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Mesenchymal Stem Cell-Based Immunomodulation

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Letter

In many cases, medical management does allow stabilization of patients with HF. In some cases, HF progresses and VAD therapy is the only option for stabilization. Progressive respiratory (requiring non-invasive and invasive support) decompensation, liver dysfunction, kidney injury and feeding intolerance are commonly reported measures of congestion and/or inadequate cardiac output (CO) that may develop despite optimal medical management. End-organ dysfunction is common in pediatric VAD patients prior to implantation, with 45% of patients intubated (paracorporeal devices 75-85% of patients compared to intracorporeal devices 21%), 94% on inotropes, 64% requiring feeding tubes/TPN, 40% with hyperbilirubinemia and 30% having a glomerular filtration rate (GFR) < 60 mL • min−1 •1.73 m. These findings are notable given end-organ dysfunction is associated with poor outcomes among VAD patients and following transplantation and timely implantation can result in reversal of end-organ dysfunction and better outcomes.

Although pre-operative renal, hepatic, respiratory and nutritional failure have been associated with worse post-VAD outcomes, many patients have pre-operative end-organ dysfunction. This likely is due to late presentation, late diagnosis or delayed timing for implantation. Irreversible renal dysfunction has been considered a relative contraindication to VAD implantation in the past but identifying irreversible dysfunction remains a significant challenge. Current data is complicated by various definitions of renal dysfunction including: serum creatinine > 1.6 mg/dl for patients aged > 10 years, or creatinine > 1.0 mg/dl for patients aged ≤ 10 years, or by the estimated glomerular filtration rate (eGFR) using the Schwartz formula being < 90 ml/min/1.73 m In the 3rd Pedimacs report, the threshold was defined as <60 mL/min1/1.73 m^2 and found that 30% of patients had renal insufficiency with 5% found to have an eGFR <30 mL/min1/1.73 m^2 or requiring dialysis. Post-VAD outcomes have been shown to be worse if the patient has renal dysfunction prior to VAD implantation.

"Right heart failure" (RHF) in children after LVAD implant is difficult to quantify, but has been shown to have an incidence as high as 42%. Although right ventricular dysfunction is common, this can typically be managed medically as BiVAD is relatively uncommon in the pediatric VAD population. Many clinical and imaging parameters have been used to assess the right ventricular (RV) function prior to VAD, however none of the individual parameters have been a sole predictor of the need for RV support. Echocardiography may be used to qualitatively assess RV systolic function, and semi quantitative measures such as tricuspid annular plane systolic excursion (TAPSE) and RV fractional area change can be used for RV functional assessment; however, the value of any individual echocardiographic parameter in predicting RV failure and/or the need for BiVAD support is limited. Cardiac catheterization to measure CO, central venous pressure (CVP), and pulmonary capillary wedge pressure often occurs prior to VAD placement, but this is neither practical nor safe in all patients. Finally, assessment of cardiac rhythm is imperative. Sustained ventricular arrhythmias not controlled by pharmacologic measures may contribute to RHF and need for BiVAD support in the perioperative period. After establishing that a patient requires a VAD, an important subsequent step is determining the kind of support needed. This refers to the support of the systemic or LV alone (SVAD or LVAD) versus biventricular support (BiVAD). While support of the RV alone (RVAD) may also be considered, it is uncommon. Consideration of LVAD versus BiVAD support is relevant only to patients with biventricular circulations. For patients with single ventricle circulation, however, it is critical to recognize that adequate support of the circulation with a systemic VAD (SVAD) may result in suboptimal outcomes if the patient's circulatory derangement results wholly or in part from perturbations in the Fontan pathway. Children with HF are often underweight as a result of poor appetite, increased metabolic demands of the failing heart, neurohormonal activation from heart failure, and poor gastrointestinal perfusion. VAD support provides a window for optimization of nutritional status prior to HT. BMI less than the 5th percentile at the time of HT is an independent predictor of decreased graft survival, though that finding is not universal. Nutritional status stratified by the percentage of ideal body weight at listing or at HT in children aged < 2 years was associated with the increase in waitlist mortality, but not associated with post-transplant outcomes.

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