and treatment with broad-spectrum antibiotics were associated with increased risk.[85,91] The relationship of blood product transfusion with the development of postoperative infections has been well described and is thought to be due to more extensive surgical injury, anemia, and the immunosuppressive effects of blood products.[89,91-93] In a group of cardiac surgery patients, the risk of pneumonia increased by 5% per unit of red blood cells (RBC) or platelets received. Additionally, there was an increased risk of pneumonia for each day that the blood was stored, lending some evidence to immunosuppressive effects increasing the risk for pneumonia.[94]

Most pneumonias after cardiac surgery are attributed to Gram-negative organisms. However, a more recent prospective study found that pneumonia occurring within 3 days of CABG is likely to be caused by Gram-positive organisms that were present in the sputum prior to surgery. Risk factors for the development of such pneumonia included preoperative smoking, preoperative positive tracheal aspirate, low cardiac output, and the transfusion of more than 4 units of packed RBCs.[95]

Pneumonias occurring later in the postoperative course are typically due to Gram-negative organisms. Patients, especially those receiving mechanical ventilation, become colonized with pathogenic Gram-negative bacteria, such as *Pseudomonas aeruginosa, Acinetobacter, Klebsiella* and *Enterobacter*, which are becoming increasingly resistant to antibiotics. This resistance is not surprising given the routine prophylactic use of broad-spectrum antibiotics, such as cephalosporins, during the intraoperative and immediate perioperative periods.

The source of these bacteria is thought to be microaspiration of small amounts of oropharyngeal secretions—the "gastro-pulmonary hypothesis".[96] This risk is greater in patients with overt acute cerebrovascular events but is also increased in patients with diabetes mellitus, COPD, previous myocardial infarction, prior cerebrovascular accident and age of 75 years or older.[82] In mechanically ventilated patients, endotracheal tube cuffs are effective in preventing large volumes of fluid from passing into the lower trachea but do not prevent microaspiration.

Risk factors that increase the chances of microaspiration of oropharyngeal secretions include the supine position and the presence of a nasogastric tube. H_2-receptor blocking agents used as prophylaxis against upper gastrointestinal bleeding have been implicated as increasing the colonization of gastric fluid with many Gram-negative bacteria, which can then be microaspirated.

Specific measures that have been suggested to prevent VAP include using multi-use, closed-system suction catheters, no routine changing of ventilator breathing circuits, continuous subglottic suctioning, maintaining patients semi-recumbent, avoiding H_2-blockers and early enteral feeding. However, a large (1200 patients) multicenter study showed that H_2-blockers do not significantly increase the risk of VAP or mortality compared with sucralfate, an agent that does not affect intragastric pH.[97] Continuous aspiration of subglottic secretions is feasible using special endotracheal tubes. However, this technique has not been placed into routine use, partially because a prospective trial failed to show that it reduced the incidence of VAP; it only delayed its appearance.[98]

Another strategy to decrease infectious complications and reduce multiple system organ failure is to use intensive insulin therapy to maintain postoperative blood glucose concentrations below 110 mg/dL even in nondiabetic patients.[99] It is the glycemic control not the insulin that is beneficial.[100] In diabetics, maintaining the glucose below 200 mg/dL in post-CABG patients also reduced infectious complications.[101]

Pulmonary Edema

Diffuse parenchymal processes, and cardiogenic and noncardiogenic pulmonary edema are among the causes of acute respiratory failure after cardiac surgery. Cardiogenic (or hydrostatic) pulmonary edema occurs when there is transudation of fluid into the interstitial lung spaces and alveoli caused by high pulmonary microvascular pressure. Noncardiogenic pulmonary edema occurs as the consequence of increased permeability of pulmonary capillaries with exudation of protein-rich fluid into the alveoli. It is called noncardiogenic pulmonary edema because it occurs with PCWP below 18 mm Hg.

Cardiogenic Pulmonary Edema

Cardiogenic pulmonary edema that is due to reduced left ventricular function is among the lead-

ing reasons for prolonged mechanical ventilation after cardiac surgery. The reduced left ventricular function may be a preoperative condition or may result from intraoperative events. Examples of patients with preexisting reduced left ventricular function include those undergoing mitral valve surgery for mitral regurgitation secondary to dilated cardiomyopathy and CABG for ischemic cardiomyopathy.[102,103] Importantly, a low preoperative left ventricular ejection fraction has a greater correlation with postoperative respiratory failure than does decreased preoperative pulmonary function.[10] The treatment of cardiogenic pulmonary edema involves improving the underlying cardiac function with inotropic agents, afterload reduction, and diuretics. An intra-aortic balloon pump (IABP) may be inserted to support cardiac function. Such patients have a high mortality (34% in one series); 67% of the patients who were weaned from the IABP, but subsequently died, had respiratory failure and pneumonia.[104]

Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) is a group of conditions characterized by noncardiogenic pulmonary edema. The clinical criteria for its diagnosis are the presence of bilateral interstitial infiltrates on chest radiograph, a PCWP of less than 18 mm Hg, and the presence of arterial hypoxemia to such a degree that the PaO_2/FiO_2 ratio is less than 200. Acute lung injury (ALI) is less severe than ARDS and is characterized by the same criteria, but with a PaO_2/FiO_2 ratio between 200 and 300. ARDS is usually associated with decreased lung compliance. ARDS can range from mild to severe, leading to a variety of clinical presentations. Full blown ARDS after CPB occurs in less than 2% of patients, with mortality rates as high as 80%.[105] ARDS is a component of multiple organ system dysfunction, which also occurs in less than 2% of patients undergoing cardiac surgery, with mortality rates of up to 75%.[106,107] Lesser degrees of acute lung injury that manifests as reduced oxygenation, increased V/Q mismatch, and decreased lung compliance, occurs in up to 12% of patients after CPB.[108]

ARDS among patients undergoing cardiac surgery has many possible causes. CPB has been implicated as causing postpump ARDS. The mechanism is thought to be the triggering of a systemic inflammatory response that leads to increased pulmonary endothelial permeability.[109] Many studies have shown that CPB triggers a cascade of substances associated with the systemic inflammatory response. Details of this inflammatory response to cardiac surgery were recently reviewed by Laffey et al.[110] This response entails mediators such as the cytokines and endothelium-derived factors (e.g., nitric oxide), as well as activation of the complement and coagulation-fibrinolytic cascades. Clinical studies have associated this response with postoperative pulmonary complications. For example, high blood concentrations of intracellular adhesion molecule-1 (ICAM-1) after CPB were correlated with the development of respiratory insufficiency.[111] These adhesion molecules aid in the sequestration of neutrophils, and so these findings are consistent with prior reports of the sequestration of large numbers of neutrophils in the pulmonary capillaries during rewarming from CPB. This sequestration is associated with an elevation in lysosomal enzyme activity,[112,113] which is evidence for a localized inflammatory reaction that can result in increased capillary permeability.

Further evidence of postbypass pulmonary injury consistent with ARDS comes from histologic studies. Examination of pre- and 20 minutes post-CPB lung specimens revealed that after CPB, there was extensive injury to the air–blood barrier with swelling, and even necrosis, of endothelial cells and type I and type II pneumocytes. Additionally, in many alveoli, surfactant was not evenly distributed because of cellular edema.[114]

Despite these injuries, most of the patients had uneventful recoveries.[114] This finding is consistent with clinical observations wherein only a small minority of patients actually developed full-blown ARDS, while many have more subtle changes in pulmonary function, such as mildly impaired oxygenation.

Among the possible triggers for the inflammatory response is blood coming in contact with the artificial surface of the perfusion circuit, resulting in leukocyte activation with the subsequent release of cytokines and other inflammatory substances.[115,116] Heparin-coated circuits reportedly attenuate the release of cytokines and other mediators, leading to better post-CPB lung compliance and pulmonary vascular resistance. However, such circuits do not appear to provide any clinical benefit.[117]

Another trigger may be that the low tissue perfusion during CPB causes intestinal hypoperfusion and ischemia that is thought to translocate enteric endotoxins and trigger a systemic inflam-

matory response.[107] Furthermore, the reperfusion of intestines and other underperfused areas at the termination of CPB might initiate the reperfusion syndrome, which also activates the inflammatory cascade.

There is some evidence that membrane oxygenators cause less postoperative accumulation of extravascular lung water and atelectasis then bubble oxygenators, but this does not appear to translate into less clinically evident postoperative respiratory dysfunction.[108,118] More recently there has been interest in hollow fiber membrane oxygenators, because they cause less leukocyte activation than flat sheet membrane oxygenators. However, no clinically significant differences in respiratory dysfunction were observed between the two types of oxygenators.[119]

Attempts at modulating the stress response with glucocorticoids (methylprednisolone, 0.3 mg/kg every 6 hours for 4 doses starting 1 hour before surgery) were studied in a randomized, prospective, double-blinded, placebo-controlled trial. No differences were noted in the duration of postoperative mechanical ventilation, peak expiratory flow rates or A-aO_2 differences.[120] Another study of similar design used larger doses of methylprednisolone (30 mg/kg during sternotomy and the initiation of CPB). The steroids resulted in prolonged intubation and greater increases in A-aO_2 gradient and shunt.[121] Steroids are not indicated to decrease the inflammatory response or reduce the incidence of postoperative respiratory dysfunction.

CPB may not be the only cause of ARDS after cardiac surgery. Other proposed etiologies include the administration of protamine, hypothermia, cessation of ventilation during CPB, and untoward reactions to blood products. Risk factors for ARDS development included previous cardiac surgery, shock, emergency surgery, low preoperative ejection fraction and significant (> 4 units) transfusion of blood products.[122,123] The dilemma is whether the latter is due to the blood products themselves activating the inflammatory cascade or is just a marker of severe surgical injury and shock is unclear. Moreover, ARDS is cited as one of the complications of re-exploration for bleeding, again pointing out this dilemma.[124]

Attempts at attenuating the activation of the inflammatory cascade through the use of leukocyte-depleted blood transfusions was proposed as a method of reducing postoperative ARDS and infectious complications.[125] However, this has not been confirmed by clinical studies.[126] It has also been postulated that pleurotomy prior to CPB and positive fluid balance during CPB may accentuate post-CPB pulmonary edema.[127] Despite the many factors that can potentially trigger ARDS during and after cardiac surgery, the incidence of clinically significant ARDS is less than 2%. Therefore, there is still much to be learned about why ARDS develops in only some of the patients who suffer from the potential triggering factors.

Is postpump lung still a major cause of postoperative morbidity in light of improved CPB techniques? In two series of cardiac surgery patients (with CPB) published in the early 1980s and mid 1990s 1.0% to 1.3% developed ARDS, with reported mortality rates of 53% to 68%.[128,129] More recent reports revealed incidences of 0.4% and 0.5% with mortality rates of 15% and 91%, respectively.[122,123] In addition, the incidence of multiple system organ failure, which ARDS is one of the components, was lower in the more recent studies. In a series of autopsies from patients undergoing cardiac surgery from 1985 to 1995, 4% of 147 autopsies demonstrated ARDS.[5] A more recent postmortem study showed that 2% (of 108 patients) had ARDS.[6,130] The reduction in the incidence of ARDS was ascribed by the authors of these studies to the use of membrane rather than bubble oxygenators, better myocardial preservation techniques, and the reduced use of hypothermia below 32°C during CBP. As yet there are no reports of the incidence of ARDS in large, multicenter series of off-pump patients, so it is unknown whether the incidence of ARDS is lower after such operations.

The ventilatory support of patients with ARDS has undergone changes over the past decade. The current scheme, dubbed the *protective lung strategy*, aims to avoid ventilator-associated pulmonary mechanotrauma. Mechanotrauma involves damage to the alveoli and other small lung structures that results from repetitive over-stretching owing to large tidal volumes—"volutrauma"—and cyclic recruitment-derecruitment of collapsed areas of the lung. It is thought that such mechanical stress activates humoral lung responses, such as the release of cytokines, thus intensifying the injury to the lungs. To attenuate this ventilator-induced lung injury, there has been a shift towards the use of small tidal volumes (approximately 6 mL/kg) and limitation of airway plateau pressures. These smaller tidal volumes are often accompanied by mild-to-moderate elevations in PaCO_2 (e.g., 50–60 mmHg with concomitant decreases in pH). This permissive hy-

percapnia has not been found to have detrimental effects.[131] In a multicenter study of ARDS, tidal volumes of 6 mL/kg resulted in a 25% reduction in mortality compared with tidal volumes of 12 mL/kg.[132] It is not yet been shown whether this strategy has specifically impacted the mortality or morbidity rates of ARDS following cardiac surgery.

Pulmonary Embolism

A problematic complication after all types of surgery is the development of deep venous thrombosis (DVT) with embolization of thrombotic material to the lungs. The reported incidence of pulmonary embolism after cardiac surgery ranges from 0.3% to 9.5%. Mortality after pulmonary embolism was high, 18.7% vs 3.3% for those with no embolism, although the incidence of fatal pulmonary embolism was 0.5%.[133-135] The incidence is lower after valve surgery than CABG, perhaps because many of the former patients are anticoagulated soon after surgery.[133]

The reported rate of DVT after CABG ranged from 17% to 46%, although most cases had no significant symptoms.[133,135] The higher incidences were reported from series that examined entire populations with lower extremity ultrasound.[135] The DVT occurred not only in the legs from which saphenous vein grafts were harvested but also in contralateral legs.[133,136] It is important to note that after CABG, many patients receive aspirin to prevent graft thrombosis as well as other DVT prophylaxis, especially elastic graded compression stockings. Post-CABG patients (n = 270) admitted to a rehabilitation unit all underwent lower extremity ultrasound examinations. DVT was detected in 17%, and 2 patients subsequently developed pulmonary emboli.[142] Age over 65 years, female gender, and postoperative complications predicted the development of DVT. When bedridden patients were excluded, heparin prophylaxis that was started soon after surgery until transfer to the rehabilitation unit and continued for more than 3 days reduced the incidence of DVT compared to prophylaxis for less than 3 days after surgery.[137] Among 147 autopsies after cardiac surgery, death was attributed to pulmonary embolism in 4%.[5]

The current recommendations for DVT prophylaxis are aspirin and elastic gradient compression stockings in CABG patients who ambulate within 2 to 3 days after surgery and low-molecular-weight heparin and sequential compression stockings in patients bedridden for longer periods.[135] These recommendations are based on a randomized trial where prophylaxis with sequential pneumatic compression stockings provided no added protection against DVT in ambulating CABG patients treated with aspirin and elastic gradient compression stockings.[138]

Off-pump surgery has raised the question of whether such patients develop a hypercoagulable state similar to that seen after major noncardiac surgery.[139] The level of anticoagulation during such operations is lower than during CPB operations. In a study that compared 500 off-pump with 1476 on-pump CABGs, there were 5 (1%) and 8 (0.5%) venous thrombotic and thromboembolotic complications in each of the two groups;[140] however, this difference did not achieve statistical significance. The authors recommended that off-pump patients also receive anticoagulant prophylaxis.

Phrenic Nerve Injury

Phrenic nerve injury is an especially problematic respiratory complication of cardiac surgery. Poor diaphragmatic function should be suspected if there is paradoxical motion during spontaneous breathing, an elevated diaphragm on chest radiograph, or a decreased vital capacity. The diagnosis is made with fluoroscopy or ultrasonography. Phrenic nerve injury most often occurs on the left side, and though it often is short-lived, it may interfere with discontinuation of mechanical ventilation. Unfortunately in some patients, the dysfunction may persist for 6 or more months and interfere with activities of daily living.[76]

Such injury is usually caused by irrigation of the pericardial space with cold solution for myocardial preservation during CPB.[141] Electrophysiologic evidence of nerve injury was seen in 32% of patients when ice slush was used and in 2% to 6% when cold saline was used.[142] The prevalence of clinically significant diaphragmatic dysfunction has been estimated to be 2.1% when the heart is cooled without an insulation pad protecting the phrenic nerve and about 0.5% without any topical cooling.[76,143] Nerve injury was rarely seen when only intracoronary cardioplegia was used.[141] Furthermore, the incidence of such injury has decreased now that often cardioplegia is administered in retrograde fashion through a coronary sinus catheter and there is less use of

surface cooling. Another cause of phrenic nerve injury may be direct trauma during the incision or manipulation of the pericardium.

Clinically evident phrenic injury may rarely occur during the harvesting of the internal mammary artery, since on the left side the nerve crosses the path of the artery and on the right side the two are parallel.[144] However, subclinical injury is more common. A retrospective study of postextubation chest radiographs hinted at subclinical phrenic nerve dysfunction in 42% of patients who had internal mammary artery harvesting versus only 12% of those who did not.[145] After high, free-graft right internal mammary artery harvesting in 783 patients, 31 (4%) had evidence of phrenic nerve injury, with 12 requiring diaphragmatic plication.[146] All cardiac surgery patients who fail to easily wean from mechanical ventilation and who have no other obvious cause for respiratory failure should be investigated for phrenic nerve injury.

Pneumothorax

Pneumothoraces may occur after cardiac surgery because of direct injury to the lung during surgery or central venous cannulation, spontaneous rupture of pulmonary blebs, and barotrauma during mechanical ventilation. The overall incidence of pneumothorax after cardiac surgery is reportedly 0.7% to 1.7%,[147,148] although the incidence following CABG with internal mammary harvesting is as high as 5.3%.[50]

Mediastinal and often also pleural tubes are routinely placed in the chest cavity to evacuate air and blood immediately before closing the chest. However, pneumothoraces may occur immediately after surgery when air accumulates in unopened pleura surrounding damaged lung tissue. In addition, mediastinal or pleural tubes may be unable to evacuate all the leaking air because of misplacement or blockage caused by kinking, obstruction with blood clots, or pleural loculations secondary to lung disease. Because many cardiac surgery patients are mechanically ventilated after surgery, injuries to the lung causing air leaks may present as tension pneumothoraces. Furthermore, pneumothoraces may only become apparent after the removal of mediastinal and pleural tubes.

Minimally invasive cardiac surgery and surgery through a ministernotomy present special problems because injury to the lung may not be recognized during surgery so that pneumothoraces may only become evident once the thoracic cavity is closed. This situation can lead to a prolonged air leak owing to the inability to repair significant lung lacerations.[149] In general, most pneumothoraces resolve with tube thoracostomy treatment; however, a few cases have been reported of chronic broncho-pleural fistulae following CABG that required surgical repair.[150]

There have been many recommendations on how to prevent pneumothoraces from developing immediately after surgery. These include opening both pleurae so that mediastinal tubes can drain pleural air and placing pleural tubes in the cavity where the internal mammary artery has been dissected. It is also important that the nursing and medical staff maintain the patency of the mediastinal and pleural tubes.

Barotrauma is one of the complications of positive pressure mechanical ventilation with the dramatic manifestation being the development of a tension pneumothorax if intrapleural air is not evacuated. Additionally, pneumomediastinum, pneumopericardium, and interstitial and subcutaneous emphysema also occur, but usually do not cause any clinically significant problems. Lung collapse secondary to a pneumothorax causes clinical problems when it leads to hypoxemia, elevated intrapleural pressures causing hemodynamic compromise (tension pneumothorax), or air leaks that prevent sufficient effective ventilation.

Among the conditions that increase susceptibility to developing barotrauma are chronic interstitial lung disease, status asthmaticus, and COPD. In the latter two conditions, if insufficient time is allowed for expiration, dynamic hyperinflation may occur leading to overdistention of the alveoli and barotrauma.[151] Therefore, ventilator strategy in such situations should include prolonged expiratory time, even if tidal volume and respiratory rate must be reduced and thus resulting in moderate elevations in $PaCO_2$ (permissive hypercapnia). Acute conditions that predispose to ventilator-associated barotrauma include overdistention of the lung and reduced integrity of the lung tissue. Lung tissue may be compromised by necrotizing infections, preexisting blebs, and direct surgical damage. Positive airway pressure, if excessive, may by itself cause barotrauma. In ARDS, the lungs can be so stiff (i.e., compliance so reduced) that high airway pressures do not cause barotrauma since little pressure is transmitted to the pleural surface; thus the alveolar-pleural pressure gradient is low. Among mechan-

ically ventilated patients with ARDS and acute lung injury, barotrauma occurred in 13%.[152] When patients were ventilated with low tidal volumes and limited airway pressures, the incidence was 6.5%.[152]

Sternal Wound Infection and Mediastinitis

Deep sternal wound infection and mediastinitis are devastating complications of median sternotomy with mortality of 10% to 47%.[153] Although they are not by definition pulmonary infections, they have much influence on pulmonary function. Such patients often need one or more operations and so require reintubation and mechanical ventilation for variable lengths of time. The unstable sternum and the associated pain prevent deep breathing and interfere with effective coughing, thus increasing susceptibility to pneumonia. Mediastinitis may result in unilateral or bilateral pleural effusions in up to a third of patients with mediastinitis.[154] The risk factors for developing deep sternal wound infections include many of those associated with developing postoperative pneumonia, including older age, smoking, obesity, and prolonged postoperative ventilation.[155] Therefore, it is not surprising that postoperative pulmonary problems and infections at another site, such as pneumonia, are among the independent risks for the development of a sternal infection.[153,156]

Postoperative Pulmonary Management

Mechanical Ventilation after Cardiac Surgery

Traditional practice was to mechanically ventilate patients for up to 24 hours after cardiac surgery so as to allow patients to rewarm, emerge from anesthesia, stabilize hemodynamically, and ascertain if there was excessive bleeding. It was postulated that continued mechanical ventilation would insure control over ventilation, reduce metabolic demands, and negate the need to induce anesthesia and reintubate in case of return to the operating room for bleeding. This process was based upon intuitive thinking and not supported by published studies.

More recent practice has been to discontinue mechanical ventilation as early after surgery as possible—ideally within 4 to 6 hours.[157] This tendency toward earlier extubation was demonstrated in a study of 4400 patients from 21 European centers that showed that the overall median time to extubation was 12 hours, with 8 centers having median times of 10 hours or less.[158] The reasons that earlier extubation was introduced were both clinical (prolonged ventilation is associated with greater morbidity from nosocomial infection) and economic (shorter ICU and hospital stays).

"Fast-tracking," or rapid weaning, is traditionally practiced in selected, elective, hemodynamically stable patients with adequate gas exchange who have no evidence of cardiac failure, excessive bleeding, or neurologic injury. However, there have been reports of successful fast-tracking in elderly patients and those with poor ventricular function.[159] Fast-tracking requires the use of short-acting anesthetic techniques and appropriate postoperative sedation,[160,161] including drugs such as remifentanil, alfentanil, propofol, inhalation anesthetics, and avoidance of longer-acting muscle relaxants such as pancuronium.[162-164] However, the most important feature of any fast-track anesthetic technique is the proper timing and dosing of anesthetic drugs, as shown by the successful use of longer-acting agents, such as sufentanil, for fast-tracking.[165]

Among the rationales for fast-tracking patients is that it permits them to ambulate and cough soon after surgery, and thus, it would be expected to reduce the incidence of respiratory complications. A retrospective, matched cohort study demonstrated that patients extubated early after surgery had significantly less atelectasis than those extubated later.[166] Additionally, on postoperative day 5, VC and FEV_1/FVC were higher in the group of patients extubated early after surgery.[166] In a study of two consecutive cohorts of patients, the fast-track patients had a 7.3% nosocomial pneumonia rate versus a 14.7% rate in nonfast track patients.[167] Another study of fast-tracked patients showed low pneumonia rates: 3.4% of those less than 70 years of age and 4.4% of those older than 70 years developed pneumonia.[168]

A systematic review of 10 fast-track trials found that reintubation of such patients is rare.[169] In a series of 572 patients selected for early extubation (mean time after surgery, 190 minutes) only one developed respiratory failure that required reintubation and mechanical ventilation.[170] It appears that there is some evidence that fast-tracking reduces respiratory complications. However, it is important to remember that in the nonrandomized studies, fast-track patients tended

to be those at lower risk. Unfortunately, a systematic review of six clinical trials was only able to show that the benefits of early extubation were shorter ICU (7 hours) and hospital (one day) stays because the trials were not designed to adequately assess other more clinically oriented end points.[159]

The experience with fast-tracking has led some centers to extubate selected patients in the operating room. This practice does not appear to be problematic, since patients extubated before leaving, compared with those extubated within 6 to 8 hours of leaving the operating room, did not have any differences in oxygenation, lung volumes, or chest radiograph evidence of atelectasis up to 4 days after surgery.[171-172] Similarly, extubation within 6 hours, compared with 6 to 24 hours, after completion of surgery did not reduce the length of ICU or hospital stay. However, patients extubated only after 24 hours had longer hospital stays and more postoperative complications.[173] This delayed extubation was associated with poor left ventricular, renal, and pulmonary function, as well as the longer duration and greater urgency of surgery.[181]

With off-pump CABG, many patients are successfully extubated very soon after surgery, including in the operating room, without any subsequent pulmonary complications. The time to extubation was shorter in off-pump than in on-pump CABG patients (3.4 vs 8.3 hours).[174] In a series of 160 patients extubated in the operating room, the 5 subsequent reintubations were for reoperation for mediastinal bleeding and not respiratory failure.[175] Among 64 MIDCAB patients, 85% were extubated in the operating room without complications.[176]

Prolonged Mechanical Ventilation

The small numbers of patients requiring prolonged mechanical ventilation after cardiac surgery represent a subset of patients with a high incidence of respiratory complications. Data from 503,478 CABG patients operated upon from 1997–1999 (Society of Thoracic Surgeons [STS] National Adult Cardiac Surgery Database) found that 5.96% were ventilated for more than 48 hours.[177] Such patients had a higher mortality (11.3%) than an entire study population (1.5%) of 995 patients.[178] Another study using STS data from 496,797 CABG patients found that 44% of the 29,781 (6%) patients who had prolonged ventilation stayed in the hospital for more than 14 days. Alternately, 50% of the 26,008 patients with stays of more than 14 days had prolonged ventilation.[179]

Prolonged ventilation is often due to cardiac dysfunction (low cardiac output state) causing cardiogenic pulmonary edema, but may also be due to noncardiogenic pulmonary edema or pneumonia. Patients who develop atrial fibrillation after cardiac surgery have a higher incidence of re-intubation.[180] Other causes of prolonged mechanical ventilation and re-intubations include persistent postoperative bleeding, neurologic complications, acute renal failure[181] and intra-abdominal complications, such as acalculous cholecystitis and postoperative hepatic dysfunction.[182] Surgical reexploration for bleeding also is a strong independent risk factor for prolonged mechanical ventilation.[183] Forty-one (2%) of 2615 postcardiac surgery patients developed severe sepsis and required mechanical ventilation for longer (31 ± 21 [SD] days) than nonseptic patients (0.9 ± 0.1 days).[184] Similarly, patients who developed a bloodstream infection within 96 hours of surgery were mechanically ventilated for an extended period (117 ± 22 hours; controls, 18 ± 9 hours).[181] Prolonged ventilation after cardiac surgery for causes other than primary pulmonary complications was associated with poor long-term function and poor hospital survival.[185]

Off-pump CABG with its theoretical smaller physiological insult than on-pump CABG should result in fewer patients requiring prolonged ventilation, as was shown in a nonrandomized study of 208 on-pump patients where 7.7% were ventilated for more than 48 hours and 112 off-pump patients where 1.8% were so ventilated.[186] Similar results were obtained in other nonrandomized studies,[187] as well as in patients with reoperative single-vessel CABG and COPD.[196] None of the COPD patients who underwent off-pump CABG required prolonged mechanical ventilation as opposed to 9.3% of on-pump CABG patients.[188]

Predictors of Prolonged Mechanical Ventilation

One can surmise that patients with reduced preoperative pulmonary function are at increased risk of developing postoperative pulmonary complications. However, this is not born out by the literature. Many studies show little correlation between the results of preoperative pulmonary function tests and the risk of postoperative pulmonary

dysfunction.[189] In some, but not all, studies, a history of current cigarette smoking was the only predictor of delayed extubation after cardiac surgery.[177,178] Patients with severe chronic obstructive pulmonary disease (COPD) have been shown to have a similar incidence (60%) of pulmonary complications after CABG with CPB as after major abdominal surgery (56%).[190] COPD is not a component of the Parsonnet Risk Scale, which uses preoperative variables to compute surgical risk. However, COPD with the long-term use of bronchodilators or steroids is a component of the EuroScore.[191]

In a retrospective study of 191 COPD patients (defined as those undergoing active treatment for COPD or having a FEV_1 <75% of predicted) undergoing CABG, the mortality was 7% and morbidity was 50%. Pulmonary complications caused 12% of the morbidity and prolonged mechanical ventilation caused 4%. A subgroup of COPD patients more than 75 years old treated with steroids was identified as having a prohibitive risk for CABG. Canver et al[192] found that COPD patients, irrespective of age, stay in the ICU and hospital longer than non-COPD patients; those with mild-to-moderate COPD do not have higher mortality rates.

Pre- and postoperative factors that predict delayed extubation (> 24 hours) after cardiovascular surgery have been identified.[193] Spivak et al[194] identified preoperative histories of smoking, diabetes, unstable angina, and congestive heart failure as such factors. Dunning et al[195] examined the records of 3070 patients who underwent cardiac surgery and found that a Parsonnet score of greater than 7, a poor left ventricular ejection fraction, a pulmonary artery systolic pressure over 35 in patients over 65 years old, and reoperation for bleeding or cardiac arrest identified 50% of the patients requiring prolonged postoperative ventilation. In over 3000 patients who underwent cardiovascular surgery, Rady et al[196] found that 12% of patients on admission to the cardiovascular ICU had early acute pulmonary dysfunction, defined as a FiO_2/PaO_2 ratio of less than 150 and an abnormal chest radiograph. The factors that predicted early dysfunction are found in Table 1.

Thompson et al[197] studied 139 patients who required at least 7 days of mechanical ventilation after cardiac surgery. They found that such varied factors as urban residence, COPD, prolonged operation, and CPB time were predictive of prolonged ventilation. Patients with preoperative hypoalbuminemia are at increased risk of prolonged mechanical ventilation after cardiac surgery.[198] Some also identified preexisting renal failure and chronic dialysis as risk factors for prolonged ventilation.[177] Others found that intraoperative and immediate postoperative issues such as poor cardiac function, as evidenced by the need for IABP, emergency transfusions, and reoperation, predict prolonged mechanical ventilation.[178,179] Canver and Chanda[199] defined respiratory failure as the need for mechanical ventilation for more than 72 hours any time after surgery. They found that 491 (5.6%) of 8802 CABG with CPB patients had respiratory failure. Preoperative determinants included IABP, congestive heart failure, COPD, age, low left ventricular ejection fraction. Intraoperative determinants were prolonged CPB, while postoperative determinants were postoperative septic endocarditis, gastrointestinal bleeding, stroke, sternal wound infection, reoperation

Table 1. Risk Factors for Early Pulmonary Dysfunction after Cardiothoracic Surgery

Preoperative Variables
• Age ≥ 75 Years
• Body mass index ≥ 30 kg/m²
• Mean pulmonary artery pressure ≥ 20 mmHg
• Stroke volume index ≤ 30 mL/m²
• Low serum albumin
• History of cerebrovascular disease
• Emergency surgery
• Total cardiopulmonary bypass time ≥ 140 min
Postoperative Variables
• Hematocrit (immediate postoperative) ≥ 30%
• Mean systemic arterial pressure ≥ 90 mmHg
• Cardiac index ≥ 3.0 L/min/m²
Pulmonary dysfunction associated with
• Postoperative increase in serum creatinine
• Neurologic complications
• Nosocomial infections
• Prolonged mechanical ventilation
• Length of stay in the cardiovascular ICU and hospital
• Death

Rady MY, et al. Crit Care Med 25:1831, 1997.

for bleeding, and renal failure. Dissection of both internal mammary arteries without opening the pleuras reduced the incidence of prolonged mechanical ventilation (> 24 hours), atelectasis, and pleural effusions.[200] Prolonged ICU stay (> 3 days) was associated with preexisting lung disease.[201,202]

Discontinuing Mechanical Ventilation in Cardiac Surgical Patients

The period of discontinuing mechanical ventilation after cardiac surgery is characterized by increased metabolic and cardiovascular stress thought to be due to a combination of increased work of breathing, anxiety, pain, and emegence from sedation.[203] The magnitude of this stress response is dependent on the complexity of the surgery and tends to be smaller in patients who underwent uncomplicated cardiac surgery.[204] Some cardiac surgical patients poorly tolerate the increases in endogenous catecholamines that accompany weaning and extubation.[205] It is possible that patients may develop myocardial ischemia owing to their increased heart rate.[206] Such patients may need heart rate reduction with a short acting β-blocker during the periextubation period. Esmolol was able to attenuate hypertension and tachycardia during the extubation after cardiac surgery.[207]

Discontinuing positive ventilation may also exacerbate cardiac failure. In general, the decrease in intrathoracic pressure owing to spontaneous ventilation increases venous and cardiac preload.[126] This is not usually a problem in patients with cardiac function that is able to compensate for the increased preload. However, patients with marginal cardiac function may require optimization of heart function through diuresis, afterload reduction, or inotropy. Paulus et al[208] found that administering the inotropic agent enoximone, a phosphodiesterase III inhibitor, to nine patients who previously had been unable to wean, increased the cardiac index so that seven of the patients could be successfully weaned.

Readmission to the ICU

Among the gauges of the impact of pulmonary complications on the postoperative course after cardiac surgical patients is their effect on readmissions to the ICU. In a study of 2117 CABG patients, 75 (3.6%) were readmitted to the ICU, 10 of them more than once.[209] The readmissions were for respiratory reasons (47%) and for cardiac problems (20%). The most common respiratory etiology for the readmission was difficulty in clearing secretions, followed by pneumothorax, COPD exacerbation, and large pleural effusion. Others also noted that respiratory problems are the leading reason for readmission.[188,210] One study concluded that the predictors of ICU readmission were preoperative renal failure and prolonged (> 24 hours) postoperative mechanical ventilation, while another found that nonelective surgery, a body mass index of more than 27, the need for elevated FiO_2, and rapid respiratory rates were such predictors.[209,210] Readmission to the ICU of fast-track patients was 3.3% (53 of 1613 patients): 43% were readmitted for pulmonary problems and a third needed to be reintubated and mechanically ventilated.[211] Respiratory problems are the leading reason that patients get readmitted to the ICU after cardiac surgery, once again demonstrating the important nature of respiratory complications following surgery.

Pain Management

Pain following cardiac surgery is dependent on the type of thoracic incision and whether saphenous veins were harvested. In general, the pain experienced following median sternotomy is self-limited to the first few postoperative days and often is successfully managed with oral pain medications (e.g., oxycodon plus acetaminophen) by the first or second day after surgery. In fact, the pain of the leg incisions used to harvest saphenous veins is reportedly more intense than the pain from a well-stabilized sternotomy. In contrast to the pain from a median sternotomy, the pain associated with a thoracotomy is more severe since, unlike sternotomy, it involves incising muscles. Anterior minithoracotomies, which involve removal of costal cartilages and opening of the pleura,[212] are also quite painful. This finding was demonstrated by the significantly higher pain scores seen during forced inspiration 1 and 3 days after MIDCAB performed through anterior thoracotomies than the scores after CABG performed through median sternotomies.[29] Thoracotomy patients have intense pain, not only from the inci-

sion itself but also from intercostally placed chest tubes. In one series of MIDCAB, intercostals nerve cryoablations were routinely performed to reduce postoperative pain.[213]

The role of postoperative pain management in reducing pulmonary morbidity after cardiac surgery has not been extensively studied. Gust et al[214] demonstrated smaller volumes of atelectasis when patient-controlled rather than nurse-controlled analgesia was used after CABG. Whether this translates into lower morbidity is unclear.[215] Patient-controlled analgesia (PCA) is not commonly used for patients in ICUs and intermediate care units with high patient:nurse ratios for the initial portion of their postoperative convalescence; they also tolerate oral pain medications within a day or two of surgery.[216] After CABG that involves the harvesting of saphenous veins, it is most important to provide good analgesia for the resultant leg pain so that patients can ambulate comfortably early after surgery and so reduce pulmonary complications. Additionally, pain should be evaluated not only at rest but also while the patient is performing chest therapy maneuvers such as coughing, incentive spirometry, and deep breathing exercises so that the level of analgesia is sufficient to render these maneuvers pain-free. Yet, the level of analgesia needed during chest therapy must not cause respiratory depression when the patient is at rest nor should it prevent the patient from ambulating. Therefore, the use of nonrespiratory depressant nonopioid analgesics such as acetaminophen, and NSAIDS, plus intermittent small doses of narcotics may be useful.[217]

There is a need for further examination of pain management techniques for use after minimally invasive surgery performed through anterior thoracotomies and via thoracoscopy because of the tendency for early extubation.[218] Experiences with thoracotomies and thoracoscopies for lung parenchymal surgery support the importance of effective analgesia to facilitate coughing and prevent pulmonary complications.

Intrathecal Morphine

It is surmised that postoperative pain plays a role in the development of postcardiac surgery changes in pulmonary function; therefore, one would expect that optimal epidural or intrathecal analgesia would lead to improved pulmonary function. The subarachnoid administration of small doses, 5–30 μg/kg, of morphine has been used to provide postoperative pain relief following all types of cardiac surgery. The theoretical advantage of this method is excellent pain relief provided for up to 24 hours using very small doses of narcotics injected into the lumbar subarachnoid space.

Clinical studies have examined whether intrathecal morphine is advantageous. Many investigations have been performed using the time to extubation after surgery as their end-point. A randomized, but small (n = 45), study where intravenous (IV) PCA morphine analgesia alone, was compared to intrathecal morphine (4 μg/kg) plus clonidine (1 μg/kg), the time to extubation was shorter in the latter group (medians: 225 minutes vs 330 minutes).[219] Mean time to extubation was also reduced (means: 156 minutes to 258 minutes) when anesthesia with IV remifentanil plus intrathecal morphine (2 mg) was compared with an IV fentanyl anesthetic.[220] In both groups, IV morphine was administered after surgery as needed. It is important to note that in these two studies the differences in the median/mean times to extubation between the intrathecal and other groups group was about 100 minutes. However, there are studies that showed no differences in time to extubation with intrathecal morphine.

In a randomized, placebo plus two doses of morphine (250 μg and 500 μg) trial (n = 50), the two morphine doses did not significantly affect time to extubation, but did reduce the need for supplementary IV morphine.[221] Similar results were obtained when a desflurane anesthetic was used with either a remifentanil infusion plus intrathecal morphine (8 μg/k) or a sufentanil infusion.[222] In another study where 10 μg/kg of intrathecal morphine was compared with intrathecal placebo, not only was there no difference in the time to extubation but 4 patients in the morphine group had extubation prolonged by respiratory depression.[223] Other trials using the same dose of intrathecal morphine noted that some patients developed respiratory depression, and the mean time to extubation in the morphine group was prolonged (7.6 hours vs 10.9 hours).[224,225] The prolongation of the time to extubation appears to be at least partially a dose-response effect.

Thoracic Epidural Anesthesia and Analgesia

There has been recent enthusiasm for using thoracic epidural analgesia (TEA) in cardiac surgery

because of its potential benefits of providing excellent postoperative analgesia, coronary vasodilation, attenuation of the stress response, reduced supraventricular arrhythmias, lower incidence of renal failure, and less postoperative confusion.[226] However, there is no consensus in the literature as to whether neuraxial analgesia has beneficial effects on pulmonary function after cardiac surgery performed through a median sternotomy.[226]

The pulmonary effects of TEA are dependent on the level of the block and whether it involves partial or complete motor block. With a motor blockade below T10 there is little decrease in expiratory reserve volume, while a higher level of total motor blockade results in expiratory reserve volume, but not inspiratory capacity, falling towards zero.[227] As expected, TEA with local anesthetics also decreased the rib cage contribution to breathing. However, the reduced rib contribution does not seem to have major effects on lung volumes, because in the supine position the abdominal contribution predominates.

Tenling et al[227] showed that maximal expiratory pressure, but not any other spirometric parameter (FVC, FEV_1 or maximal inspiratory pressure) was better preserved by TEA.[227] Others[228] noted better preserved FEV_1 and peak expiratory flow rates with postoperative TEA. However, there were no differences in postoperative pulmonary function between epidural buprenorphine administered via either the lumbar or thoracic routes or TEA with ropivacaine plus fentanyl.[211,229] Whether the instances where the epidural analgesia preserves lung volumes translates into better outcomes has been the focus of clinical investigations.

A number of clinical studies have compared the effects of TEA in patients given a general anesthetic plus thoracic epidural analgesia using a local anesthetic (bupivacaine/ropivacaine) plus a narcotic (fentanyl/morphine) mixture, or intravenous morphine (some as PCA) analgesia. Some found that epidural analgesia facilitated earlier extubation associated with greater expiratory lung volumes and greater cooperation with physiotherapy.[229-231] Others did not observe earlier extubation,[232] and a few found that early extubation was hindered.[233] Importantly, Scott et al[230] showed a lower incidence of respiratory tract infections when patients treated with TEA were compared with those treated with a target-controlled infusion of alfentanil.[230] Although there is no doubt that neuraxial analgesia provides effective pain relief, evidence that it might prevent pulmonary complications after cardiac surgery is minimal.

Among patients undergoing off-pump CABG surgery either through a median sternotomy or a small left anterior thoracotomy (MIDCAB), thoracic epidural analgesia has been successfully used and permitted the early extubation.[234,235] However, no large randomized trials have been performed to examine whether the use of epidural analgesia reduces pulmonary complications in off-pump surgery.

Elderly Patients

Longer life spans have led to more cardiac surgery being performed, not only in septuagenarians and octogenarians but even in nonagenarians and centenarians.[236] Operations, including CABG, are being performed with improved outcomes in terms of mortality and morbidity compared with previous decades.[237-240] These improved outcomes have been ascribed to improved anesthetic and surgical techniques, along with better preoperative preparations, myocardial protection, and postoperative care. However, these patients represent a special challenge because of coexisting diabetes mellitus, renal, pulmonary, and neurologic diseases. They have high incidences of postoperative delirium, up to 32% in one study, and higher complication and mortality rates than younger patients, so it is possible to hypothesis that they have significant rates of postoperative pulmonary problems.[241,242]

However, do the older members ($\geq$ 75 years old) of the cardiac surgical population have a greater incidence of pulmonary complications than younger patients? In patients exceeding 80 years old, more than 60% had at least one nonfatal postoperative complication and 7% to 8% had pulmonary complications. Pneumonia was found to be more common in octogenarians after both CABG and valve procedures (3.9% vs 2.1%) as was prolonged ventilation (6.7% vs 4%).[241] Similarly, CABG patients more than 75 years old had a 6% incidence of pneumonia; no cases occurred in younger patients.[243] In a study of octogenerians, 4 (6%) of 70 CABG and 15 of 100 aortic valve replacement patients had postoperative pneumonia.[244] Among the 36 patients who required more than 48 hours of mechanical ventilation, 19 had pneumonia.[244] Others observed lower pneumonia rates (4%) requiring mechanical ventilation after aortic surgery in octogenarians.[245]

Among the 662,033 patients in the STS National Database (1997–2000) who were more than 50 years old who underwent both CABG and valve procedures, 1097 were nonagenarians and centenarians.[236] They had greater mortality and morbidity than octogenarians, including a higher rate of prolonged (> 24 hours) mechanical ventilation (6%, 50–79 years; 10.5%, 80–89 years, and 12.2%, 90+ years). In a smaller study of 42 nonagenarians, 7% were reported to have suffered postoperative respiratory complications (pneumnia, reintubation, and respiratory failure).[246]

Interestingly, among patients more than 75 years old, those with low body mass indices (< 23) had greater risks of perioperative complications, including respiratory complications (respiratory failure) than those with higher indices, including those classified as overweight and obese. This finding is not unexpected, given that in general, low body mass in the elderly, unlike in younger patients, is associated with greater mortality.[247]

There has been interest in performing off-pump CABG to reduce the mortality and morbidity observed with on-pump techniques. Hoff et al,[248] in a retrospective review of patients more than 80 years old, reported lower rates of complications, including less prolonged ventilation (1.7% vs 11.8%), after off-pump surgery. Similarly, in a retrospective review of patients more than 75 years old, there were fewer cases of pulmonary edema/ARDS after off-pump than after on-pump CABG.[249]

Newer Techniques and Respiratory Complications

Do the newer minimally invasive and non-CPB techniques reduce the incidence of pulmonary complications? No large, multicenter randomized trials have examined whether the respiratory complication rates are lower after off-pump and minimally invasive surgery. Therefore, it is dificult to definitively ascertain whether the newer techniques lower the respiratory complication rates. The available evidence comes from nonrandomized, single-institution case series and is based on the incidence of pneumonia, ARDS, and length of mechanical ventilation after cardiac surgery. However, it is improtant to realize that the duration of mechanical ventilation is influenced by many factors other than respiratory complications.

Median Sternotomy Without Bypass

Retrospective reviews of elderly patients more than 80 years old reported less prolonged ventilation and fewer cases of pulmonary edema/ARDS among off-pump patients.[248,249] In two large, nonrandomized retrospective studies, there was no difference in the incidence of postoperative ARDS in patients who underwent on-pump or off-pump CABG surgery.[241,242] However, one study observed that more patients in the on-pump group were ventilated for more than 24 hours.[242] This finding was not born out in a propensity analysis on 17,969 off-pump and matched on-pump patients from the STS database.[250] Another case series of 5,163 patients, 2,223 of whom underwent off-pump CABG, found that the incidence of parenchymal (ARDS and pneumonia) and extraparenchymal (pneumothorax and pleural effusion) complications along with re-intubation, tracheostomies, and ventilation for more than 24 hours were higher in both low- and high-risk (based on preoperative factors) patients undergoing on-pump than off-pump surgery.[251] One can conclude, based on these studies, that the incidence of pulmonary complications in "off pump" surgery appears to be lower.

Ministernotomy

In two small randomized studies (n = 80 and 40), the incidences of pleural effusions, pneumothoraces, respiratory insufficiency, prolonged ventilation, and atelectasis were not different between aortic valve replacements performed through ministernotomies or full median sternotomies.[25,261] In a small case series, aortic valve replacement through an "I" ministernotomy, resulted in a shorter duration of mechanical ventilation than with full median sternotomy.[253]

Anterior Thoracotomies

In a report of a series of 153 patients undergoing aortic valve surgery with the port-access method (Heartport, Redwood City, CA) through a 5 cm right anterior thoracotomy, 3 (2%) had pneumonia.[254] Another study compared aortic and mitral valve surgery performed through a 8- to 10-cm right parasternal (2-5 costal cartilage) minithoracotomy with that performed through a median sternotomy. Although the incidence of pulmonary

complications were not reported, the bypass and operative times were longer in the minithoracotomy group, while the duration of postoperative mechanical ventilation and ICU stays were not different.[255] A report of a small series of COPD patients undergoing CABG either with a median sternotomy plus bypass, sternotomy without bypass, or MIDCAB, claimed that there were more advantages to the latter procedures in COPD patients based on lesser decreases in FEV_1 and earlier extubation after MIDCAB.[256]

Endoscopy and Thoracoscopy

To further reduce to invasive nature of cardiac surgery there is increasing use of endoscopic techniques. The techniques range from thoracoscopic harvesting of the internal mammary artery combined with MIDCAB to the entire surgery being performed through three or four ports with the aid of a telemanipulating robot.[257,258] These latter surgeries may be performed off-pump or on-pump using the port-access method.[258] Whether these techniques further reduce postoperative pulmonary complications has yet to be demonstrated.

Conclusions

This review examines the available information on the incidences, consequences, and treatments of postcardiac surgery respiratory complications. This examination was a major challenge because of the dearth of large, randomized, multicenter clinical trials. Instead, conclusions were drawn from either large databases, clinical trials performed at a single center, or nonrandomized case series from individual hospitals. In addition, the literature is dominated by studies of CABG with far less written about valve replacement and repairs. This finding is to be expected, since most patients having cardiac surgery undergo coronary artery revascularization. However, compared to CABG, valve replacement and repair is associated with longer CPB durations, more and longer postoperative support, and more bleeding complications.[259]

Cardiac surgery, especially when performed using CPB, results in major disturbances in body homeostasis, including major changes in the structure and function of the respiratory system. Atelectasis forms immediately upon the induction of general anesthesia, positive pressure ventilation alters physiologic V/Q matching, and violation of the chest cavity with the manipulaton of its contents directly affects lung function and structure. CPB offers additonal insults to the respiratory system, both directly through the activation of the inflammatory response and indirectly through the decreased perfusion and lack of ventilation of the lungs.

The postoperative period offers further challenges, including pain and mechanical ventilation. Given that many patients undergoing cardiac surgery have underlying lung disease or a history of smoking, it is remarkable that more patients do not suffer major pulmonary complications during and after cardiac surgery. Advances in anesthetic, surgical, and critical care have, for example, reduced the physiologic insults of surgery (e.g., better myocardial preservation techniques) and streamlined care in the immediate postoperative period (e.g., early extubation). Moreover, the development of minimally invasive surgery and nonbypass techniques are further evidence of the attempts at reducing the homeostatic disruptions of cardiac surgery.

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