Review

Airway Management

Early extubation after pediatric cardiac surgery

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Early extubation after pediatric cardiac surgery has come full circle from being practiced in the early days of pediatric cardiac surgery, falling out of favor with opioid-heavy cardiostable anesthesia, and resurfacing again in more recent times as part of enhanced recovery after surgery practice. Early extubation is variably defined, but is mostly accepted as extubation that occurs within 6–8 h from the end of surgery. In recent years, the debate has shifted from early extubation in the intensive care unit to immediate extubation in the operating theatre. In this review, we examined the benefits and pitfalls of early and immediate extubation, factors that influence the success of early extubation, and potential guidelines for practice and implementation.

Keywords: Airway extubation; Anesthesia, cardiac procedures; Enhanced recovery after surgery; Pediatric anesthesia; Postoperative care.

INTRODUCTION

Early extubation is most commonly defined as extubation within 6 h of cardiac surgery [1-4]. Immediate extubation, also known as on-table extubation, extubation in the operating theatre, or very early extubation [3-5], is a subset of this condition. Early extubation is recommended for adult cardiac surgery as part of the guidelines for perioperative care in cardiac surgery by the Enhanced Recovery After Surgery (ERAS) Society [2], because it is recognized to be safe and beneficial even for high-risk patients [6]. More recently, there has been a push for immediate extubation in the operating theatre for adult cardiac surgery [7].

The concept of early extubation in pediatric cardiac surgery is not new. In the early years of pediatric cardiac surgery, closed-heart surgery and limited resources, such as ventilators and drugs, resulted in anesthetics that relied predominantly on the use of potent inhalational agents. This allows for the rapid return of spontaneous ventilation, which facilitates early extubation [8]. However, with more complex congenital heart surgeries involving cardiopulmonary bypass developed in the 1950–1960s, a high-dose opioid-based anesthetic with routine mechanical ventilation for at least 6–20 h has been advocated [9]. With further advances in medicine, reports of early [3,10] and very early extubation [5,11] began emerging in the 1970–1980s and the 1990s respectively. In recent years, there has been an increasing number of immediate extubations performed [12] with a push for fast track [8,13]. The practice of early or immediate extubation in the operating room is variable [14], and the debate on early and very early extubation continues [4,15]. In this review article, we examined the benefits and pitfalls of early and immediate extubation, factors that influence the success of early extubation, and potential guidelines for practice and implementation.

BENEFITS OF EARLY EXTUBATION

The benefits of early extubation are related to the physiological effects of spontaneous ventilation and reduction in

the requirements for sedation and muscle relaxation. These include better hemodynamics associated with less inotropic and fluid support; decreased airway and pulmonary complications related to intubation; reduced sedation-related complications such as hypotension and delirium; early start of mobilization, feeding, and interaction with parents; and potential cost savings from the reduced intensive care unit (ICU) and hospital stay [4,8,16].

Better hemodynamics and less inotropic support

Positive-pressure ventilation increases intrathoracic pressure, resulting in decreased venous return, right ventricular filling, and preload. An increase in intrathoracic pressure also increases pulmonary vascular resistance and, hence, right ventricular afterload. This results in decreased right ventricular stroke volume. Increased intrathoracic pressure also decreases the intrathoracic to extrathoracic aortic pressure gradient, which decreases the left ventricular afterload and stroke work [17]. This activates the neurohormonal system, resulting in increased secretion of antidiuretic hormone and a decrease in atrial natriuretic peptide levels [18,19]. Hence, depending on the volume status and cardiac function of the patient, positive pressure ventilation may result in worse outcomes, especially in hypovolemic patients or those with right ventricular dysfunction, or in better outcomes in patients with left ventricular systolic failure [17].

Conversely, with spontaneous ventilation, the negative intrathoracic pressure created during inspiration increases venous return and promotes an increase in cardiac output [17]. The benefits of these effects are more pronounced in patients with single-ventricle physiology who have undergone bidirectional Glenn and Fontan circulation [20,21], although they have also been observed in patients who have undergone other types of cardiac surgery, such as those with right ventricular pressure overload [1,3,5,6,8,10,22]. Morales and Kintrup demonstrated in their respective studies on Fontan patients that those extubated immediately had significantly lower mean pulmonary arterial pressure, lower mean common atrial pressure, and higher mean arterial blood pressure, especially in the first 12 h postoperatively, thus requiring a shorter duration of inotropic support. Those extubated immediately also had less pleural effusion and need for chest tube placement, less intravenous fluid administration, and less metabolic acidosis 3–4 h after surgery compared to the group that was extubated in the ICU [20,21]. Nawrocki et al. [22] demonstrated that patients with right ventricular

pressure overload conditions, such as tetralogy of Fallot or double-outlet right ventricle with pulmonary stenosis, who were extubated immediately after chest closure had better hemodynamics than those who were extubated in the ICU. Feng et al. [16] conducted a randomized study involving infants and toddlers undergoing surgery for atrial septal defects and/or ventricular septal defects and showed that those who were randomized to immediate extubation had significantly lower inotropic requirements and lactate levels.

Avoidance of pulmonary and airway complications associated with intubation

Early extubation decreases the risk of pulmonary complications, such as barotrauma, atelectasis, or ventilator-associated infections. Endotracheal tube related complications like kinking, accidental extubation and laryngotracheobronchial trauma are also avoided [1,3-5,11,23,24]. It also results in decreased suction-related complications, such as stimulation, resulting in the precipitation of a pulmonary hypertensive crisis [5,11]. Early extubation is also associated with earlier diagnosis and management of diaphragmatic palsy [23]. In a prospective observational study by Garg et al. [23], diaphragmatic palsy, a complication of cardiovascular surgery, was detected within 12 h in patients extubated immediately in the operating theatre, compared to 48–96 h later in those who were not. Thus, early extubation of patients with this complication could be managed definitively earlier. Those with delayed extubation were suspected of having this complication only after multiple failed attempts at weaning from ventilation in the ICU [23].

Reduction of use of sedatives/paralysis

Patients who are not extubated early would generally require sedation with occasional paralysis to promote endotracheal tube tolerance and avoid ventilator desynchronization [25]. As sedatives and general anesthesia may be associated with poor neurodevelopmental outcomes [26,27] or hemodynamic compromise, the reduced need for sedatives in patients extubated early can be beneficial. Prolonged use of neuromuscular blocking agents may result in diaphragmatic atrophy and weakness, which in turn increase the risk of extubation failure [28]. Therefore, avoiding the prolonged use of neuromuscular blocking agents is desirable.

Reduced length of ICU and hospital stay

Several studies have reported a reduction in the length of ICU stay by at least 1 to 1.7 days and hospital stay by at least 2– 2.7 days in patients who were extubated early [8,11,16,22,29]. While this allows for better utilization of the limited ICU beds [4,11], whether this translates into actual cost savings may depend on the healthcare cost structure and reimbursement schemes of the country [30,31]. The Pediatric Heart Network Collaborative Learning Study reported cost savings of about $13,000 or 27% for Tetralogy of Fallot repairs after implementation of early extubation practice, but none for the coarctation of the aorta repair cohort [32]. A low case mix index is a reflection of the lower clinical complexity and required resources in a patient population over a period of time. Murin et al. [30] reported that despite faster ICU bed turnovers and good outcomes, the lower mean case mix index of the fast-track infant cardiac surgery group resulted in 27% less reimbursement compared to the non-fast-track cardiac surgery group. Nasr and DiNardo [15] opined that cost savings need to consider both the cost of ICU resources and other costs, such as the additional time in the operating theatre required to facilitate early extubation. In that light, she estimates that 1-day ventilator cost is negated by 7.5 min extra time spent in the operating theatre to achieve immediate extubation.

PITFALLS AND CONCERNS OF EARLY EXTUBATION

The primary concern in early extubation is failed extubation with the need for reintubation within 72 h [28,33,34]. The overall rate of failed extubation after cardiac surgery has been reported to range from 0% to 27% [15,23,28,35,36]. Although mild to moderate respiratory acidosis has been observed in some cases of early extubation, in most instances, it is transient and resolves spontaneously within 1–2 h [23,37]. Indeed, it has been postulated that after bidirectional Glenn anastomosis, mild hypercapnia may be beneficial because it results in improved systemic oxygenation and increased systemic, pulmonary, and cerebral blood flow [38]. Most extubation failures occur within the first 24 h, particularly within the first 6–12 h [28,39]. Another concern is that premature extubation may exacerbate a low cardiac output state and trigger arrhythmias and cardiac arrest. Reasons for failed extubation include upper airway obstruction due to airway anomalies or airway edema, cardiogenic shock or low cardiac output, cardiac arrest, arrhythmia, diaphragmatic palsy, pulmonary edema, chylothorax, atelectasis, seizures, sepsis, bleeding requiring re-exploration, sedation for agitation resulting in respiratory depression or apnea, endotracheal bleed due to late onset reperfusion injury or pulmonary arterial hypertension, hypercarbia and hypoxemia [39-43].

Extubation failure has been independently associated with a worse clinical outcome, particularly in neonates [28,42-44]. In a study by Mastropietro et al. [28], neonates who failed their first extubation had a higher mortality rate (23% compared to 0.4%). Gaies' report from the Pediatric Cardiac Critical Care Consortium showed that when controlling for patient factors, extubation failure was associated with an increased length of ICU stay (median, 15 days vs. 3 days), hospital stay (24 days vs. 7 days), and in-hospital mortality (7.9% vs. 1.2%) compared with those who were successfully extubated [39]. Byrnes et al. [45] showed in their multisite study of 18,278 hospitalizations that extubation failure is associated with a 10 times increase in mortality and a 3–4 times increase in the length of hospital stay. The cause of extubation failure may be important: Harkel et al. [43] reported that extubation failure due to cardiorespiratory failure was associated with a 65% mortality rate compared to 0% for those who had extubation failure due to upper airway obstruction [44].

However, what is clear is that reintubation rates after immediate extubation is lower than those extubated later in the ICU [23,39-41,44]. In a study by Gupta that examined the risk factors for mechanical ventilation and reintubation after pediatric heart surgery in 27,398 patients from 62 centers, the reintubation rate was 6% for 6,810 patients who underwent immediate extubation and 10% for 20,588 patients who were extubated in the ICU [40]. Similarly, Gaies et al. [39] showed that 3% of 503 patients who underwent immediate extubation required reintubation, versus 9% of 975 patients extubated in the ICU.

FEASIBILITY AND SAFETY OF EARLY EXTUBATION

Numerous studies have suggested the safety and feasibility of immediate extubation after pediatric cardiac surgery [5,8,23,46,47]. A systematic review by Alghamdi et al. [48] of early extubation concluded that, although the studies were mostly retrospective in nature and of generally poor methodological quality with heterogeneity, there was no statisti-

cal difference in the rate of reintubation between those extubated immediately and those within 6 h post-surgery. Early mortality rates were also lower in the immediate extubation group, although this may be confounded by the fact that patients who are clinically less complicated are more likely to be extubated immediately. In a review of fast tracking after repair of congenital heart disease by Garg et al. [46], immediate extubation rates were reported to be high, ranging from 41 to 90.2%. Although most studies in this review were retrospective studies conducted in cardiac centers with fast-track processes in place, it should be noted that half of the studies included neonates, and the majority included infants. A retrospective study involving 32 neonates undergoing an arterial switch operation for D-transposition of the great arteries reported an immediate extubation rate of 56%, with no difference in reintubation rates compared to those who had delayed extubation [49]. Garg reported an immediate extubation rate of 90.2% in his center that sees 10–12 pediatric cardiac surgeries performed daily, and a reintubation rate of 1.25% [46]. Notably, other studies have suggested that the rate of reintubation within 72 h of immediate extubation, are low, ranging from 0–12% [5,11,23,40,41,44,46,50]. Two randomized studies examining anesthetic management facilitating immediate extubation suggested that immediate extubation is safe, with no significant difference in reintubation rates compared to elective delayed extubation [16,29]. Immediate extubation does not necessarily significantly prolong the duration of time spent in the operating theatre if the appropriate anesthetic technique is used, with an additional time as low as two extra minutes reported by Shinkawa [46,51].

RISK FACTORS FOR EXTUBATION FAILURE

To understand the factors that determine the success of early extubation, we need to examine the risk factors for extubation failure, which is most commonly defined as the need for reintubation within 72 h of extubation [28,44]. Studies examining the risk factors of extubation failure have identified patient, surgical, anesthetic, and postoperative factors. Extubation failure is more likely to be determined by a combination of factors rather than by a single factor.

Patient risk factors

These include neonates and infants [45,52], males [45], airway anomalies [28], lower weight for age z-score as recognized by failure to thrive [40,52], the presence of extracardiac/chromosomal anomalies [52,53], pulmonary hypertension [40,54], need for preoperative ventilation [28,33,35], more complex cardiac lesions such as Society of Thoracic Surgeons-European Association for cardiothoracic surgery mortality categories (STAT) 4–5 versus STAT 1–3 [44,52], and preoperative pneumonia [55]. Associations have been found among ethnicity, race, and extubation failure, but these may be difficult to explain [45]. Trisomy 21 has been identified as a risk factor for failed extubation [4,20] and a longer period of mechanical ventilation [37] because airway compromise is eight times more likely in patients with trisomy 21 and hypoxemia appears more common [53]. Rooney et al. [52] also identified the presence of major preoperative risk factors such as hepatic dysfunction, chest compression within 48 h of surgery, mechanical circulatory support, neurological and renal deficits, and shock at the time of surgery as risk factors for extubation failure.

Surgical risk factors

These include the type of surgical procedure, duration of cardiopulmonary bypass, and delayed sternal closure. Byrnes et al. [45] conducted a retrospective multicenter cohort study of prospectively collected data from the Pediatric Cardiac Critical Care Consortium (PC4) registry between 2013–2018 and analyzed 18,278 extubations. The early extubation failure rate (within 48 h) was 5.2%, and the late extubation failure rate (48–168 h) was 2.5%. Norwood and orthotopic heart transplants were found to have the highest odds of early extubation failure compared with ventricular septal defect repair. Tetralogy of Fallot, Fontan, arterial switch operation, and ventricular septal defect were procedures with the lowest odds of extubation failure [45]. The presence of residual cardiac lesions may increase the risk of extubation failure, particularly if not recognized earlier [47]. The longer the duration of cardiopulmonary bypass (CPB) and aortic cross-clamp, the higher the risk of extubation failure. In Joshi's study of 448 patients of whom 92% underwent immediate extubation, a CPB time greater than 120 min increased the chances of not extubating in the operating theatre by an adjusted odds ratio of 5.5 [41]. In his study on extubation in neonates, Mastropietro found that open sternotomy of 4 days or more was associated with a significant increased risk of extubation failure and noted that most of those with delayed sternal closure were more likely to receive neuromuscular blocking agents (87%) compared to the rest of the co-

hort (39%) [28].

Anaesthesia risk factors

Anesthesia risk factors for extubation failure include the use of uncuffed endotracheal tubes (ETT) [28], oral intubation [45] and the use of high doses of opioids (fentanyl > 25 µg/kg). The higher incidence of failed extubation with uncuffed ETTs and oral intubation has been postulated to be related to the increased likelihood of a larger uncuff tube and head movement, resulting in more movement contact, leading to glottic edema and upper airway obstruction [45]. Higher doses of opioids and sedatives can result in increased respiratory depression and higher incidence of failed extubation [56].

Postoperative risk factors

Postoperative risk factors for extubation failure include the duration of postoperative ventilation, a higher Pediatric Index of Mortality (PIM) 2 score, vocal cord paralysis, surgical complications, and quality of postoperative care.

The duration of postoperative ventilation, not just preoperative ventilation, is a risk factor for extubation failure [28,39,40]. Gaies et al. [39] conducted a multicenter (9 hospitals) analysis of 1,734 mechanical ventilation episodes involving 1,478 patients showed that the extubation failure rate after immediate extubation failure was 3% compared to 4% when ventilation was less than 24 h, 9% after 24 h, and 13% after 7 days. However, the association between ventilation duration and extubation failure in neonates after cardiac surgery is less clear [28].

A higher PIM 2 score, which generally indicates that a patient is more likely to die, was associated with an increased risk of extubation failure [40].

The presence of postoperative complications such as acute lung injury, pleural effusion, or diaphragmatic palsy leads to respiratory compromise and failure to extubate [40,45]. Byrnes et al. [45] demonstrated in their analysis that the risk of diaphragmatic palsy leading to early extubation failure is increased after surgery for the repair of coarctation of the aorta via thoracotomy, ventricular septal defect, superior cavopulmonary (Glenn) anastomosis, atrioventricular canal, arterial switch with ventricular septal defect, orthotopic heart transplant, and Fontan procedure. Similarly, the risk of early extubation failure due to pleural effusions increases with the following surgeries: arterial switch opera-

tion, Norwood, ventricular septal defect, coarctation of the aorta, arterial switch operation with ventricular septal defect, Tetralogy of Fallot, and superior cavopulmonary (Glenn) anastomosis [45].

Some studies have suggested that quality of postoperative care is an important risk factor for extubation failure. Higher extubation failure rates are associated with the lack of dedicated cardiac ICU [40] and lower-volume cardiac centers [24,40,52], possibly because of the lack of staff trained specifically in the postoperative care and monitoring of cardiac patients or the lack of standardized management protocols. In an observational study by Gupta et al. [40] that examined the risk factors for mechanical ventilation and reintubation after pediatric cardiac surgery from data provided by 62 cardiac centers, centers with a dedicated cardiac ICU, longer nursing hours, and more critical-trained nurses had lower odds of mechanical ventilation and reintubation. Nighttime and extubation during shift changes have been linked to a greater risk of early extubation failure [45].

POTENTIAL GUIDELINES FOR PRACTICE AND IMPLEMENTATION OF EARLY EXTUBATION

It is important to recognize that no single factor guarantees the success or failure of early extubation. Each institution must consider its resources and experience to determine patient suitability and develop a perioperative management plan that seeks to maximize the success of early extubation. This is in line with the recommendations of The American Association for Thoracic Surgery Congenital Cardiac Surgery Working Group (2021) comprehensive perioperative approach to enhanced recovery after pediatric cardiac surgery [57].

Development of a protocol

The decision-making process for early extubation can be complex. Studies have demonstrated that a fast-track or early extubation protocol can be useful to guide the practice of early extubation within an institution and reduce the time to extubation [2,3,10,42,47,58]. The Pediatric Heart Network centers engaged in a collaborative learning initiative involving nine centers, four of which were active sites and 5 controls [59]. The rate of early extubation increased from 11.7 to 66.9%, the mean duration of extubation decreased from 21.2 to 4.5 h, and the duration of ICU stay decreased at active

sites [59]. Although there are examples of ERAS protocols published to take reference from [13,46,58,60,61], each institution should consider the resources available in the creation of a protocol for early extubation to determine which patients underwent what surgical procedure, and which anesthetic and analgesia management would be suitable for early or immediate extubation. However, even with a protocol in place, there may still be challenges to its implementation [41]. In a survey of anesthetists, despite the presence of a protocol, only 7% of respondents said that they strictly followed the inclusion criteria for immediate extubation [12]. It is also expected that the protocol and practice of immediate or early extubation in an institution may change over time as more experience is gained; for example, increasingly smaller babies may undergo immediate or early extubation [42].

Multidisciplinary approach

A multidisciplinary team approach comprising a dedicated team of cardiac anesthetists, surgeons, cardiologists, and the ICU team (physicians, nurses, and respiratory therapists) is necessary to determine the inclusion and exclusion criteria and obtain buy-ins from all stakeholders. Without this, the successful and sustained implementation of an early extubation protocol is challenging [14,62]. This was seen by the regression in early extubation rates from 67 to 30% and increase in time to first extubation from 4.5 to 13.5 h in 3 of the 4 active centers that participated in the Pediatric Heart Network collaborative learning initiative clinical practice guidelines, over the 1 year period after conclusion of the study [59,62]. Bates et al. [14] in their study showed that even with the same protocol in place in 4 centers, there was variation in the implementation and outcomes, resulting in mean extubation times varying from 0.3 to 5.3 h (from 15.4–35.5 h) and differences in the magnitude of change. They identified barriers to change as concerns regarding analgesia and sedation, workflow changes, and resistance to change, particularly if the track record of outcomes in a center has historically been good. Achieving team buy-in requires staff engagement, education, development of complementary protocols for sedation and analgesia, data collection and review with team members, and attentiveness to concerns and reasons for delayed extubation. These elements are crucial for the success of early extubation or fast-track cardiac programs [14,58,62]. Given the involvement of many disciplines in patient care, role clarification and effective communication are imperative. Practically, this could take the form of huddles immediately before surgery, and multidisciplinary meetings or rounds that are planned during the perioperative period.

Patient considerations

Even though we know that there are patient risk factors that are associated with extubation failure, there are no universally accepted inclusion and exclusion criteria. Age and weight limits are commonly considered in the exclusion criteria, but there is considerable variation in the cutoff values [13,44,53]. Neonates and premature infants successfully underwent immediate extubation [46,63,64] even for complex surgical procedures [23,46,51,64]. Patients with genetic and chromosomal disorders, particularly trisomy 21, are at increased risk of extubation failure; however, Joshi's study reported successful immediate extubation in 16 out of 18 patients [41]. Similarly, pulmonary hypertension may not necessarily preclude immediate extubation, as demonstrated by Vida and Garg [23,37,46]. Major preoperative morbidities could exclude early extubation [52]. These include heart failure, hepatic dysfunction, preoperative cardiac arrest requiring chest compression/cardiac assist devices or extracorporeal membrane oxygenation (ECMO), and renal failure. Patients who require preoperative ventilation for > 24 h before surgery may also not be suitable candidates for early extubation.

Surgical considerations

Considered alone, surgical complexity can influence the decision to extubate because there is likely a correlation between the duration of cardiopulmonary bypass (CPB), aortic cross-clamp, and deep hypothermic circulatory arrest, and the development of complications such as bleeding, diaphragmatic palsy, significant pleural effusions, residual cardiac lesions, low cardiac output, and ventricular dysfunction. The risk adjustment for congenital heart surgery score (RACHS) is a risk-adjustment tool for short-term mortality from all forms of congenital heart disease surgery [65], whereas the STAT system analyzes the risks of in-hospital mortality from congenital heart surgery procedures [28]. A lower mortality risk was observed in the lower categories of both scoring systems. Patients with RACHS categories 1–2 or STAT 1–3 categories should be considered for early extubation because their success rate is high [41]. These procedures include ventricular septal defects, atrial septal defects, pacemaker generator changes, vascular ring repair, AVSD repair,

bidirectional Glenn, coarctation of the aorta repair (end-to-end), patent ductus arteriosus ligation, coronary artery origin anomaly repair, Fontan surgery, new pacemaker implantation, Tetralogy of Fallot repair, valve replacement, arterial switch operation for transposition of the great arteries, atrioventricular septal defect or canal repair, conduit placement, and the Rastelli procedure. Repeat surgeries are not necessarily a contraindication for early extubation if bleeding and residual lesions are not an issue. While a CPB time of more than 120 to 150 min, an aortic cross-clamp time of more than 60–100 min, use of hypothermic arrest, and a longer procedure time have been considered reasons to avoid early extubation, Garg stated that as long as hemostasis is maintained, immediate extubation can still be considered [46].

Intraoperative goals and management

If the goal is immediate or early extubation, attention should be paid to fluid balance, pain management, anesthetic techniques, good surgical repair, hemostasis, and preservation of organ function to ensure a hemodynamically stable patient who is awake, comfortable, pain-free, and able to breathe well by the end of surgery.

Intraoperative fluid management is crucial to prevent the development of pulmonary edema and acute lung injury. Anesthetists and perfusionists play important roles in this regard. Excessive increases in body water can be avoided by reducing the prime volume using a miniaturized CPB circuit, meticulous monitoring of systemic venous drainage on CPB, and the utilization of conventional (CUF) and modified ultrafiltration (MUF) to remove excess water [23,46]. Management of blood products is important. The use of fibrinogen concentrates, prothrombin complexes, and antifibrinolytic agents such as tranexamic acid guided by thromboelastography can help limit exposure to blood products that are known to cause acute lung injury and other complications that may delay extubation.

The surgeon plays an important role in performing good surgical repair with minimal residual lesions while minimizing the duration of CPB, aortic cross-clamp time, or circulatory arrest. Therefore, meticulous surgical hemostasis is essential. Attention to organ preservation strategies such as appropriate temperature management is important to ensure minimal neurological, myocardial, pulmonary, and renal dysfunction in patients at the end of surgery.

A good anesthetic plan should allow for good pain relief and smooth and rapid awakening.

Although there are many approaches to achieve this outcome, they center around using multimodal analgesia that allows for opioid-sparing effects, tailored use of neuromuscular blocking agents, and limited use of sedatives or anesthetic agents. A depth of anesthesia monitoring device such as processed electroencephalogram (EEG) monitoring, is useful in guiding the use of intravenous or inhalational anesthetic agents, both on and off CPB. Monitors such as cerebral oximetry, urine output, temperature, and transesophageal echocardiography can help determine organ perfusion and detect problems such as inadequate surgical repair with significant residual cardiac lesions, allowing for early and appropriate intervention. Inadequate administration of anesthetics can result in awareness; however, excessive administration can result in burst suppression, which is associated with an increased risk of delirium [66] and delayed awakening. Both sevoflurane and isoflurane have been used successfully for immediate extubation, but sevoflurane allows for a more rapid recovery from anesthesia [67]. The use of a neuromuscular blocking agent, such as rocuronium, reduces the amount of anesthetic agent required to achieve a still surgical field. Full reversal of neuromuscular blockade and a train of four ratio of at least 90% must be performed before extubation to reduce the risk of respiratory complications related to inadequate neuromuscular blockade reversal [68]. The use of a cuffed ETT should be considered as suggested by Mastropietro's study in neonates, which found an association between extubation failure and the use of uncuffed ETTs [28]. If used, the cuff pressure should be maintained below 20 cmH$_2$0.

Various analgesic agents and techniques have been successfully used in various combinations to ensure good pain relief, which is crucial for the patient to breathe well postoperatively. Although high-dose opioids have traditionally been used to blunt the stress response of cardiac surgery, alternative techniques can be used to achieve this while limiting the total dose of opioids used intraoperatively. Intravenous acetaminophen (10–15 mg/kg) [41,58,69], non-steroidal anti-inflammatory drugs (NSAIDs) [58] like ketorolac (0.5 mg/kg 6 h to max 30 mg per dose) or ibuprofen (10 mg/kg 6 h, max 400 mg per dose) [58,61,69], low analgesic doses of ketamine (0.25–0.5 mg/kg) and dexmedetomidine infusions have been used in fast track protocols to decrease opioid requirements in the perioperative period [58]. Although there is limited information on the pharmacokinetics of ketorolac in children [70], and paracetamol may not be effective in acute pain management in children less than 2 years of age

[71], both of these drugs, particularly when used in conjunction with a regional anesthetic technique such as caudal blocks, have been shown to result in less opioid usage in infants aged 6 months and older [69].

Intravenous ibuprofen has been approved for use in infants aged 6 months and above, and therefore can be considered if there are concerns with intravenous ketorolac use [72], provided there are no contraindications to the use of NSAIDs. As a precaution, NSAIDs may be initiated only when hemostasis is achieved in the postoperative period. Regional anesthesia blocks, such as caudal [13,23,41,44,50], thoracic epidural [12], intercostal nerve [12], and paravertebral blocks [60], are viable techniques that have been shown to reduce intraoperative and postoperative intravenous opioid requirements and blunt the neurohumoral stress response. For children less than 5 years of age with a favorable anatomy and coagulation profile, caudal with preservative free morphine 50–100 µg/kg with or without 0.25% bupivacaine [11,53,73], clonidine 1–2 µg/kg [11,44,69] or dexmedetomidine 1 µg/kg [46] diluted to 1 ml/kg [46], provides good intraoperative and postoperative analgesia [23,69]. Intravenous dexmedetomidine 0.4–1 µg/kg/h has been advocated as a useful adjuvant for intra-and postoperative sedation and analgesia, with the ability to blunt the neurohumoral stress response while sparing opioid and benzodiazepine use [74] and facilitating early extubation [75]. In a meta-analysis that focused on dexmedetomidine used at an infusion rate of 0.5–1 µg/kg/h, dexmedetomidine was found to significantly reduce the duration of mechanical ventilation, reduce ICU and hospital stay, and reduce the incidence of junctional ectopic tachycardia [74].

To facilitate early extubation, the total amount of intraoperatively administered opioids must be limited. The limits to intraoperative fentanyl have been cited in various studies to range between 5 µg/kg to a maximum of 20 µg/kg [23,42]. Remifentanil has also been used to provide rapid titratable analgesia, although long-acting analgesic alternatives are required for postoperative care [58]. In studies, the total intraoperative morphine dose generally does not exceed 0.15 mg/kg, and fentanyl does not exceed 9 µg/kg if early extubation is considered to avoid significant respiratory depression with a high dose opioid [44,58].

Even with excellent anesthesia and analgesia plans, patients with the following characteristics may not be suitable for immediate or early extubation:

1. Premature neonates
2. Pre-existing pulmonary disease, preoperative pneumonia, mechanical ventilation preoperatively for > 24 h [33,35,55]
3. Airway concerns such as known airway anomalies or difficult airways, history of failed extubation, or post-extubation stridor
4. Major preoperative comorbidities such as cardiac failure, hepatic dysfunction, preoperative cardiac arrest requiring chest compression/cardiac assist device or extracorporeal membrane oxygenation (ECMO) and renal failure
5. Tracheal bleeding as evidenced by blood in the endotracheal tube or thick tracheal secretions
6. Complex surgical procedures (STAT 4 or 5), especially Norwood, orthotopic heart transplantation, truncus arteriosus, arterial switch-ventricular septal defect, superior cavopulmonary anastomosis (Glenn), coarctectomy, and atrioventricular canal
7. Severe pulmonary arterial pressure (mean pulmonary arterial pressure [MPAP]/mean systemic arterial pressure [MSAP]) > 0.7, requiring pulmonary vasodilators.
8. Patients who are hemodynamically unstable or have low cardiac output state, with an inotropic score of 10–15 or an vasoactive inotropic score of 20 [50,76] e.g. requiring dopamine or dobutamine 10 µg/kg/min with adrenaline 0.05 µg/kg/ min–0.1 µg/kg/min and milrinone 0.75 µg/kg/min [29,46]
9. Ventricular dysfunction or significant residual cardiac lesion on echocardiogram
10. Significant surgical site bleeding or coagulopathy
11. Poor urine output
12. Inadequate recovery from sedation/conscious level state
13. High ventilatory settings: $FiO_2 \geq 50\%$, peak inspiratory pressure ≥ 25 cmH$_2$0, pressure support > 10 cmH$_2$0
14. Poor respiratory mechanics, such as failure to achieve 6 ml/kg tidal volume despite full reversal of neuromuscular blockade, respiratory rate of more than 30 beats per min
15. Unsatisfactory arterial blood gas results: arterial oxygen tension (PaO_2) < 80 mmHg in patients with full repair and < 55 mmHg in patients who underwent palliative procedures on FiO_2 0.5, arterial carbon dioxide tension ($PaCO_2$) > 55 mmHg, pH < 7.3 [46].
16. Base deficit > 4 mEq/L for full repair and > 6 mEq/L for palliative procedure [10]
17. Hypothermia: temperature less than 35°C
18. Open sternum

The timing of extubation is another factor that needs consideration because night extubations or afternoon cases are known to be a risk factor of failed extubation [5,13].

Postoperative care

It is crucial to provide good postoperative support in the ICU in the form of trained critical care nurses and physicians who understand the physiological responses of a child and can detect and manage early signs of respiratory or cardiac compromise. This includes tolerating respiratory acidosis with mild hypercarbia of up to 55–60 mmHg during the immediate postoperative period [46].

Cardiologists should perform transthoracic echocardiography soon after the child arrives in the ICU to understand the baseline postoperative function and whenever the child deteriorates. It may be worthwhile to note that infection control measures extend to transthoracic echocardiography which should include disinfecting the probe and using sterile gel to enhance contact.

It is important that the patient remains comfortable and calm in the postoperative period with regular paracetamol, NSAIDs and low doses of opioid given as required (intravenous fentanyl 0.5 µg/kg or morphine 0.05 mg/kg titrated to effect, or as a morphine infusion of 10–20 µg/kg/h). Dexmedetomidine infusion is continued for the first 24 h prior to weaning. Garg et al. [46] advised that neonates and young infants should be handled minimally to avoid episodes of breath-holding, which can lead to desaturation, and adequate sedation should be given during stimulating procedures. Management of agitation should include non-pharmacological means like parental presence, cuddling, distraction and early feeding in addition to appropriate use of anxiolytics like benzodiazepines or clonidine (0.9–3.3 µg/kg), and analgesics if pain is the likely cause of agitation [42,46]. Early removal of chest drains and pacing wires will help reduce analgesic requirements, and should be considered.

Some patients may require some form of non-invasive respiratory support to avoid reintubation. These include continuous positive airway pressure, non-invasive positive pressure ventilation, nasal high-frequency oscillatory ventilation, and high-flow nasal cannula [36]. Therefore, the ICU should be equipped with at least one of these modalities.

CONCLUSION

Although the majority of studies included were retrospec-

tive observational studies that carry inherent limitations, such as selection bias and inability to control for all potential confounders, the experiences reported strongly suggest that early extubation should be practiced whenever possible for pediatric congenital heart surgery. Nevertheless, appropriate patient selection based on the availability of institutional resources and expertise is important, because extubation failure may result in additional morbidity and mortality. For a successful early extubation program, a dedicated multidisciplinary team approach is necessary to ensure appropriate patient selection, good clinical judgement, and common goals. Finally, good postoperative ICU support is necessary to avoid early extubation failure.

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CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

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