Useful References in Pediatric Cardiac Intensive Care: The 2017 Update*

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Objectives: Pediatric cardiac intensive care continues to evolve, with rapid advances in knowledge and improvement in clinical outcomes. In the past, the Board of Directors of the Pediatric Cardiac Intensive Care Society created and subsequently updated a list of sentinel references focused on the care of critically ill children with congenital and acquired heart disease. The objective of this article is to provide clinicians with a compilation and brief summary of updated and useful references that have been published since 2012.

Data Selection: Pediatric Cardiac Intensive Care Society members were solicited via a survey sent out between March 20, 2017, and April 28, 2017, to provide important references that have impacted clinical care. The survey was sent to approximately 523 members. Responses were received from 45 members, of which some included multiple references.

Data Extraction: Following review of the list of references, and removing editorials, references were compiled by the first and last author. The final list was submitted to members of the society's Research Briefs Committee, who ranked each publication.

Data Synthesis: Rankings were compiled and the references with the highest scores included. Research Briefs Committee members ranked the articles from 1 to 3, with one being highly relevant and should be included and 3 being less important and should be excluded. Averages were computed, and the top articles included in this article. The first (K.C.U.) and last author (K.M.G.) reviewed and developed summaries of each article.

Conclusions: This article contains a compilation of useful references for the critical care of children with congenital and acquired heart disease published in the last 5 years. In conjunction with the prior version of this update in 2012, this article may be used as an educational reference in pediatric cardiac intensive care. (*Pediatr Crit Care Med* 2018; 19:553–563)

Key Words: pediatric cardiac intensive care; pediatric cardiac surgery; pediatric cardiology; pediatric intensive care

***See also p. 584.**

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A list of "One Hundred Useful References in Pediatric Cardiac Intensive Care" was originally compiled by Anthony Chang, MD, MBA, and the Board of Directors of the Pediatric Cardiac Intensive Care Society (PCICS) in 2004. The list was distributed at the fifth International PCICS Conference, 2004, Miami, FL, and subsequently updated in 2012 (1). Pediatric cardiac intensive care continues to evolve, with evolving research and improvement in clinical outcomes. The objective of this article is to provide clinicians with a compilation and brief summary of updated and useful references that have been published since 2012.

METHODS

Members of the PCICS were solicited via a survey e-mailed weekly from March 20, 2017, to April 24, 2017 requesting references for peer-reviewed references that had the greatest impact on clinical care for critically ill infants and children with cardiac disease. References were considered for inclusion if they were published after January 1, 2012. The original 2004 list and subsequent 2012 compilation (1) were used as a guide to solicit new references. The initial e-mail survey was sent to 582 PCICS members, and the last e-mail was sent to 523 members. The decrease in potential respondents was reflective of members who unsubscribed from e-mails and those with unpaid society dues.

Responses were received from 45 PCICS members, who submitted a total of 56 references for inclusion. Editorials and published guidelines from national organizations (e.g., American Heart Association, European Association for Cardio-Thoracic

Surgery [EACTS]) were excluded. After removing duplicates and references that did not meet inclusion criteria, 36 publications remained. Seven members of the PCICS Research Briefs Committee ranked submitted references on a scale of 1–3 in order to provide an objective measure of each reference's impact on the field. Votes were cast in the following manner for each article: a vote of "1" signified definitely include the article, "2" strongly consider for inclusion, and "3" a good article, but not in the top. References were excluded if greater than or equal to four committee members assigned a score of 3. After rankings were received, four references were excluded, leaving 31 for inclusion in the 2017 update.

SUMMARY OF REFERENCES

The following articles represent the 2017 update of important contributions to the literature as judged by members of the PCICS. Articles are grouped according to subject matter. A brief summary of each article is provided. An index of summarized articles is provided in **Table 1**.

Glucose Homeostasis

Agus MS, Wypij D, Hirshberg EL, et al; HALF-PINT Study Investigators and the PALISI Network: Tight glycemic control in critically ill children. *N Engl J Med* 2017; 376:729–741 (2)

In this 35-center prospective controlled clinical trial, critically ill children with confirmed hyperglycemia (excluding patients who had undergone cardiac surgery) were randomly assigned to one of two ranges of glycemic control: 80–110 mg per deciliter (lower target group) or 150–180 mg per deciliter (higher target group). In the intention-to-treat analysis, the median number of ICU-free days did not differ significantly between treatment groups. Patients in the lower target group had significantly lower glucose levels and had higher rates of healthcare-associated infections than those in the higher target group, as well as higher rates of severe hypoglycemia, defined as a blood glucose level below 40 mg per deciliter. Critically ill children with hyperglycemia did not benefit from tight glycemic control targeted to a blood glucose level of 80–110 mg per deciliter, compared with a level of 150–180 mg per deciliter.

Ventricular-Ventricular and Cardiopulmonary Interactions

Penny DJ, Redington AN: Function of the left and right ventricles and the interactions between them. *Pediatr Crit Care Med* 2016; 17(8 Suppl 1):S112–S118 (3)

This comprehensive review of original studies found in Medline and PubMed focuses on interactions between the left and right ventricle and how they modulate each other. The differences between the function of each ventricle relates to differences in respective arterial loads. Function of the left ventricle requires an assessment of the temporal changes in pressure and volume, as well as the time-varying changes between them. This pressure-volume relationship provides insights into ventricular function, energetics, and the way in which left ventricle is coupled to the arterial vasculature. The functioning of the right ventricle is interdependent on the left ventricular function, and there is constant cross-talk in both normal and disease states. Enhanced understanding of the ventricular interactions will facilitate improved therapies for critically ill cardiac patients.

Cardiac Arrest and Extracorporeal Membrane Oxygenation

Eastaugh LJ, Thiagarajan RR, Darst JR, et al: Percutaneous left atrial decompression in patients supported with extracorporeal membrane oxygenation for cardiac disease. *Pediatr Crit Care Med* 2015; 16:59–65 (4)

The purpose of this single-center retrospective study was to describe and compare techniques, adequacy, and impact of timing of left atrial decompression on patient outcomes in a group of pediatric patients supported with veno-arterial extracorporeal membrane oxygenation (ECMO) for cardiac failure. All techniques (vent placement, static balloon dilation, and stent implantation) were equally successful and significantly reduced left atrial pressure and pulmonary edema. Survival to hospital discharge was not associated with ECMO duration prior to left atrial decompression, change in left atrial pressure, or technique used.

Howard TS, Kalish BT, Wigmore D, et al: Association of extracorporeal membrane oxygenation support adequacy and residual lesions with outcomes in neonates supported after cardiac surgery. *Pediatr Crit Care Med* 2016; 17:1045–1054 (5).

This single-center retrospective study examined a cohort of neonates cannulated to ECMO after cardiac surgery to evaluate factors associated with in-hospital mortality. The influence of adequacy of ECMO support, residual structural lesions, and timing of intervention for residual lesions on mortality in this cohort was also evaluated. Eighty-four neonates were cannulated to venoarterial ECMO after cardiac surgery. Survival to discharge was 50%. Prematurity, pre-ECMO pH less than or equal to 7.17, need for inotrope support during ECMO, and ECMO duration greater than 168 hours were all associated with increased mortality (5). Although pre-ECMO lactate was not significantly different between survivors and nonsurvivors, unresolved lactic acidosis greater than or equal to 72 hours after cannulation was associated with increased mortality. Clearance of lactate is an important therapeutic target for patients cannulated to ECMO. Finally, 70 of 84 patients (83%) were noted to have residual lesions after cardiac surgery, and time to diagnosis or correction of residual lesions was significantly shorter in survivors.

Lasa JJ, Rogers RS, Localio R, et al: Extracorporeal cardiopulmonary resuscitation (E-CPR) during pediatric in-hospital cardiopulmonary arrest is associated with improved survival to discharge: A report from the American Heart Association's Get With The Guidelines-Resuscitation (GWTG-R) registry. *Circulation* 2016; 133:165–176 (6)

The main purpose of this retrospective registry study was to determine whether patients with prolonged in-hospital cardiopulmonary resuscitation (CPR) (≥ 10 min) with cannulation to ECMO support (i.e., extrapulmonary CPR [E-CPR]) were more likely to survive to discharge and survive with a favorable neurologic outcome when compared with conventional CPR alone (any event without ECMO). Of the 3,756 patients evaluated in the American Heart Association "Get with the Guidelines" multicenter registry, 591 received E-CPR and 3,165 received conventional CPR. Survival to hospital discharge and survival with a favorable neurologic outcome were higher in the E-CPR group (40% and 27%, respectively) compared with the conventional CPR group (25% and 18%, respectively). After adjusting for covariates, the odds of survival to hospital discharge was 2.8 times greater in those receiving E-CPR (95% CI, 2.1–3.7; $p < 0.001$). Similarly, the odds of survival with a favorable neurologic outcome was 2.4 times greater in the E-CPR group compared with the conventional group (95% CI, 1.9–3.6; $p < 0.001$). This association persisted in a propensity score–matched cohort analysis. Thus, E-CPR is associated with improved survival to discharge and survival with a favorable neurologic outcome compared with conventional CPR following an in-hospital cardiac arrest.

Moler FW, Silverstein FS, Holubkov R, et al; THAPCA Trial Investigators: Therapeutic hypothermia after in-hospital cardiac arrest in children. *N Engl J Med* 2017; 376:318–329 (7)

In this prospective multicenter randomized controlled trial (37 children's hospitals), children who experienced an in-hospital cardiac arrest were randomized to one of two temperature interventions (33°C or 36.8°C). Randomization occurred within 6 hours of return of spontaneous circulation and included children age greater than 48 hours old and less than 18 years old. Cooling occurred for 48 hours with subsequent warming and maintenance of normothermia for the subsequent 120 hours. The primary outcome was survival at 12 months after an arrest with a Vineland Adaptive Behavior Scale (VABS)–II score (second edition) of greater than or equal to 70. The trial was terminated early because of futility after 329 patients had been randomized. In those in whom a VABS-II score could be evaluated before the arrest, there was no difference in outcomes between the normothermia and hypothermia groups. There was also no difference between groups in secondary outcomes including blood product use, infection, serious adverse events, 28-day mortality, and 1-year survival.

Early Extubation

Ödek Ç, Kendirli T, Uçar T, et al: Predictors of early extubation after pediatric cardiac surgery: A single-center prospective observational study. *Pediatr Cardiol* 2016; 37:1241–1249 (8)

Prolonged mechanical ventilation may affect cardiac hemodynamics and places patients at increased risk for worse outcomes, including longer length of stay (LOS), higher risk for complications, and increased morbidity and mortality. In this single-center prospective observational study, the authors aimed to determine the perioperative predictors of early extubation (< 24 hr of mechanical ventilation) in a cohort of children after cardiac surgery. Ninety-nine patients were included in the study, of which 61% extubated early, with four failures at the initial attempt. In a multivariable analysis, lower surgical complexity and lower number of organ failures after surgery were associated with early extubation.

Blinder JJ, Thiagarajan R, Williams K, et al: Duration of mechanical ventilation and perioperative care quality after neonatal cardiac operations. *Ann Thorac Surg* 2017; 103:1956–1962 (9)

This single-center retrospective chart review was performed to determine whether the duration of mechanical ventilation could be used to benchmark the quality of care after neonatal cardiac operations. Of the 601 patients included, multiple risk factors were associated with prolonged duration of mechanical ventilation, including higher STAT (Society of Thoracic Surgeons [STS] and the EACTS STS-EACTS Congenital Heart Surgery Mortality) categories, lower weight, worse technical performance score, and the development of complications. Preoperative risk factors increased the duration of mechanical ventilation by 1.23 days, a worse (class 3) technical performance score by 2.16 days, and development of postoperative complications by 2.03 days.

Neuro Critical Care

Naim MY, Gaynor JW, Chen J, et al: Subclinical seizures identified by postoperative electroencephalographic monitoring are common after neonatal cardiac surgery. *J Thorac Cardiovasc Surg* 2015; 150:169–178; discussion 178–180 (10)

Neonates undergoing cardiac surgery are at risk for seizures in the postoperative period, with a frequency reported from 5% to 20%. As a quality improvement project, the authors implemented postoperative electroencephalographic (EEG) monitoring within 6 hours of ICU admission in all patients less than or equal to 30 days old (corrected gestational age < 44 wk) after cardiac surgery. The purpose of the study was to determine the frequency of subclinical seizures and identify risk factors for development of seizures. Postoperative EEG monitoring was performed in 161 subjects over an 18-month period. EEG (clinical and subclinical) seizures were identified in 8% of neonates, with a median time to onset of 20 hours after admission to the ICU. Seizures were subclinical in 11 patients (85%). Risk factors for seizures included younger neonates with longer bypass and deep hypothermic circulatory arrest (DHCA) times, single ventricle defects with arch obstruction, delayed sternal closure, postoperative cardiac arrest, and use of ECMO. In the multivariable analysis, only delayed sternal closure and longer DHCA time were associated with seizures.

Patel AK, Biagas KV, Clarke EC, et al: Delirium in children after cardiac bypass surgery. *Pediatr Crit Care Med* 2017; 18:165–171 (11)

In this article, the authors performed a single-center prospective observational study evaluating the frequency of delirium and associated risk factors for its development in children after cardiac surgery. The study included 194 children age 1 day to 21 years old, and delirium was measured using the Cornell Assessment of Pediatric Delirium (CAPD) tool. Patients were categorized as never having delirium or having greater than 24 hours of delirium. Forty-nine percent of subjects experienced delirium, defined by a score greater than or equal to 9 on the CAPD tool in developmentally normal children or by a score

TABLE 1. Index of Included References

S. No.	Article Title, Authors	Journal	Year	Type of Study
1	Tight glycemic control in critically ill children; Agus et al (2)	*New England Journal of Medicine*	2017	Prospective multicenter RCT
2	Function of the left and right ventricles and the interactions between them; Penny et al (3)	*Pediatric Critical Care Medicine*	2016	Review: Medline and PubMed
3	Percutaneous left atrial decompression in patients supported with extracorporeal membrane oxygenation for cardiac disease; Eastaugh et al (4)	*Pediatric Critical Care Medicine*	2015	Single-center retrospective chart review
4	Association of extracorporeal membrane oxygenation support adequacy and residual lesions with outcomes in neonates supported after cardiac surgery; Howard et al (5)	*Pediatric Critical Care Medicine*	2016	Single-center retrospective chart review
5	Extracorporeal cardiopulmonary resuscitation (E-CPR) during pediatric in-hospital cardiopulmonary arrest is associated with improved survival to discharge: A report from the American Heart Association's Get With The Guidelines-Resuscitation (GWTG-R) registry; Lasa et al (6)	*Circulation*	2016	Retrospective registry study
6	Therapeutic hypothermia after in-hospital cardiac arrest in children; Moler et al (7)	*New England Journal of Medicine*	2017	Prospective multicenter RCT
7	Predictors of early extubation after pediatric cardiac surgery: A single-center prospective observational study; Odek et al (8)	*Pediatric Cardiology*	2016	Single-center prospective observational study
8	Duration of mechanical ventilation and perioperative care quality after neonatal cardiac operations; Blinder et al (9)	*Annals of Thoracic Surgery*	2017	Single-center retrospective chart review
9	Subclinical seizures identified by postoperative electroencephalographic monitoring are common after neonatal cardiac surgery; Naim et al (10)	*Journal of Thoracic and Cardiovascular Surgery*	2015	Quality improvement study
10	Delirium in children after cardiac bypass surgery; Patel et al (11)	*Pediatric Critical Care Medicine*	2017	Single-center prospective observational study
11	Association of digoxin with interstage mortality: Results from the pediatric heart network single ventricle reconstruction trial public use dataset; Oster et al (12)	*Journal of the American Heart Association*	2016	Multicenter retrospective database study
12	Vasopressin after the fontan operation; Kumar et al (13)	*World Journal for Pediatric and Congenital Heart Surgery*	2016	Single-center retrospective chart review
13	Reduced pleural drainage, length of stay, and readmissions using a modified Fontan management protocol; Pike et al (14)	*Journal of Thoracic and Cardiovascular Surgery*	2015	Single-center retrospective chart review
14	Risk factors for longer hospital stay following the fontan operation; Sasaki et al (15)	*Pediatric Critical Care Medicine*	2016	Single-center retrospective chart review
15	Central venous to arterial Co_2 difference after cardiac surgery in infants and neonates; Rhodes et al (16)	*Pediatric Critical Care Medicine*	2017	Single-center retrospective chart review
16	Perioperative near-infrared spectroscopy monitoring in neonates with congenital heart disease: Relationship of cerebral tissue oxygenation index variability with neurodevelopmental outcome; Spaeder et al (17)	*Pediatric Critical Care Medicine*	2017	Single-center retrospective chart review

(*Continued*)

TABLE 1. (*Continued*). Index of Included References

S. No.	Article Title, Authors	Journal	Year	Type of Study
17	Postoperative cerebral and somatic near-infrared spectroscopy saturations and outcome in hypoplastic left heart syndrome; Hoffman et al (18)	*Annals of Thoracic Surgery*	2017	Single-center retrospective chart review
18	Efficacy and safety of sedation with dexmedetomidine in critical care patients: A meta-analysis of randomized controlled trials; Constantin et al (19)	*Anesthesia, Critical Care and Pain Medicine*	2016	Meta-analysis of RCT (PubMed and Cochrane database)
19	Early versus late parenteral nutrition in critically ill children; Fivez et al (20)	*New England Journal of Medicine*	2016	Prospective multicenter RCT
20	Peritoneal dialysis vs furosemide for prevention of fluid overload in infants after cardiac surgery: A randomized clinical trial, Kwiatkowski et al (21)	*JAMA Pediatrics*	2017	Single-center RCT
21	Fluid overload is associated with higher mortality and morbidity in pediatric patients undergoing cardiac surgery; Lex et al (22)	*Pediatric Critical Care Medicine*	2016	Single-center retrospective chart review
22	Vasoactive-ventilation-renal score reliably predicts hospital length of stay after surgery for congenital heart disease; Scherer et al (23)	*Journal of Thoracic and Cardiovascular Surgery*	2016	Single-center prospective observational study
23	Establishment of pediatric cardiac intensive care advanced practice provider services; Gilliland et al (24)	*World Journal for Pediatric and Congenital Heart Surgery*	2016	Review
24	The effect of critical care nursing and organizational characteristics on pediatric cardiac surgery mortality in the United States; Hickey et al (25)	*Nursing administration*	2014	Multicenter retrospective database study
25	Utilizing the PCICS nursing guidelines in managing the CICU patient; Justice et al (26)	*World Journal for Pediatric and Congenital Heart Surgery*	2015	Quality improvement Review
26	Nurse decision making regarding the use of analgesics and sedatives in the pediatric cardiac ICU; Staveski et al (27)	*Pediatric Critical Care Medicine*	2014	Multicenter prospective nonexperimental mixed methods study
27	A developmental care framework for a cardiac ICU: A paradigm shift; Torowicz et al (28)	*Advances in Neonatal Care*	2012	Quality improvement Review
28	Survival and surgical interventions for children with trisomy 13 and 18; Nelson et al (29)	*JAMA*	2016	Multicenter retrospective database study
29	Outcomes and predictors of perinatal mortality in fetuses with ebstein anomaly or tricuspid valve dysplasia in the current era: A multicenter study; Freud et al (30)	*Circulation*	2015	Multicenter retrospective chart review
30	Parental perspectives on suffering and quality of life at end-of-life in children with advanced heart disease; Blume et al (31)	*Pediatric Critical Care Medicine*	2014	Cross-sectional multicenter survey study
31	Bleeding and thrombosis in pediatric cardiac intensive care; Giglia et al (32)	*Pediatric Critical Care Medicine*	2016	Review: Medline and PubMed

JAMA = *Journal of the American Medical Association*, RCT = randomized controlled trial.

greater than or equal to 9 with a change from baseline as determined by the practitioner in developmentally delayed patients. Delirium most often developed within the first 3 days after surgery. Age less than 2 years, developmental delay, higher surgical complexity score, cyanotic heart disease, and a serum albumin level of less than 3 mg/dL were independently associated with delirium in a multivariate model. The presence of delirium was also an independent predictor of longer postoperative hospitalization, with each day of delirium increasing the LOS by 1.6 days.

Single Ventricle Palliation: Pre-, Peri- and Postoperative Management and Outcomes

Oster ME, Kelleman M, McCracken C, et al: Association of digoxin with interstage mortality: Results from the pediatric heart network single ventricle reconstruction trial public use dataset. *J Am Heart Assoc* 2016; 5 (12)

Early mortality after stage 1 Norwood procedure remains high (7–19%), and interstage mortality among those discharged home before stage II palliation (bidirectional Glenn) is 2–12%. The authors conducted a multicenter retrospective study using data from the Pediatric Heart Network Single Ventricle Reconstruction Trial. The primary objective was to evaluate the association of outpatient digoxin use and interstage mortality in infants with single ventricle congenital heart disease. In this study, interstage mortality was defined as death before stage II palliation. Of the 330 eligible patients, 102 (31%) were discharged on digoxin. Interstage mortality for those not on digoxin was 12.3%, compared with 2.9% among those treated with digoxin, with an adjusted hazard ratio of 3.5. The number needed to treat to prevent one death was 11 patients.

Kumar TK, Kashyap P, Figueroa M, et al: Vasopressin after the fontan operation. *World J Pediatr Congenit Heart Surg* 2016; 7:43–48 (13)

The authors conducted a single-center retrospective chart review to assess associations between the use of postoperative vasopressin infusions and volume and duration of chest tube drainage. They also sought to assess for association between vasopressin administration and early postoperative fluid balance and hospital LOS. Sixty-two patients (between January 2004 and June 2014) underwent an extracardiac nonfenestrated Fontan procedure and were included in the analysis. A peritoneal catheter was placed for passive drainage in high-risk patients (Fontan pressure > 16 mm Hg). The primary endpoints were volume of pleural fluid and duration of drainage, measured in days. The authors found that the vasopressin group had significantly lower chest tube output, a shorter duration of chest tube days, and shorter hospital LOS compared with the nonvasopressin group. They also achieved a greater negative early postoperative fluid balance.

Pike NA, Okuhara CA, Toyama J, et al: Reduced pleural drainage, length of stay, and readmissions using a modified Fontan management protocol. *J Thorac Cardiovasc Surg* 2015; 150:481–487 (14)

In this single-center retrospective study of patients undergoing the Fontan operation, the authors compared chest tube drainage and LOS after implementing a postoperative Fontan management protocol ($n = 60$) to historical controls ($n = 60$). The protocol included initiation of furosemide on postoperative day 1, use of captopril, hydrochlorothiazide and aldactone, restriction of fluids to 80% maintenance, 0.5 L nasal cannula oxygen until chest tube removal and a low-fat diet (30% of daily calories from fat) for 6 weeks, and systemic anticoagulation with warfarin. There were no significant differences in baseline, operative, and postoperative characteristics between the two patient groups. However, those who underwent Fontan after implementation of a management protocol had a reduced number of chest tube days, with only 12% ($n = 7$) having a chest tube for greater than 7 days compared with 38% ($n = 23$) in the preimplementation group. The quantity of pleural fluid and hospital LOS were also reduced in the postimplementation group. Although not statistically significant, the use of the Fontan protocol showed a total cost savings of 22% and 29% for hospital LOS and readmission, respectively.

Sasaki J, Dykes JC, Sosa LJ, et al: Risk factors for longer hospital stay following the fontan operation. *Pediatr Crit Care Med* 2016; 17:411–419 (15)

The purpose of this single-center retrospective study was to evaluate the pre- and intraoperative risk factors for longer hospital stay and describe the perioperative course in 218 patients following the Fontan operation over a 15-year time period. In this study, prolonged LOS was defined as greater than 75th percentile of the institution after cardiac surgery, which was 15 days. Independent pre- and intraoperative risk factors for prolonged LOS included higher hemoglobin, higher mean pulmonary artery pressure, and lower aortic saturation. When patients with hepatic vein inclusion were excluded, higher hemoglobin, lower aortic saturation, and the presence of a fenestration were associated with a longer LOS.

Invasive and Noninvasive Monitoring

Rhodes LA, Erwin WC, Borasino S, et al: Central venous to arterial Co2 difference after cardiac surgery in infants and neonates. *Pediatr Crit Care Med* 2017; 18:228–233 (16)

Venous to arterial Co_2 partial pressure difference ($AVco_2$) measures circulatory clearance of tissue Co_2 and is correlated with cardiac output in critically ill adults. A widening $AVco_2$ represents the imbalances between cardiac output and Co_2 production. The purpose of this single-center retrospective study in infants after cardiac surgery was to determine if $AVco_2$ is associated with low cardiac output syndrome after surgery via correlation with traditional bedside surrogates (lactate, arterial-venous oxygen difference [AVo_2], and mixed venous saturation [Svo_2]). There were 139 infants enrolled between October 2012 and May 2015. There were 296 arterial and venous blood gas pairs at 6, 12, and 24 hours after cardiac surgery. In this study, $AVco_2$ was moderately correlated with AVo_2 and Svo_2, but not lactate. A poor outcome (defined as a composite of inotrope score > 15, death, cardiac arrest, ECMO, or unplanned surgical reintervention) occurred in 34 of 139 patients, and in this group, the admission $AVco_2$ was significantly higher (8.3 vs 5.4 mm Hg) (area under the curve = 0.69). In a multivariable analysis, surgical complexity, admission $AVco_2$, and open chest status were predictions of poor outcome (odds ration [OR] = 1.3) and mortality (OR, 1.2).

Spaeder MC, Klugman D, Skurow-Todd K, et al: Perioperative near-infrared spectroscopy monitoring in neonates with congenital heart disease: Relationship of cerebral tissue oxygenation index variability with neurodevelopmental outcome. *Pediatr Crit Care Med* 2017; 18:213–218 (17)

The authors developed a new measure of cerbral tissue oxygenation index variability using the root mean of successive squared differences of averaged 1-minute cerebral tissue oxygenation index values for both intraoperative and the first 24 postoperative hours. The investigators conducted a single-center retrospective cohort study to determine if lack of variability in this novel index was associated with abnormal neurodevelopmental outcomes. Of the 62 patients who had cerebral near-infrared spectroscopy (NIRS) monitoring, 44 underwent subsequent neurodevelopmental testing at 6, 15, and 21 months old. Patients with abnormal neurodevelopmental testing had lower postoperative cerebral tissue oxygenation index variability when compared with patients with normal neurodevelopmental testing. After adjusting for class of congenital heart disease and duration of DHCA, lower postoperative cerebral tissue oxygenation index variability was associated with poor neurodevelopmental outcome. Reduced cerebral tissue oxygenation variability may be a surrogate for impaired cerebral metabolic autoregulation.

Hoffman GM, Ghanayem NS, Scott JP, et al: Postoperative cerebral and somatic near-infrared spectroscopy saturations and outcome in hypoplastic left heart syndrome. *Ann Thorac Surg* 2017; 103:1527–1535 (18)

In this single-center retrospective chart review, data from an existing registry of 48-hour hemodynamic measures after stage 1 palliation of neonates with hypoplastic left heart syndrome were analyzed to test the hypothesis that NIRS-derived cerebral and somatic/renal regional saturations can predict survival. Complete data for comparative analysis of physiologic predictors were available from 194 patients. The authors conclude that the use of cerebral and somatic NIRS monitoring in the first 6 postoperative hours can predict outcomes of early mortality and ECMO use. The predictive power of oximetric data from two-site NIRS was superior to that from $\mathrm{Svo_2}$ (18). Because outcomes were strongly determined by NIRS measures at 6 hours, early postoperative NIRS measures should be considered rational targets for goal-directed interventions.

Nutrition and Pharmacotherapy

Constantin JM, Momon A, Mantz J, et al: Efficacy and safety of sedation with dexmedetomidine in critical care patients: A meta-analysis of randomized controlled trials. *Anaesth Crit Care Pain Med* 2016; 35:7–15 (19)

This meta-analysis of original studies identified in a search of the PubMed and Cochrane databases was conducted to evaluate the association between dexmedetomidine use with efficacy and safety outcomes. Included were 1,994 patients from 16 randomized controlled trials comparing dexmedetomidine with other sedative agents in nonpostcardiac surgery critically ill adult patients. Comparators were lorazepam, midazolam, and propofol (19). Dexmedetomidine use was associated with a reduction in ICU LOS, mechanical ventilation duration, and delirium frequency. Dexmedetomidine use was also associated with an increase in bradycardia and hypotension (19).

Fivez T, Kerklaan D, Mesotten D, et al: Early versus late parenteral nutrition in critically ill children. *N Engl J Med* 2016; 374:1111–1122 (20)

A multicenter, randomized, controlled trial involving 1,440 critically ill children was conducted to investigate whether withholding parenteral nutrition for 1 week (i.e., providing late parenteral nutrition) in the PICU is clinically superior to providing early parenteral nutrition. Late parenteral nutrition resulted in fewer new infections and a shorter duration of dependency on intensive care. In addition, late parenteral nutrition was associated with a shorter duration of mechanical ventilatory support than was early parenteral nutrition as well as a smaller proportion of patients receiving renal replacement therapy.

Fluid Overload and Acute Kidney Injury

Kwiatkowski DM, Goldstein SL, Cooper DS, et al: Peritoneal dialysis vs furosemide for prevention of fluid overload in infants after cardiac surgery: A randomized clinical trial. *JAMA Pediatr* 2017; 171:357–364 (21)

The authors conducted a single-center randomized control trial in which infants were randomized to receive furosemide or peritoneal dialysis for the presence of postoperative oliguria, defined as 4 total hours of less than 1 milliliter per kilogram of urine output during the first 24 hours. The dialysis prescription was standardized for patients in that group, and patients in the furosemide group received 1 milligram per kilogram every 6 hours for two doses, with subsequent dosing at physician discretion. Seventy-three patients were included in the final analysis. There was no significant difference in the proportion of patients who obtained a negative fluid balance on postoperative day 1, but patients randomized to furosemide were three times more likely to develop 10% fluid overload. The furosemide group also had a three times greater odds of prolonged mechanical ventilation (defined as ventilation for > 3 d), a longer duration of inotrope use, and a higher need for electrolyte replacements.

Lex DJ, Tóth R, Czobor NR, et al: Fluid overload is associated with higher mortality and morbidity in pediatric patients undergoing cardiac surgery. *Pediatr Crit Care Med* 2016; 17:307–314 (22)

This study was a single-center retrospective chart review from January 2004 to December 2008. The primary aim was to investigate the relationship between fluid overload adverse outcomes in a large heterogeneous cohort of pediatric patients undergoing cardiac surgery. Included in the analysis were 1,520 patients, of which 6% died, 25% had postoperative low cardiac output syndrome, and 7% received renal replacement therapy. The vast majority (90%) had cumulative fluid overload of less than 5%, whereas 8% developed fluid overload between 5 and 10%, and 2% had fluid overload greater than 10%. Nonsurvivors had a higher percent fluid overload on the day of surgery and postoperative day 1. In a multivariable analysis, fluid overload on the day of surgery was independently associated with mortality (OR, 1.14) and low cardiac output syndrome (OR, 1.2).

Scherer B, Moser EA, Brown JW, et al: Vasoactive-ventilation-renal score reliably predicts hospital length of stay after surgery for congenital heart disease. *J Thorac Cardiovasc Surg* 2016; 152:1423–1429.e1 (23)

Previously, the Vasoactive-Ventilation-Renal (VVR) score calculated at 48 hours after cardiac surgery was shown to be a robust predictor of short-term clinical outcomes, outperforming the vasoactive inotrope score and serum lactate levels. The authors performed a prospective observational study to further validate the findings of the VVR score from January to June of 2015. The primary outcome was LOS defined by the upper 25% of all cardiac surgery admissions. The VVR score for predicting LOS greater than 17.5 days was greatest at 12 hours after cardiac surgery, with an area under the curve of 0.93. In a multivariable regression analysis, adjusting for confounding variables (nitric oxide, noncardiac anatomic abnormalities), the VVR remained a predictor of LOS (OR, 1.15; 95% CI, 1.1–1.2).

Pediatric Cardiac Intensive Care Nursing and Advanced Practice Providers

Gilliland J, Donnellan A, Justice L, et al: Establishment of pediatric cardiac intensive care advanced practice provider services. *World J Pediatr Congenit Heart Surg* 2016; 7:72–80 (24)

This review article describes mechanisms for developing, implementing, and sustaining advance practice nursing services in pediatric cardiac ICUs (PCICUs). Key aspects include 1) PCICU advanced practice provider (APP) role definition, 2) description of differences between acute care pediatric nurse practitioners and physician assistants, 3) development of a proposal to gain institutional support for a PCICU APP service, 4) key cardiac center leadership roles, 5) description of critical elements of PCICU APP services, and 6) implementation strategies for a sustainable PCICU APP service.

Hickey PA, Gauvreau K, Curley MA, et al: The effect of critical care nursing and organizational characteristics on pediatric cardiac surgery mortality in the United States. *J Nurs Adm* 2014; 44(10 Suppl):S19–S26 (25)

This multicenter retrospective database study explored pediatric critical care nursing and organizational factors that impact in-hospital mortality for cardiac surgery patients across children's hospitals in the United States. Nursing leaders from 38 children's hospitals that contribute data to the Pediatric Health Information System dataset completed an organizational assessment for years 2009 and 2010. These data were linked with patient-level data. These data are the first to link clinical nursing experience with pediatric patient outcomes. A cut point of 20% registered nurses or greater with 2 years clinical experience or less was significantly associated with higher risk–adjusted inpatient mortality (25).

Justice L, Ellis M, St George-Hyslop C, et al: Utilizing the PCICS nursing guidelines in managing the CICU patient. *World J Pediatr Congenit Heart Surg* 2015; 6:604–615 (26)

This quality improvement review describes the PCICS Nursing Guidelines developed to provide an evidence-based resource for bedside cardiac ICU nursing care. Guideline topics include postoperative care, hemodynamic monitoring, arrhythmia management, and nutrition. Utilization of these guidelines in practice is illustrated for single ventricle stage 1 palliation, Fontan operation, and repair of truncus arteriosus and atrioventricular septal defect.

Staveski SL, Lincoln PA, Fineman LD, et al: Nurse decision making regarding the use of analgesics and sedatives in the pediatric cardiac ICU. *Pediatr Crit Care Med* 2014; 15:691–697 (27)

This prospective nonexperimental mixed methods study of PCICU nursing practice was conducted in three tertiary academic pediatric heart centers in the United States to describe nurse decision-making and patient responses associated with the administration of analgesics and sedatives in the PCICU. Nurses identified 28 symptoms managed with analgesia and sedation. The most frequent symptoms included hypertension, tachycardia, crying, pain, and agitation. Nurses identified 20 patient changes that resulted from their interventions. The most prevalent changes included improved hemodynamics, calm state, sleep, comfort, and relaxed state. PCICU nurses use many nonspecific indicators to describe patient level of comfort collectively. Decisions for managing patient comfort were influenced by their patients' overall hemodynamic stability.

Torowicz D, Lisanti AJ, Rim JS, et al: A developmental care framework for a cardiac intensive care unit: A paradigm shift. *Adv Neonatal Care* 2012; 12(Suppl 5):S28–S32 (28)

The purpose of this quality improvement review article was to review the process of implementing a development model of care in a cardiac ICU. Five core measures to support evidence-based developmental care practices 1) sleep, pain, and stress assessment; 2) management of daily living; 3) positioning, feeding, and skin care; 4) family-centered care; and 5) a healing environment are described. The authors implemented these measures following neonatal cardiac surgery in a PCICU.

Quality of Life and Outcomes

Nelson KE, Rosella LC, Mahant S, et al: Survival and surgical interventions for children with trisomy 13 and 18. *JAMA* 2016; 316:420–428 (29)

Surgical interventions remain controversial in patients with trisomy 13 and 18. The authors conducted a multicenter retrospective study to describe survival and surgical procedures over a 22-year period (1991–2012) among children in Ontario, Canada, using multiple health administrative and demographic data sources in the single payer healthcare system. Survival was calculated using the Ontario vital statistics death file. During the study period, data were available for 174 children with trisomy 13 and 254 children with trisomy 18. The median survival times were 12.5 days (interquartile range [IQR], 2–195 d) for trisomy 13, and 9 days (IQR, 2–92 d) for trisomy 18. The mean 1-year survival was 19.8% for trisomy 13, and 12.6% for trisomy 18. Among children who underwent surgical interventions, 1-year survival was higher. For trisomy 13 patients, mosaic or translocation type was associated with longer term survival. For trisomy 18, higher birth weight and mosaic or translocation type were associated with longer term survival. Patients with trisomy 18 also had more neurologic diagnoses and admissions during the first year of life. Having a cardiac or neurologic deficit was not associated with a shorter survival. In the entire cohort, a majority of children who survived 6 months lived 10 years or longer. Survival from surgery likely reflects careful patient selection and procedural benefit.

Freud LR, Escobar-Diaz MC, Kalish BT, et al: Outcomes and predictors of perinatal mortality in fetuses with ebstein anomaly or tricuspid valve dysplasia in the current era: A multicenter study. *Circulation* 2015; 132:481–489 (30)

In this multicenter retrospective study, the outcomes and factors associated with mortality after fetal diagnosis of Ebstein anomaly and tricuspid valve dysplasia in 243 patients encountered from 2005 to 2011 were examined. The primary outcome was perinatal mortality, defined as fetal demise or death before neonatal discharge. Overall perinatal mortality was 45%. Independent predictors of mortality at the time of diagnosis were gestational age less than 32 weeks, larger tricuspid valve annulus diameter *z* score, pulmonary regurgitation, and a pericardial effusion. Nonsurvivors were more likely to have pulmonary regurgitation at any gestational age.

Blume ED, Balkin EM, Aiyagari R, et al: Parental perspectives on suffering and quality of life at end-of-life in children with advanced heart disease: An exploratory study*. *Pediatr Crit Care Med* 2014; 15:336–342 (31)

This cross-sectional multicenter survey study from two tertiary care pediatric hospitals describes parent perspectives regarding the end-of-life experience of children with advanced heart disease. Parents of children younger than 21 years old with primary cardiac diagnoses who died in the hospital 9 months to 4 years before the survey date were surveyed by mail ($n = 50$; 39% response rate). According to their parents, many children with advanced heart disease experienced suffering in the end-of-life care period. The symptoms parents perceived to be causing the most suffering were breathing and feeding difficulties in children under 2 years and fatigue and sleeping difficulties in older children. For most parents, realization that their child has no realistic chance of survival does not occur until late and in some cases not until death is imminent. Once this realization occurs, however, parents perceive peacefulness, a "good death," and excellent quality of care.

Bleeding and Thrombosis

Giglia TM, Witmer C: Bleeding and thrombosis in pediatric cardiac intensive care. *Pediatr Crit Care Med* 2016;17(8 Suppl 1):S287–S295 (32)

Using studies identified in MEDLINE and PubMed, the authors reviewed the particular tendencies as well as specific concerns of bleeding and clotting secondary to intrinsic as well as extrinsic factors in children with critical cardiac disease. Therapies for thrombosis prevention and treatment in the cardiac ICU are discussed.

DISCUSSION

Several notable features of this 2017 update of useful references in pediatric cardiac intensive care warrant specific comment. For several clinical issues, understanding within the field has evolved substantially since the 2012 update. For example, one study included in the 2012 update reported strong, risk-adjusted associations between elevated glucose levels and adverse outcomes after pediatric cardiac surgery (33). However, recently conducted multicenter randomized clinical trials in critically ill children, including those recovering from cardiac surgery and cardiac medical patients found no benefit of tight glycemic control on important clinical outcomes (2, 34). Another study included in the 2012 update was a randomized, multicenter clinical trial which found that the administration of an empiric milrinone infusion was effective for decreasing the frequency of low cardiac output syndrome following complex two ventricular repairs (35). Milrinone use subsequently became common following such operations as well as the Fontan procedure. However, a recent randomized trial in children undergoing the Fontan operation concluded that empiric milrinone was no more efficacious than placebo when early outcomes were assessed (36). Furthermore, a recent retrospective single-center study included in the 2017 update suggested that empiric vasopressin infusion may be more appropriate, perhaps due in part to its vasoconstrictor effect on the precapillary resistance vessels thus decreasing the capillary hydrostatic pressure (13). A prospective trial would shed further light on the potential role of empiric vasopressin infusions after Fontan surgery.

Both updates contain a sizable number of articles about mechanical circulatory support (4–6, 37–46). Challenges in adequately and safely supporting small children and those with complex congenital heart disease persist and should be the focus of future investigations. Another issue that was featured in both updates is the inflammatory response and fluid overload that is associated with cardiopulmonary bypass (21, 22, 47–51). Ongoing clinical multicenter clinical trials should provide high-quality evidence regarding the use of corticosteroids for neonates undergoing cardiac operations that require cardiopulmonary bypass (NCT01579513 and NCT03229538).

Research studies focusing on acute brain injury and neurodevelopmental outcomes were highlighted in both updates (7, 10, 17, 28, 38, 52–60). Although the neurodevelopmental phenotype of children with complex congenital heart disease has been well characterized, clinicians are still awaiting proven strategies to improve outcomes for at risk patients.

Investigations focusing on thrombotic complications and bleeding (32, 61–63) continue to be published. More research is needed to identify best practices to safely prevent thromboembolic events in critically ill pediatric cardiac patients.

In the 2017 update, five references were included that focused on the practice of bedside and advanced practice nurses (24–28), whereas no such studies were included in the 2012 update. This shift likely reflects the growth in nursing members of the PCICS as well as growing focus on the multidisciplinary teams that are essential to achieve optimal outcomes in pediatric cardiac intensive care.

Of note, both the 2012 and 2017 updates suggest that investigators continue to use many different types of study designs to address important questions relevant to pediatric cardiac intensive care. In the 2012 update, the most common study design was a single-center retrospective chart review (47%), followed by single-center prospective study (19%), single-center randomized clinical trial (12%), review article (7%), analysis of administrative or clinical registry data (6%), multicenter randomized clinical trial (3%), multicenter retrospective study (2%), meta-analysis (2%), and translational study (2%). In this 2017 update, once again the most common study design was a single-center retrospective chart review (42%). Other designs included review article (16%), analysis of administrative or clinical registry data (10%), multicenter randomized clinical trial (10%), multicenter retrospective study (6%), multicenter prospective nonrandomized trial (6%), and single-center prospective study, meta-analysis, and single-center randomized clinical trial (3% for each type). Although the above percentiles only reflect articles included in the two updates, these data present a general profile of the types of study designs being used to address the most pressing issues in our field. In addition, the rare frequency and heterogeneity of congenital heart disease make designing prospective trials challenging.

One of the potential limitations of this article is that there may be associated bias in the references provided by members, and thus, other important references may not have been included in this summary. Importantly, no list of references is inclusive, and the reader should use this and previously published versions (1) as a foundation to expand knowledge.

CONCLUSIONS

This article contains a compilation of references for the critical care of children with congenital and acquired heart disease that have been published in the last 5 years and judged to be important by members of the PCICS and its Research Briefs Committee. In conjunction with the 2012 update (1), this article may be used as a reference for education in pediatric cardiac intensive care.

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