Prolonged postoperative recovery following surgical repair for congenital heart disease in young children

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Abstract

Introduction: We aimed to draw a profile of young children undergoing surgical repair for congenital heart disease (CHD), who have prolonged postoperative recovery, and compared this profile with the profile of a shorter postoperative recovery time group.

Material and methods: Data of 147 consecutive patients aged younger than 36 months undergoing cardiac surgery for CHD were reviewed, and they were allocated to two groups based on the duration of intensive care unit (ICU) stay equal to or less than 7 days (group I, n=114), and more than 7 days (group II, n=33).

Results: The patients in group II were significantly younger (10.2±3.9 months vs. 19.9±5.8 months; P<0.001). Aortic cross-clamp times were 39.1±3.6 min in group I, and 50.4±8.7 min in group II (P<0.05). Extubation failures (more than 48 hours) occurred in 3 cases in group I, compared to 29 patients in group II (P<0.0001). A total of 28 patients (7 in group I, and 21 in group II) developed pulmonary complications. These patients contributed to the majority of total ventilator days (69%) as well as ICU stay (58%). Fourteen percent of patients underwent staged operations in group I, compared to 48.5% in group II (P<0.002).

Conclusions: Pulmonary complications seem to be one of the most important causes of delayed recovery following cardiac surgery in young children. We suggest that extubation time is a crucial factor for development of pulmonary problems. This factor might be more important for infants who undergo staged operations.

Key words: congenital heart disease, infant, postoperative care, surgery.

Introduction

The scope of cardiac surgical critical care includes prediction and prevention of problems as well as investigation and intervention. However, preventing deterioration is more effective than attempting salvage at a later stage.

Congenital heart disease (CHD) covers a large spectrum of clinical entities, ranging from isolated cardiac defects to very complex multiple cardiac malformations, and in the vast majority of cases, surgical repair or palliative procedures are needed. Innovations in surgical techniques and in perioperative care have allowed for successful surgical repair of complicated CHD previously considered inoperable.

Early mobilization after cardiac surgery in children may be limited by various postoperative problems. These are mainly congestive heart failure, respiratory insufficiency, general or local infections, postoperative cardiac arrhythmias, and a number of other postoperative complications [1].

We undertook a 14-month retrospective review of young (younger than 36 months old) children undergoing cardiac surgery at our institution, and attempted to identify important characteristics that may underlie prolonged postoperative recovery in this patient population.

Material and methods

Hospital records of 149 consecutive patients, aged younger than or equal to 36 months, who underwent palliative or corrective surgery for CHD at our centre during a 14-month period were retrospectively reviewed. Two patients who died within 48 hours after surgery (immediate mortality) were excluded. Therefore, the study population included a total of 147 patients. The cardiac diagnoses were established by echocardiography, cardiac catheterization, and/or cineangiography. The following variables were recorded: demographics, cardiac diagnosis, surgical procedure, intraoperative information [total duration of surgery, cardiopulmonary bypass (CPB) time, and aortic cross-clamp time], postoperative inotropic support, and duration of postoperative mechanical ventilation (MV). Patients were allocated to two groups based on the duration of Intensive Care Unit (ICU) stay: ≤7 days (group I), and >7 days (group II). The decision of this cut-off time was based on the fact that 7 days was the 95th percentile of the mean duration of ICU stay for all young children undergoing cardiac surgical repair in our centre.

According to demographic variables and intra- and post-operative parameters, patients' profiles were drawn and compared for both groups.

The clinical course during the ICU stay was reviewed and complications were identified based on written reports and/or laboratory and other ancillary data. In the patients in whom complications affected more than one system, attempts were made to identify the dominant system most likely to contribute to the adverse clinical course based on a consensus among the investigators. The group with pulmonary complications was further subdivided by types of complication: phrenic nerve dysfunction, pulmonary vascular hypertension, pleural effusion and others. Criteria for the diagnosis of phrenic nerve palsy included the presence of an elevated dome of the diaphragm on chest X-ray. Atelectasis was defined as the radiographic finding of a lobar infiltrate and volume loss in the absence of clinical or laboratory signs of infection. Pulmonary hypertension was identified from echocardiographic estimates and/or catheterization measurements (a pulmonary artery catheter was inserted for almost all of the patients after induction of anaesthesia). Patients with pleural drainage >5 ml/kg/day, and patients requiring continued chest tube drainage beyond the third postoperative day were considered to have pleural effusion, and the nature of the pleural fluid was noted.

Patients were extubated based on ongoing ICU algorithm protocols and the decision of the staff anaesthesiologist. Extubation criteria were open consciousness, no pneumothorax, no pleural effusions, optimal filling cardiac pressures, minimal inotropic support and existence of the following parameters: more than 15 ml/kg vital capacity, more than 350 mm Hg of alveolar-arterial difference (with 100% oxygen), more than 7.35 pH, less than 45 mm Hg of $PaCO_2$, minimum –20 to –30 mm Hg inspiratory force. When a patient was re-intubated and mechanically ventilated within the first 48 hours after planned extubation, it was considered to have failed (*failed extubation*). Overall durations of the ICU stay and the hospital stay were also documented. Early postoperative mortality (first 30 days) was assessed.

For surgery performed by cardiopulmonary bypass, these agents were added to the prime solution: heparin (100 IU/100 ml), 20% mannitol (3 ml/kg), prednisolone (10 mg/kg), aprotinin (30000 IU/kg), sodium bicarbonate (1 ml/kg) and cefazolin (20 mg/kg). The volume of blood to be added to the prime solution was calculated according to this formula:

Volume = (body weight × total body blood volume) × (patient Htc/target Htc) – (body weight × total body blood volume).

Target haematocrit was defined as 30% in our clinic. If haematocrit was too high, fresh frozen plasma (FFP) was added to the circuit. To increase haematocrit level haemofiltration was used, and blood was added to the system, if necessary.

After surgery, depending on the case and postoperative course, dopamine (2.5-4 mg/kg/min) and dobutamine (4-8 mg/kg/min) perfusions as inotropes, and nitroglycerin (0.5-1.5 mg/kg/min) perfusion as a vasodilator in the ICU were used. For more complicated cases or for patients with long cardiopulmonary bypass time, adrenaline (0.03-0.05 mg/kg/min) perfusion and IV phentolamine (0.1 mg/kg × 3-4 per day) inotropic support were added as inotrope and vasodilator agents, respectively. Ilomedin, iloprost, milrinone and NO were used for severe pulmonary hypertension cases. Furosemide (0.1-0.5 mg/kg) perfusion was preferred for forcing diuresis. After extubation, oral digoxin and captopril were used on a case-by-case basis.

Statistical analysis

Most of the data are expressed as mean ± SEM. For some parameters, the median value is also calculated. Comparisons between groups I and II were performed using one-way analysis of variance followed by post hoc tests or unpaired t tests as appropriate. Linear regression analysis with calculation of regression coefficients was employed for assessment of the potential relationship between bypass time and duration of MV or ICU stay (for the pump patients). A P value of less than 0.05 was considered statistically significant.

Results

Pre-, peri- and postoperative data of the patients are shown in Table I. Group I consisted of 114 patients, representing 77.6% of the study population. All of the patients were Caucasian. The mean age was 19.9±5.8 months (range: 3-36 months, median: 22 months), and there were 66 male infants in group I. The mean weight percentile was 24.2±5.2% (according to the Turkish curve). Group II included 33 infants (22.4%), 20 of whom were male, and their mean weight percentile was 28.5±5.6% [P>0.05, not significant (NS)]. The patients in group II were significantly younger (mean age: 10.2±3.9 months, range: 4 days-36 months, median: 12 months; P<0.001). The mean preoperative ejection fraction was 41.1±4.9% (range: 25-60%) and 39.3±4.5% (range: 23-55%) in group I and group II, respectively (NS). The cardiac diagnoses and surgical procedures for each group are shown in Tables II and III, respectively. Mean surgical duration was 135.1±8.1 min for group I and 162.4±11.9 min for group II (NS). Total CPB and aortic cross-clamp times were 61.9±4.6 min and 39.1±3.6 min, respectively, in group I, and 78.4±11.2 min (P<0.05) and 50.4±8.7 min (P<0.05) in group II. The duration of MV in group I [1.4±0.4 days (range: 0.3-6 days, median: 1 day)] was significantly shorter than in group II [23.8±3.3 days (range: 2-86 days, median: 8 days)] (P<0.0001). Similarly, mean durations of ICU and hospital stay were 3.1±0.8 days (range: 1-6 days, median: 2 days) and 9.0±6.3 days (range: 1-38 days, median: 7 days), respectively, for group I and 30.1±17.4 days (range: 7-132 days, median: 14 days) (P<0.001) and 45.2±26.3 days (range: 8-193 days, median: 22 days) (P<0.001), respectively, for group II. We further examined the relationship between CPB time and the duration of MV and ICU stay, and found that no significant correlations were present. In group I, there were 3 extubation failures, whereas 29 extubation failures were recorded in group II (P<0.0001).

Arrhythmia resulting in pacemaker dependency was noted in 4 patients (3.5%) in group I, and 2 patients (6.1%) in group II (NS).

Postoperative inotropic support was required by 37 patients (32.5%) in group I, and 14 patients (42.4%) in group II (NS).

Postoperative blood (concentrated erythrocyte suspension) [85.8±64.6 vs. 136.8±99.5 ml (P<0.05)] and fresh frozen plasma [92.5±68.1 vs. 185.0±101.1 ml (p<0.01)] usage were more frequent in group II.

Table I. Preoperative, perioperative, and postoperative characteristics in group I and group II

Characteristics	Group I (n=114)	Group II (n=33)	P value
Age [month]	19.9±5.8	10.2±3.9	<0.001
Sex, M [%]	66 (57.9%)	20 (60.1%)	NS
Weight, mean percentile [%]	24.2±5.2	28.5±5.6	NS
Ejection fraction [%]	41.1±4.9	39.3±4.5	NS
Perioperative data			
Surgical duration [min]	135.1±8.1	162.4±11.9	NS
CPB time [min]	61.9±4.6	78.4±11.2	<0.05
Cross-clamp time [min]	39.1±3.6	50.4±8.7	<0.05
Postoperative data			
Mechanical ventilation [day]	1.2±0.2	19.4±3.0	<0.001
ICU stay [day]	3.1±0.8	30.1±17.4	<0.001
Hospital stay [day]	9.0±6.3	45.2±26.3	<0.001
Blood usage [ml]	85.8±64.6	136.8±99.5	<0.05
Fresh frozen plasma usage [ml]	92.5±68.1	185.0±101.1	<0.01
Inotropic support [%]	37 (32.5%)	14 (42.4%)	NS
Pacemaker dependency [%]	4 (3.5%)	2 (6.1%)	NS
Extubation failures [%]	3 (2.6%)	29 (88.9%)	<0.0001
Respiratory complications [%]	7 (6.1%)	21 (63.6%)	<0.0001

Table II. Cardiac diagnosis in patients with group I and group II

Cardiac diagnosis	Group	
	I	II
Aortic stenosis	1	1
Atrial septal defect	13	–
Atrioventricular canal defect	2	5
Coarctation of aorta	5	2
Tricuspid atresia	2	–
Hypoplastic left heart syndrome	–	1
Patent ductus arteriosus	17	–
Pulmonary atresia	1	–
Transposition of great arteries	5	5
Tetralogy of Fallot	14	2
Truncus arteriosus	–	1
Ventricular septal defect	16	1
Ventricular septal defect + atrial septal defect	–	1
Double aortic arch	1	–
Total anomalous pulmonary venous connection	2	–
Complex congenital heart diseases	33	14
Aortopulmonary window	2	–
Total	**114**	**33**

Table III. Cardiac surgical procedures required in patients group I and group II

Surgical procedure	Group	
	I	II
Aortic valvuloplasty	3	–
Aorto pulmonary window repair	2	–
Arterial switch	3	3
Atrial septal defect repair	13	–
Atrial septal defect repair and ventricular septal defect repair	2	1
Atrioventricular canal repair	4	5
Blalock-Taussig shunt	3	6
Coarctation repair	5	2
Fontan procedure	5	1
Glenn procedure	7	2
Double aortic arch repair	1	–
Norwood procedure stage 1	–	1
Pulmonary artery augmentation	2	–
Pulmonary artery banding	–	6
Patent ductus arteriosus repair	17	–
Rastelli procedure	1	2
Total anomalous pulmonary venous connection repair	2	–
Tetralogy of Fallot repair	14	2
Truncus arteriosus repair	–	1
Ventricular septal defect repair	28	1
Senning procedure	1	–
Mustard procedure	1	–
Total	**114**	**33**

The number of patients who had staged operations (Blalock Taussig shunt, etc.) were 15 (14.0%) in group I, and 16 (48.5%) in group II ($P<0.002$).

Total morbidities (hepatic, renal, gastrointestinal and neurological complications, bleeding, arrhythmia and pulmonary complications) were noted in 15 patients (12.3%) in group I, and 26 patients (78.8%) in group II ($P<0.0001$). Differences in pulmonary complications seemed more important than non-pulmonary complications. In group I, 7 patients (6.1%), and in group II, 21 patients (63.6%) developed clinically significant pulmonary complications ($P<0.0001$). Pulmonary complications included phrenic nerve dysfunction, pleural effusion, severe pulmonary hypertension, pneumothorax, and pulmonary infections, and they were determined to be the major factor associated with prolonged MV. These 28 patients contributed to the majority of total ventilator days (69%) as well as ICU stay (58%).

Pleural effusions were noted in 9 patients (four in group I, and five in group II). Bilateral serous pleural effusions complicated the postoperative course in two patients, while unilateral effusions occurred in the other patients.

Moderate to severe pulmonary hypertension was present in seven patients. All the patients were managed with the standard protocol for postoperative pulmonary hypertension, which included sedation, neuromuscular paralysis, hyperoxygenation, and respiratory alkalosis.

Nineteen of the patients (2 in group I and 17 in group II) had developed pulmonary infections. These infections were either primary or secondary to the other pulmonary complications. Isolated agents by culture were *Staphylococcus aureus* (80%), *Escherichia coli* (5%), *Pseudomonas aeroginosa*, *Klebsiella* and *Enterococcus*.

Early (first 30 days) deaths were noted in 8 patients (7.0%) and 6 patients (18.2%), respectively in groups I and II ($P<0.05$). Causes of death were pulmonary infection and sepsis in 6 patients in group I, and 5 patients in group II. The other three patients were lost because of cardiac arrest unresponsive to cardiopulmonary resuscitation.

Discussion

Improvements in surgical techniques and postoperative care have resulted in a reduction in ICU stay after open heart surgery. Duration of stay

in the ICU is one of the major factors contributing to the high cost associated with surgical interventions in complex CHD. Indeed, studies examining the impact of ICU stay have shown that ICU utilization accounts for about 20% of total hospital costs [2]. Thus, it is not surprising that with reforms in health care, early and more aggressive extubation after cardiac surgical procedures in children and neonates has been attempted and, in fact, it has been shown to be both safe and feasible by several investigators [3, 4]. In an effort to identify risk factors associated with prolonged MV, Kanter and colleagues [5] retrospectively reviewed a series of 140 patients, younger than two years old, who underwent surgical cardiac repair. The need for preoperative MV, longer CPB and aortic cross-clamp durations, and additional surgical interventions were all identified as independent variables associated with prolonged MV and ICU stay. More recently, preoperative measurements of pulmonary vasculature physiological variables, such as systemic and pulmonary resistance, were highly correlated with the duration of MV in patients undergoing repair of ventricular septal defects (VSD) [4]. However, there is a paucity of information regarding the relative contribution of respiratory tract pathology to the need for prolonged MV and ICU stay in these patients. While postoperative diaphragmatic dysfunction is a well-recognized complication contributing to prolonged MV, acquired or congenital tracheobronchomalacia with significant airway obstruction complicating the postoperative period has only been reported in case report format in patients undergoing repair for CHD [6]. In this study, we show that pulmonary complications are common among young children undergoing surgical repair of congenital cardiac conditions, and account for a substantial proportion of the postoperative requirements for mechanical ventilatory support and the overall utilization of the ICU. The difference for non-pulmonary complications seems less significant [6.2 vs. 15.2% in groups I and II, respectively ($P<0.05$)], while pulmonary complications reflect a very significant difference between the groups [6.1 vs. 63.6% in groups I and II, respectively ($P<0.0001$)].

In the literature, several studies suggest that 18 to 41% of infants will require prolonged mechanical ventilatory support following cardiac surgery [7, 8].

The perioperative course of the cardiothoracic patient is frequently complicated by respiratory compromise for various reasons. The postoperative cardiac surgical patient is in a *special biological situation* with a whole body inflammatory response due to the effects of CPB [9]. Therefore, duration of CPB should be important for postoperative outcome. During CPB, the lungs may be partially or completely atelectatic for lengthy periods, compromising lung mechanics for a variable time after resuming ventilation. Needless to say, the beneficial effects of corrective surgery in infants with increased pulmonary blood flow outweigh any transient detrimental effects of cardiopulmonary bypass [10]. Infants with congenital cardiac anomalies often manifest with respiratory symptoms secondary to cardiac dysfunction, increasing the work of breathing and impairing gas exchange. Mechanical ventilation may be required to unload the failing heart from the increased work of breathing.

Lesions associated with increased pulmonary blood flow or pulmonary artery pressure (e.g. ventricular septal defect, complete canal, patent ductus arteriosus, atrial septal defect) have raised vascular pressures within the lung, causing fluid to accumulate in the interstitium and alveoli. Airway resistance is increased by compression of bronchial airways by peribronchial oedema or engorged vessels [11-13]. Respiratory problems from lesions obstructing the inflow or outflow of the systemic ventricle are caused by pulmonary venous and lymphatic congestion leading to pulmonary oedema. Respiratory symptoms are usually more severe than those of shunt lesions. This is especially true for children with obstructed pulmonary venous return, severe coarctation, or aortic stenosis.

Analysis of risk factors for prolonged ventilatory support requirements assigns independent risk to the preoperative clinical status, to intraoperative elements such as CPB and cross-clamp durations, to the underlying cardiac defect, and to the nature of the surgical procedure [2, 4, 9]. In general, patients with simple shunt lesions, such as atrial septal defect (ASD), VSD, and patent ductus arteriosus (PDA), and patients undergoing extracardiac palliation are frequently extubated in the operating room and therefore require minimal ICU stays. The current study supports such a contention, as evidenced by the low number of ventilator days and overall ICU days in group I. On the other hand, patients with more complicated perioperative pathophysiology who undergo complex cardiac surgical procedures will be expected to require longer postoperative respiratory support, and it is the general consensus that in these patients, cessation of mechanical ventilatory support is usually achievable within the first 72 postoperative hours [14]. Inability to extubate earlier than in 72 hours is indicative of a more complicated postoperative course that usually will involve dysfunction of several systems. Our current study indicates that the respiratory system is a major system contributing to this postoperative morbidity.

It has long been known that children with CHD may be at increased risk for airway complications by virtue of the anatomical proximity of the cardiac chambers and major vessels to the central airways.

Airway compression has been reported in association with dilated pulmonary arteries, left atrial enlargement, and massive cardiomegaly [15]. In the vast majority of patients, the existing airway compression is usually relieved by surgical repair of the primary cardiac defect, such that most patients will be asymptomatic. Additionally, with the advent of prosthetic devices and conduits in the central vessels, extrinsic tracheobronchial compression could also be seen [16]. The morbidity and overall medical care costs of airway involvement in this population are quite impressive.

Diaphragmatic dysfunction is primarily caused by phrenic nerve injury after CHD repair, and conservative estimates assign a 0.3 to 2.1% risk to this complication [17]. However, this relative risk may be underestimated. The mechanisms leading to phrenic nerve dysfunction probably involve cold injury from iced cardioplegic solution or result from surgical trauma to the phrenic nerve as it courses around the great vessels in the thoracic cavity. The clinical manifestations are variable, and may range from lower lobar atelectasis on the affected side to ventilatory dysfunction secondary to respiratory pump failure [18].

An increase in sympathetic stimulation and decrease of parasympathetic stimulation may also favour initiation of arrhythmias [19]. Therefore, assessments for autonomic stress, such as heart rate variability (HRV) and respiratory sinus arrhythmia (RSA), might warn clinicians about patients at risk.

Infants and children younger than 2 years of age are at particular risk for development of respiratory failure because of the high compliance of the thoracic cage, the relatively weak intercostal musculature, and the mediastinal shifts induced by paradoxical motion of the paralyzed diaphragm. Thus, these patients are at high risk for extubation failure and for prolonged ventilatory dependency.

Ordinarily, the pleural drainage during the immediate postoperative period is expected to be less than 3 ml/kg/day, such that chest tubes can be removed by the third postoperative day. Causes of excessive pleural drainage include fluid overload, pulmonary oedema, serous fluid leakage from the extracardiac shunts, chylothorax secondary to thoracic duct dysfunction [20], and increased central venous pressure as seen in patients undergoing the Fontan procedure.

Pulmonary hypertension can be a frequent complication in the postoperative period, particularly in neonates and in infants with preoperatively increased pulmonary blood flow such as those who have large VSD, AV canal defects, or truncus arteriosus. Elevated pulmonary arterial pressure and resistance increase the perioperative morbidity and mortality by compromising right ventricular function and oxygenation [21]. Aggressive efforts to improve oxygenation and alveolar ventilation and to achieve effective sedation with adequate muscle relaxation may need to be coupled with pharmacological interventions such as inhaled nitric oxide.

In a critical care unit setting, figures for extubation failure range from 17 to 19% in adults to 22 to 28% in infants [22, 23]. In a paediatric series addressing this issue, extubation failure in the absence of upper airway obstruction was observed in 16.3% of cases [24]. In our study, we found that 32 of 147 patients (3 patients in group I and 29 patients in group II), or more than one-fifth of the patients, had at least one extubation failure, suggesting that this particular population is at high risk for such a complication. It has become quite clear that extubation failure is associated with an increased number of medical complications and with significantly higher mortality rates in the critical care unit [25]. Among the 29 patients in group II who failed extubation, pulmonary dysfunction was the leading aetiological factor in 17 patients (58.6%). Therefore, we recommend that young children undergoing cardiac surgical repair be identified as a particular high-risk group for extubation failure, and that clinicians actively seek to identify specific pulmonary factors.

CPB time has been associated with higher incidence of prolonged MV in the postoperative period [4, 5]. Although the exact mechanism (s) for such association are yet to be elucidated, pulmonary function tests after CPB reveal reduced static/dynamic compliance, decreased functional residual capacity, increased alveolar-arterial oxygen gradient, and atelectasis, all of which can contribute to extended mechanical ventilatory needs [26]. However, our study does not support such a correlation between CPB duration and the duration of either MV or ICU stay. Our findings concur with those of Heinle et al. [3], who reported that the duration of CPB or aortic cross-clamp time did not prevent extubation at the conclusion of the operation in neonates and young infants after surgical repair for CHD.

Our study showed that the infants who underwent staged operations were more likely to stay longer in the ICU than those patients who underwent corrective surgery ($P<0.002$). Although this is an interesting result, we do not have enough data to do further statistical analysis. However, it can be speculated that the infants who required bridge operations might be more vulnerable to postoperative stress due to incomplete correction of the main circulatory pathology.

We also observed that both blood and plasma usages were higher in the longer ICU stay group. However, we believe that this was a result of longer stay in the ICU rather than its cause. If we consider that we did not observe any allergic reaction after

blood and blood products, we should not expect these transfusions to cause an increase in recovery time. For these small children, any extra day of stay in the ICU means approximately 25 ml blood drawing for lab studies (blood gases, CBCs, etc), and continuation of IV drug therapies, which causes haemodilution. Therefore, for the patients who stayed longer in the ICU, it was unavoidable to transfuse blood and blood products to maintain intravascular volume and haemoglobin level.

Nevertheless, it seems that the cause-effect relationship is different for pulmonary complications. The high degree of pulmonary involvement in those patients requiring prolonged ICU stay indicates that such factors are important contributors to less favourable postoperative outcomes, and should therefore be considered early rather than late in the event of extubation failure. In the ICU, provision of adequate oxygenation and ventilation while recovering from anaesthesia and surgery should be primary goals. Secondary goals should be avoidance of barotrauma, volutrauma and infection [9]. Once the patient is awake, responsive and haemodynamically stable, weaning and extubation should be done without losing unnecessary time. In other words, the clinician should make every effort toward timely extubation. Otherwise, the likelihood of developing some other complications will increase and the patient might be stuck in the ICU.

The child's body consists of different delicate systems all of which integrate and interact with each other. If there is something wrong with one component, one should expect some problems in the other systems. It seems that the pulmonary system is one of the most delicate systems in operated young children.

In conclusion, we suggest that pulmonary complications are one of the most important causes of delayed recovery following cardiac surgery in young children. Thus, early evaluation for these pulmonary conditions should be considered in any postoperative patient who fails extubation.

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