Minimizing bleeding associated with mechanical circulatory support following pediatric heart surgery


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Abstract

Objective: The use of extracorporeal membrane oxygenation (ECMO) to support patients with early postcardiotomy heart failure may be associated with catastrophic bleeding, making its use undesirable. However, postcardiotomy mechanical circulatory assistance is necessary in some patients to allow for myocardial recovery. We have assembled a centrifugal pump system (CPS) that does not require early systemic anticoagulation. This study compares postoperative bleeding in pediatric patients placed on standard ECMO versus CPS within 24 h of cardiotomy.

Methods: Between November 2002 and February 2007, 25 patients (age 0 days—1.72 years) received postcardiotomy mechanical support. Fourteen patients were placed on ECMO and 11 patients were placed on CPS within 24 h of surgical repair. Retrospective analysis was performed of chest-tube drainage at multiple time points following initiation of mechanical support. Additional variables, including Risk Adjustment for Congenital Heart Surgery-1 (RACHS-1) score, total time on mechanical support, 30-day mortality, activated clotting time, blood-product administration, circuit-related complications, and circuit changes were also analyzed.

Results: Patients on ECMO (0.30 ± 0.39 years) and CPS (0.40 ± 0.56 years) were of similar age (p = 0.64). Patients on ECMO (0.3 ± 0.1 m²) and CPS (0.3 ± 0.1 m²) had similar body surface areas (p = 0.46). Patients placed on CPS had significantly less chest-tube drainage during the first 4 h of support. Activated clotting times appeared to be higher during the first 12 h of ECMO versus CPS. There was no statistical difference between ECMO and CPS with respect to the following variables: RACHS-1 score, time on support, 30-day mortality, circuit-related complications, and circuit changes. Blood-product administration at 24 h of support was significantly less (p = 0.04) for patients on CPS versus ECMO.

Conclusions: Mechanical circulatory support can be provided without the complication of clinically significant bleeding if a specialized circuit is used. This has important implications for the decision to use mechanical support in the immediate postoperative period in the face of ventricular failure. In addition, early mechanical support can be used with a low incidence of circuit-related complications.

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1. Introduction

Clinically significant perioperative myocardial and respiratory dysfunction may occur following surgery for complex congenital heart disease. In addition to requiring increasing pharmacologic and mechanical ventilatory support, up to 6.8% of these patients may require extracorporeal cardiopulmonary support to improve oxygen delivery and facilitate myocardial recovery [1–3]. However, the use of extracorporeal life support (ECLS) immediately following open cardiac surgical repair is complicated by surgical-site bleeding in approximately one-third of patients (2008 Extracorporeal Life Support Organization (ELSO) Registry; available at: http://www.elso.med.umich.edu). The risk of significant ECLS-associated bleeding during the postoperative period leads many clinicians to preferentially escalate inotropic therapy to avoid the use of mechanical support. To reduce the risk of postoperative hemorrhage in these patients, we assembled a heparin-coated centrifugal pump system (CPS) that does not require early systemic anticoagulation. The purpose of the present study was to compare postoperative bleeding between patients supported with standard extracorporeal membrane oxygenation (ECMO) or centrifugal pump system initiated within 24 h of surgical repair.

2. Materials and methods

A retrospective review of patients undergoing cardiac surgery at Seattle Children’s Hospital between November 2002 and April 2007 was performed after receiving approval...
from the Institutional Review Board of Seattle Children’s Hospital. Of the 1358 procedures performed during this time, 29 (2.1%) patients required postoperative ECLS within 24 h of surgery. Four of these patients did not undergo surgical repair using cardiopulmonary bypass. The remaining 25 patients comprise the subjects of this study.

2.1. ECLS equipment

The standard ECMO circuit consists of Stockert SIII roller pump (Sorin Group USA, Arvada, CO, USA) with a Tygon® S-95 tubing raceway (Saint-Gobain Performance Plastics, Portage, WI, USA), a Medtronic 0800 or 1500 silicone oxygenator (Medtronic, Minneapolis, MN, USA), an ECMOthether™ II heat exchanger (Medtronic, Minneapolis, MN, USA), an external extracorporeal heating system (Cincinnati Sub-Zero, Cincinnati, OH, USA), a VRECMOS collapsible bladder (Gish Biomedical, Rancho Santa Margarita, CA, USA), and uncoated tubing (Medtronic, Minneapolis, MN, USA). The total priming volume is 350 cc when the Medtronic 0800 oxygenator is used.

A heparin-coated CPS circuit was assembled and introduced into service in August 2005. The system consists of a phosphorylcoline-coated Cobe Revolution® centrifugal pump (Sorin Group USA, Arvada, CO, USA), a heparin-bonded Minimax® hollow-fiber oxygenator (Medtronic, Minneapolis, MN, USA), an external extracorporeal heating system (Cincinnati Sub-Zero, Cincinnati, OH, USA), and heparin-bonded tubing (Medtronic, Minneapolis, MN, USA). The total priming volume is 300 cc. Patients were preferentially supported with the CPS circuit following its introduction, based on circuit availability.

2.2. Patient management

All patients were admitted to a dedicated cardiac intensive care unit (ICU) following surgery. The decision to initiate ECLS in the operating room was made by the operating surgeon, whereas the decision to initiate ECLS in the ICU was based on a consensus between the cardiac critical care specialist and the operating surgeon. Adequacy of cardiac output was based on blood pressure, heart rate, urine output, serum lactate, the presence of arterial blood acidosis, central venous oxygen saturation, extremity temperature, and cerebral and visceral near infrared spectrometry. Adequacy of respiratory function was based on arterial blood gas measurements, ventilator settings, end tidal carbon dioxide, and chest radiography. Our philosophic approach to ECLS in cardiac patients is to preferentially provide mechanical cardiopulmonary support to prevent clinically significant escalation of pharmacologic therapy.

Heparin was not reversed with protamine in patients undergoing conversion to ECMO support in the operating theater. Heparin (50–100 units kg⁻¹) was given prior to initiation of ECMO in the ICU. Heparin was reversed with protamine prior to or upon initiation of CPS support in the operating theater. Patients did not receive heparin when CPS support was initiated in the ICU. Extracorporeal pumps were adjusted to achieve initial flow rates of >100 ml kg⁻¹ min⁻¹. Activated clotting time (ACT) was measured hourly, once ECLS was initiated, using a Hemochron® Response ACT analyzer (International Technidyne Corporation, Piscataway, NJ, USA). Heparin infusion was initiated when bleeding subsided in CPS patients and when bleeding subsided or when the measured ACT was <160 s in ECMO patients. Measured ACT <160 s was included as a trigger to begin heparin administration in ECMO patients to reduce the risk of circuit-related thrombotic complications associated with lower systemic anticoagulation [4]. Once heparin therapy was initiated, the infusion rate was titrated to maintain ACT between 160 and 220 s. ECMO and CPS circuits were changed when visible thrombus developed within a circuit.

Data were obtained from perfusion, intensive care, ECLS, anesthesia, and electronic medical records. Data collection included patient demographics, diagnosis, surgical procedure, 30-day survival, Risk Adjustment for Congenital Heart Surgery-1 (RACHS-1) score, preoperative medications, cardiopulmonary bypass time, circulatory arrest time, use of aprotinin, intraoperative protamine dose, need for ELS circuit or component change, administration of blood products, heparin administration, ACT, and chest-tube drainage during the initial 96 h of postoperative care.

3. Statistical analysis

Appropriate descriptive measures were used to summarize patient characteristics and outcomes. Continuous measures are presented as mean ± standard deviation or median (interquartile range) depending on the normality of their distribution. Categorical variables are captured as frequencies and percentages. For continuous measures, differences between CPS and ECMO groups were evaluated using either an unpaired two-sided t-test or a Mann–Whitney test, depending on the normality of the distribution. Differences in the distribution of categorical variables between the groups were evaluated using a Fisher’s exact test. Figures depicting the mean and standard error of ACT and cumulative chest-tube drainage during the initial 96 h of postoperative care were generated to visually illustrate patterns in the two groups over time. A Bonferroni correction was used to adjust p values for comparisons where appropriate. Analyses were performed using STATA version 10.1, with p values <0.05 considered to be statistically significant. All reported p values are two-sided.

4. Results

Fourteen (56%) patients were supported with conventional ECMO and 11 (44%) were supported with CPS. The groups were similar with respect to age, weight, body surface area, lowest body temperature during surgery, total cardiopulmonary bypass time, circulatory arrest time, and RACHS-1 score (Table 1). Surgical procedures performed in each group are listed in Table 2. Intraoperative aprotinin was used in 18 (72%) patients (nine CPS vs nine ECMO patients, p = 0.41). Lysine analogs and recombinant activated Factor VIIa were not used in any patient. Protamine was administered to 17 (68%) patients in the operating theater (nine CPS vs eight ECMO, p = 0.23). Indications for postoperative mechanical support, including failure to wean from cardiopulmonary bypass (8%; 32%), failure to maintain adequate cardiac output following separation from cardiopulmonary bypass (8%; 32%), and severe arrhythmia (8%; 32%) were similar.

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bypass (10; 40%), and inadequate pulmonary function (7; 28%) were similar between the groups (p = 0.11). Sixteen (64%) were cannulated in the operating room. Seven (28%) patients initially received venovenous extracorporeal support; the remaining 18 (72%) initially received venoarterial support. One (4%) patient was converted from venoarterial to venovenous support during the study period. Cannulae placed at the time of surgery for cardiopulmonary bypass were used for ECLS in seven (28%) patients, new chest cannulation was performed in six (24%) patients, cervical cannulation of the right common carotid artery and internal jugular vein was used in five (20%) patients, cannulation of the right internal jugular vein using a dual-lumen venovenous cannula was performed in five (20%) patients, and two (8%) patients underwent chest cannulation for venovenous support. The method and location of cannulation were similar between groups (p = 0.21). Median ACT measured prior to initiating ECLS appeared to be slightly higher in ECMO patients than in CPS patients (145 s vs 120 s, p = 0.21). Although non-significant, this would be consistent with preferential protamine administration in CPS patients (Table 3). The median interval between separation from cardiopulmonary bypass and initiation of ECLS (0.63 h CPS vs 2.8 h ECMO, p = 0.34) and the median total duration of ECLS (127 h CPS vs 153 h ECMO, p = 0.34) were similar between the groups. However, the median interval between initiation of ECLS and administration of heparin was longer in the CPS group (17.8 h vs 0.4 h, p < 0.001). ACT levels appeared higher during the first 12 h of ECMO support when compared with CPS support, with less difference seen beyond that point (Fig. 1).

A similar pattern was observed in cumulative chest-tube drainage (Fig. 2) and a significant difference was found between the two groups at 4 h, but not at the 24-h or 96-h time points. During the initial 24 h of support, ECMO patients received greater median volume of transfused blood products (388 ml vs 100 ml, p = 0.04) and platelet transfusions (2.1 units vs 0.64 units, p < 0.001).

ECMO patients and CPS patients were similar with respect to the proportion of ECLS circuit changes required (0.29 vs 0.55, p = 0.24). One patient in each group experienced an embolic event involving thrombotic occlusion of the arterial cannula that required urgent embolectomy of the cannula.
The overall 30-day mortality rate was 32%, with four patients dying in each group (29% ECMO vs 36% CPS, \( p = 1.00 \)).

5. Discussion

Postoperative surgical-site bleeding can be an important cause of morbidity and mortality in patients who require cardiopulmonary bypass to correct congenital cardiac abnormalities [5,6]. Younger patients and patients undergoing complex surgical repairs are at increased risk [7]. Cardiopulmonary bypass results in platelet and clotting factor consumption as well as reduced platelet function related to contact activation of the hemostatic system [8]. Furthermore, the effect of hemodilution on coagulation factors, Antithrombin III levels, and number of platelets is more pronounced in younger patients [9], which increases the risk of clinically significant postcardiotomy hemorrhage. The coagulopathic impact of cardiopulmonary bypass on neonates and infants is often more pronounced due to the immaturity of the hemostatic system in these patients [9,10]. Vitamin-K-dependent factors, prothrombin, Antithrombin III, protein C, and protein S levels are depressed at birth and many factors do not achieve adult levels for several months [11]. It is estimated that life-threatening postoperative hemorrhage occurs in 2–5% of patients undergoing cardiac surgery [12,13]. Although the overall incidence of hemorrhage-related mortality in pediatric patients is not well defined, up to 1–4% of infants may require early reoperation for surgical bleeding [7,14,15].

During the past two decades, the use of ECLS to support pediatric patients with postcardiotomy cardiopulmonary failure has increased. Since its inception, ECMO has been used to provide mechanical cardiopulmonary support to more than 6000 pediatric patients in the postoperative period, according to the ELSO Registry. Several centers have reported that approximately 2–4% of neonatal and pediatric patients undergoing surgical correction require postcardiotomy ECLS [1,3,16–18], with rates as high as 6–7% being reported in centers that care for high-risk neonates [2,16]. The frequency with which ECLS is used is dependent upon the complexity of the operation, experience of the surgeon and other members of the medical team, availability of ECLS equipment, and the programmatic philosophy toward postoperative ECLS.

The overall risk of postoperative surgical-site hemorrhage is approximately 32% in pediatric cardiac surgical patients, who require ECMO (ELSO Registry data). Although the risk of bleeding is similar for neonates (31.7%), infants (34.5%), and children (31.1%), the risk of death in patients with postoperative surgical-site hemorrhage is substantially greater in neonates (72%) than in older patients (60%) (ELSO Registry data). Furthermore, neonates experience increased hemorrhage-related mortality associated with postcardiotomy ECLS (13%) when compared with older patients (7%) (ELSO Registry data). To avoid the considerable risk of bleeding in postcardiotomy patients, many centers are reluctant to use postoperative ECLS in all but the most extreme circumstances.

Several centers have reported innovative modifications of standard ECMO systems for use in postcardiotomy patients, including configuring the ECLS system for direct conversion to and from cardiopulmonary bypass to minimize new circuit surface exposure [19,20], and using heparin-coated circuit components to minimize the requirement for systemic anticoagulation [16,21,22]. During recent years, approximately 30% of centers in the United States have reported using centrifugal ECLS pumps (ELSO Registry data). Since Ojito et al. first reported their experience with a miniaturized, heparin-coated ECLS circuit in 1997 [16,21,22], more than 100 children have been supported with this system at Miami Children’s Hospital [16]. In a recent review of their experience [16], they report 55% overall 30-day survival in patients supported with postcardiotomy ECLS, with up to 65% of patients surviving in recent years. Postcardiotomy ECLS was used in 7.4% of their neonates undergoing surgery. Overall neonatal ECLS survival was 48%.

Traditional ECMO circuits, consisting of a roller pump and a silicone membrane oxygenator, require careful pharmacologic anticoagulation to prevent early circuit thrombosis. In addition, traditional circuits generally require a larger priming volume due to the size of the membrane oxygenator.
and increased circuit length. Many centers are reluctant to delay heparin administration, even in the setting of postoperative hemorrhage, to prevent early circuit thrombosis and additional blood-product exposure during subsequent circuit exchange. In an effort to reduce postoperative hemorrhage-related morbidity and mortality, we assembled a heparin-coated ECLS circuit that can be used without additional heparin. An important advantage of using a modified CPS circuit is that by incorporating a non-membrane oxygenator and shorter circuit length, the likelihood of circuit thrombosis is reduced by decreasing circuit transit time and areas of stasis within the oxygenator. In patients, who are directly transitioned from cardiopulmonary bypass to CPS, protamine is given after conversion to CPS to reverse systemic anticoagulation associated with cardiopulmonary bypass. Using this strategy, normal pre-ECLS ACT values were achieved in most CPS patients (mean 136 s vs 346 s in ECMO patients). The interval between initiation of ECLS and administration of heparin was more than sixfold longer in CPS patients than in ECMO patients. Consequently, ACT was higher in ECMO patients than in CPS patients during the first few hours of support. ACT measurements were similar between the groups after administration of heparin to CPS patients. In some cases, reversal of heparin upon initiation of CPS support in the operating theater appeared to facilitate rapid control of severe postcardiotomy hemorrhage that may have otherwise required prolonged theater time and additional blood-product administration to achieve hemostasis. Reduced heparin requirement in the CPS group resulted in less chest-tube drainage throughout the study period. At 96 h, the cumulative chest-tube drainage was greater than 3.6-fold higher in ECMO patients. Ongoing hemorrhage in the ECMO group resulted in significantly greater blood and platelet transfusions during the initial 24 h of support. Despite considerably reduced heparin use in CPS patients, this group did not experience more thrombotic or embolic complications than patients supported with ECMO. This observation underscores the degree of reduced thrombogenicity of the CPS circuit. Patients in the ECMO group appeared to have higher cumulative chest-tube drainage beyond 24 h, when the groups had similar ACT levels. Although we cannot definitively explain this observation, one may consider that the ECMO patients may have been predisposed to greater platelet dysfunction due to increased bleeding and greater blood-product transfusion during the initial 24-h period.

The results of this study must be interpreted within the context of the many limitations inherent in a retrospective investigation. Although the patients were not randomized, the study groups were similar with respect to the demographic and perioperative variables analyzed. In addition, the relatively small cohort size precluded multivariable analysis. Finally, the decision to use CPS versus ECMO was based on era, representing a fundamental change in our overall ECLS strategy during this period of time. Although this does not introduce selection bias per se, we anticipate that our threshold for initiating ECLS in the postoperative setting will be lower based on the findings outlined in this study. Despite these study limitations, we believe that the results support the concept that postoperative bleeding and transfusion requirement may be significantly reduced when a specialized, heparin-coated ECLS circuit is employed to provide postcardiotomy mechanical cardiopulmonary support. We believe that any combination of thrombosis-reducing components may be incorporated in a CPS circuit to reduce postoperative bleeding without increasing the risk of thromboembolic complications. Use of a CPS circuit is associated with improved patient safety and provides an important therapeutic modality to treat postcardiotomy heart failure. Use of this system provides early cardiopulmonary support to facilitate myocardial recovery without the additional risks associated with escalating inotropic therapy.

References


