Right ventricular dysfunction in children supported with pulsatile ventricular assist devices

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Objectives: To describe the incidence and severity of right ventricular dysfunction (RVD) in pediatric ventricular assist device (VAD) recipients and to identify the preoperative characteristics associated with RVD and their effect on outcomes.

Methods: Children bridged to transplantation from 2004 to 2011 were included. RVD was defined as the use of a left VAD (LVAD) with an elevated central venous pressure of >16 mm Hg with inotropic therapy and/or inhaled nitric oxide for >96 hours or biventricular assist (BiVAD).

Results: A total of 57 children (median age, 2.97 years; range 35 days to 15.8 years) were supported. Of the 57, 43 (75%) had an LVAD, and of those, 10 developed RVD. The remaining 14 (25%) required BiVAD. Thus, RVD occurred in 24 of 57 patients (42%). Preoperative variables such as younger age ($P = .01$), use of extracorporeal mechanical support ($P = .006$), and elevated urea ($P = .03$), creatinine ($P = .02$), and bilirubin ($P = .001$) were associated with RVD. Multiple logistic regression analysis indicated that elevated urea and extracorporeal mechanical support (odds ratio, 26.4; 95% confidence interval, 2.3-307.3; and odds ratio, 27.8; 95% confidence interval, 2.5-312.3, respectively) were risk factors for BiVAD. The patients who developed RVD on LVAD had a complicated postoperative course but excellent survival (100%), comparable to those with preserved right ventricular function (91%). The survival for those requiring BiVAD was reduced (71%).

Conclusions: RVD occurred in approximately 40% of pediatric VAD recipients and affects their peri-implantation morbidity and bridging outcomes. Preoperative extracorporeal membrane oxygenation and elevated urea were risk factors for BiVAD. Additional studies of the management of RVD in children after VAD implantation are warranted. (J Thorac Cardiovasc Surg 2014;147:1691-7)

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Mechanical bridging with ventricular assist devices (VADs) has recently become an effective treatment option for children awaiting heart transplantation. The Berlin Heart EXCOR Pediatric VAD (Berlin, Germany) has been used worldwide, and substantial experience is now available, with the indications, complications, and outcomes of EXCOR use in children.[1-3]

An important question that has not been addressed in children is the right ventricular (RV) response to implantation of a left ventricular assist device (LVAD) and how to distinguish those patients who will require biventricular assist device (BiVAD).

In adults, considerable research has been done on RV dysfunction (RVD) after LVAD implantation showing that RVD is 1 of the key determinants of the bridging outcome. Preoperative risk factors have been identified and used to assess the likelihood of RV compromise in adult VAD recipients.[4-8]

However, some of the identified risk factors for RVD in adults might not exist or be applicable to children. Moreover, several reports of VAD use in children have highlighted a reduction in the use of BiVAD over time; however, the criteria for mechanical RV support in children have varied among centers.[1,3,9]

The present study aimed to describe the incidence and severity of RVD in children bridged with the Berlin Heart EXCOR VAD; to identify the preoperative characteristics associated with RVD requiring a BiVAD; and to assess the effect RVD has on postoperative morbidity and outcomes.

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Abbreviations and Acronyms
BiVAD = biventricular assist device
DCM = dilated cardiomyopathy
ECMO = extracorporeal membrane oxygenation
LVAD = left ventricular assist device
OR = odds ratio
RRT = renal replacement therapy
RV = right ventricular
RVAD = right ventricular assist device
RVD = right ventricular dysfunction
VAD = ventricular assist device

METHODS

The present study was a retrospective, observational cohort study using the data from patients treated in 2 tertiary-care pediatric transplant centers from November 2004 to January 2011. All patients aged <16 years who were bridged to transplantation with the Berlin Heart EXCOR Pediatric VAD were identified at these centers from the databases. The databases included prospective information on the patient demographic data, VAD implantation details, and outcomes. Additional data for the study were gathered retrospectively (see the section ''Data Collection''). The respective institutional research ethics review boards of the 2 centers approved the study, and a waiver of informed consent was obtained.

VAD Management

All children were supported using a Berlin Heart EXCOR Pediatric VAD. The 2 study sites had a uniform approach to VAD implantation, with the expectation of LVAD only support in most cases. The pump size was chosen according to the Berlin Heart Company protocol, and the VAD rate was set to achieve a cardiac index of 2.4 to 2.8 L/min/m^2.[9] Left ventricular unloading, cannula placement, and RV function were assessed using intraoperative transesophageal echocardiography. When weaning off cardiopulmonary bypass, the circulating blood volume was optimized and the right ventricle was supported with inotropes, inhaled nitric oxide, and pacing, if necessary. The addition of a right VAD (RVAD) was reserved for patients who could not separate from cardiopulmonary bypass despite optimal medical right heart support. The strategy for treating children with a VAD, including anticoagulation, has been previously published.[10]

Data Collection

Preoperative and operative data. The preimplantation data included the patient demographic data, diagnosis, mechanical ventilation and intravenous inotropic support duration, extracorporeal membrane oxygenation (ECMO) period, highest central venous pressure within 24 hours before VAD implantation, and laboratory test results (hepatic and renal function, blood count, and coagulation status). The preimplantation transthoracic echocardiograms were also reviewed by a cardiologist who was unaware of the treatment group with attention to the following: right atrial and left atrial area, tricuspid regurgitation grade (0, none; 1, mild; 2, moderate; and 3, severe), tricuspid regurgitation velocity (an estimate of RV systolic pressure), tricuspid valve annulus size, RV end-diastolic dimension, and qualitative RV function (0, normal; 1, mild dysfunction; 2, moderate dysfunction; and 3, severe dysfunction). The operative data included the duration of cardiopulmonary bypass and transfusion of red blood cells and other blood products within the first 24 hours after implantation.

Outcomes

RV dysfunction. RVD was defined as LVAD with an elevated central venous pressure >16 mm Hg with inotropes (other than milrinone) and/or inhaled nitric oxide therapy >96 hours, or a need for BiVAD. Other conditions with similar clinical signs were excluded (eg, tamponade, pneumothorax, effusions, or ventricular arrhythmia).

According to the increasing severity of RVD, the patients were divided into the following categories: LVAD with no RVD (LVAD-only group), LVAD with medically managed RVD (LVAD-RVD group); and LVAD with RVD requiring an RVAD (BiVAD group).

Morbidity and mortality. Postoperative complications, such as bleeding, a requirement for mediastinal exploration or placement of a chest drain, and renal failure requiring renal replacement therapy (RRT) with peritoneal dialysis or hemofiltration, were recorded. The duration of postoperative mechanical ventilation after VAD implantation was recorded. In-hospital mortality was also recorded.

Statistical Analysis

Preoperative and operative variables and RVD. Continuous data are presented as the mean ± standard deviation for normally distributed data or the median and range otherwise. The categorical and ordinal data are presented as numbers and percentages. Comparisons between groups using continuous data were performed using analysis of variance for normally distributed data and the Kruskal-Wallis test otherwise. For comparisons using categorical or ordinal data, the χ^2 or Fisher exact test was performed. Assuming the 3 groups (LVAD-only, LVAD-RVD, and BiVAD) represented an ordered group (increasing levels of RVD), a nonparametric (Wilcoxon-type) test for trend was performed to assess the trends in continuous variables across the 3 ordered groups.

Risk factors for BiVAD. For the assessment of the risk factors for BiVAD, all patients treated with LVAD only were used as the reference group. Comparisons using continuous variables were performed using the Student's t test for normally distributed data or the Wilcoxon rank sum test otherwise. Comparisons using ordinal or categorical data were performed using the χ^2 or Fisher exact test. Variables identified as significantly associated with the need for BiVAD support were entered into a multiple logistic regression model to identify the independent risk factors for BiVAD implantation and calculation of the odds ratios (ORs) and their respective 95% confidence intervals.

Outcomes after RVD. Comparisons of the outcomes were performed for all 3 groups. Additionally, we sought to determine whether any difference was present in the outcomes in the LVAD-RVD group versus the LVAD group without RVD. Differences in the duration of postoperative ventilation and hospital length of stay were analyzed using a Kruskal-Wallis test or Wilcoxon rank sum test. Differences in the complication rates and in-hospital mortality were assessed using the χ^2 test or Fisher exact test.

Statistical analysis was performed using Stata, version 9.2 (StataCorp LP, College Station, Tex).

RESULTS

Baseline Demographics

A total of 57 children (28 males and 29 females) at a median age of 2.97 years (range, 35 days to 15.8 years) and median weight of 12.8 kg (range, 3.6-90) underwent VAD implantation during the study period. In all patients, the indication for VAD support was end-stage heart failure with the intention to bridge the patient to cardiac transplantation. Five patients with congenital heart disease (all with single ventricle physiology) who were bridged during the study period were excluded from the present study.

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