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## **Reviews:**

### **Introduction:**

It continues to be an exciting time for mechanical circulatory in the pediatric population. In this edition of "What's new in pediatric MCS", we review articles which highlight some of the unique challenges that are faced within the pediatric population, such as the complexities of pediatric palliative care and challenges of pushing the boundary on the type of devices and device selection in our smaller patients. In addition, the first analysis of PediMACS have been reported, offering us important insights into the current status of pediatric MCS and highlight areas for future improvements and necessary advances.

### Article Reviews

#### **Journal of Heart and Lung Transplantation**

- Rosenthal DN, Almond CS, Jaquiss RD, et al. Adverse events in children implanted with ventricular assist devices in the United States: Data from the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS). *The J Heart Lung Transplant* 2016; 35: 569-577

PediMACS is a national database of children less than 19 years of age which began collecting data in September 2012. The authors provide the first report on the adverse events reported in children with durable mechanical support from September 2012 to August 2014. All FDA approved devices were included and adverse event definitions are similar to INTERMACS and previously have been published.

The database captured 200 patients with a mean age 11 years and total follow up of 783 patient-months. Devices were evenly distributed between continuous (55%) and pulsatile (45%) flow devices. Overall actuarial 6-month survival was 81%. The most common adverse events were device malfunction, major bleeding, and neurologic dysfunction. Children supported with pulsatile devices had

For those on continuous flow devices, major bleeding occurred earlier, while all other adverse events appeared to be more evenly distributed. Interestingly, pericardial drainage and late device malfunction were reported more frequently to PediMACS; however, overall the authors highlight there were more similarities than differences

- Blume ED, Rosenthal DN, Rossano JW et al. Outcomes of children implanted with ventricular assist devices in the United States: First analysis of Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS). *J Heart Lung Transplant*. 2016 May; 35(5): 578-84
- Using the PediMACS database described above, Blume et al provide the first report of outcomes of children implanted with VADs in the United States. Overall 222 patients underwent durable VAD implants, which included 46% on a pulsatile device and 55% on a continuous-flow device. Underlying cardiac etiology included 73% cardiomyopathy and 18% congenital heart disease. Patient age at implant included 15% under 1 year of age, 19% age 1-5 years, 16% age 6 to 10 years, and 51% age

10 to 18 years. Type of support included 81% LVAD, 15% BiVAD support, 2% RVAD, and 3% total artificial heart.

Of the 200 patients receiving durable support, the overall 6-month survival was 81% and 1-year survival was 81%. At 6 months post-VAD, approximately 60% of all patients were transplanted. By one year, 75% of children with a VAD received a heart transplant. Overall 87% of pediatric patients on durable support had favorable survival (transplant, explant for recovery, or still alive) at 6 months. Continuous flow VAD patients had a 93% favorable survival outcome. Survival at 1 year was significantly lower for children who were INTERMACS Level 1 at the time of implant compared to those who were INTERMACS Level 2. Adverse events were common with the most frequent being infection, bleeding, device malfunction, and neurologic events.

- Rossano JW, Lorts A, VanderPluym CJ, et al. Outcomes of pediatric patients supported with continuous-flow ventricular assist devices: A report from the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS). *J Heart Lung Transplant*. 2016 May; 35(5): 585-90.

Continuous flow devices have become the mainstay of support in the adult population. In this article, Rossano et al use the PediMACS database to report the pediatric experience with continuous flow VADs. There were a total 109 patients (median age of 15 years; median weight 62 kg) with the majority having an underlying diagnosis of cardiomyopathy (82%). INTERMACs level at the time of implant was level 1 (20%), level 2 (61%) and level 3 to 7 (20%). Most patients received LVAD support (94%) for a median duration of 2.3 months.

Competing outcomes analysis at 6 months post-implant showed a favorable outcome in 92% of the patients with 61% transplanted, 31% alive with the device in place, and 8% with death before transplant. These results are favorable with the outcomes reported in adults with continuous flow devices, despite a high proportion of those implanted at INTERMACs level 1. Adverse events were also similar to those previously reported in adults. Neurologic events occurred in 10% of patients, with most events occurring within the first 3 months. Interestingly, more early psychiatric issues were seen within the pediatric population, perhaps highlighting the neuropsychiatric vulnerabilities of an adolescent population.

- Conway J, Al-Aklabi M, Granoski D, et al. Supporting pediatric patients with short-term continuous-flow devices. *J Heart Lung Transplant*. 2016 May; 35(5): 603-9.

There is growing interest in the use of short term continuous flow VADs within the pediatric population as they may offer the ability to evaluate for recovery and neurologic function while avoiding the time restraints of ECMO support. Devices such as the CentriMag, PediMag, and RotaFlow are devices which have been used in an array of cannulation strategies. However, there is little information regarding the outcomes and complications of such strategies. The authors describe the experience at Stollery Children's Hospital in Edmonton, Canada with 27 children (56% female, median age 1.7 years) with a total of STCF VAD runs. Patients were supported for a mean of 12 days, with the longest support duration of 75 days. After implant, a high proportion required the addition of an oxygenator (61%) or renal replacement therapy (64%).

With regards to outcome, 21% of patients were weaned for recovery, 9% were converted to ECMO, and 15% died while on the device or 1 month after decannulation. Adverse events included bleeding requiring reoperation (24%), neurologic events (18%), and culture-positive infection (15%). Hospital discharge was achieved in 67% of patients and at an average of 9.2 months follow up, 63% of patients had survived. Overall, the authors conclude STCF VADs are able to provide bridge pediatric patients to recovery, long-term support, or transplant with an acceptable complication rate. However, further research is needed in optimal management strategies for this higher risk patient population.

- Hollander SA, Axelrod DM, Bernstein D, et al. Compassionate deactivation of ventricular assist devices in pediatric patients. *The J Heart Lung Transplant* 2016; 35:564-567

Despite advances in the use of ventricular assist devices, the increasing organ demand and use of destination therapy will likely result in more children dying while on a device. While adult guidelines exist on the compassionate discontinuation of VAD support, there is a paucity of guidance for pediatric providers.

The authors highlight differing opinions by care providers citing a recent survey which found one-third of physicians view VAD support differently than other life sustaining measures, like mechanical ventilation dialysis, or inotropes. Furthermore, another study found that 17% of physicians refused to deactivate a VAD for ethical reasons. Given this, the authors implore pediatric heart failure and palliative care communities to come together to establish guidelines to clarify complex issues surrounding compassionate deactivation. They also suggest that a deactivation checklist should be developed to provide guidance for key points in the disease trajectory.

- Miera O, Kirk R, Buchholz H, et al. A multicenter study of HeartWare ventricular assist device in small children. *J Heart Lung Transplant*. 2016 May; 35(5): 679-81.

Continuous flow devices have become the mainstay of adult VAD therapy given the improved stroke free survival and device failure. In pediatrics, continuous flow devices have shown promising results in children with BSA >1 m<sup>2</sup>. Children who are less than 1 m<sup>2</sup> are currently supported by pulsatile paracorporeal devices, which have higher rates of thromboembolic events and do not afford children the opportunity to be discharged from the hospital. In this research correspondence, the authors describe the experience of a multicenter cohort of 13 children with a median age 8.1 years and a median BSA 0.8 m<sup>2</sup> (0.6 to 0.9 m<sup>2</sup>). The most common adverse events were bleeding, renal dysfunction, ventilator support for > 6 days, right ventricular failure, and pump thrombosis. The rate of pump thrombosis was slightly higher than that previously reported for adolescents and young adults, possibly related to a lack of anticoagulation guidance. The overall survival was 92.3% with nearly half making it to hospital discharge.

**Journal American College of Cardiology:**

- Rihal CS, Naidu SS, Givertz MM, Szeto WY, et al. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care: Endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention.

Percutaneous mechanical circulatory support with devices such as the intra-aortic balloon pump, Impella, and Tandem Heart can provide hemodynamic stability. This consensus statement provides a summary of the physiologic effects of these devices and their clinical uses. The authors highlight that percutaneous circulatory support for children is currently to ECMO, with the IABP being the only percutaneous device approved in the United States for short-term support in children. Future device development will need to accommodate small femoral vessel size to help expand percutaneous circulatory support within the pediatric population.

**JACC: Heart Failure**

- Farooqui KM, Saeed O, Zaida A, et al. 3D printing to guide ventricular assist device placement in adults with congenital heart disease and heart failure. *JACC Heart Fail*. 2016 Apr; 4(4): 301-11

Ventricular assist devices may be underutilized in adults with congenital heart disease due to anatomical variants. The authors highlight how 3D printing is able to help determine cannula positioning in patients with complex anatomies such as transposition of the great vessels following a Mustard or Senning repair and those with single ventricles who have undergone Fontan palliation.

### **Annals of Thoracic Surgery**

- Arnaoutakis GJ, Blitzer D, Fuller S, et al. Mechanical circulatory support as bridge to transplantation for the failing single ventricle. *Ann Thorac Surg*. 2016 Jul 14.

Many patients with functional single ventricles will go on to develop heart failure. Use of mechanical circulatory support within this population has been challenging given the complex anatomy. The authors describe a retrospective cohort of 5 patients (1 HeartWare, 1 SynCardia, 1 Thoratec paracorporeal VAD, and 2 Berlin Heart EXCOR). Cardiac diagnoses included pulmonary atresia with intact ventricular septum, tricuspid atresia, double-outlet right ventricle with unbalanced atrioventricular canal, and situs inversus with pulmonary atresia and left atrioventricular valve atresia. The median duration of support was 60 days (28-93 days), which was complicated by neurologic injury in 60% of patients and the need for renal replacement therapy in 20% of patients. Overall, 60% of patients went on to cardiac transplantation. While this report includes a small number of patients, it highlights the growing need and potential feasibility of MCS for patients with failing single ventricle physiologies.

- Wehman B, Stafford KA, Bittle GJ. Modern outcomes of mechanical circulatory support as a bridge to pediatric heart transplantation. *Ann Thorac Surg* 2016 Jun; 101(6): 2321-7

Due to organ scarcity, many patients with end stage heart failure will require use of mechanical circulatory support as a bridge to transplantation. In this article, the authors aim to describe the difference in post-transplant survival between children bridged with MCS to transplant versus children who proceeded directly to transplant. Using the UNOS database, the study identified 2,160 patients who went directly to transplant and 617 who required MCS as a bridge to transplant. Of those requiring MCS, 428 (69.4%) were on a VAD, 189 (30.6%) and were on ECMO. Not surprisingly, patients placed on ECMO were younger and weighed less. Actuarial survival was greater in the direct to transplant group compared to those bridged with ECMO, but were similar those bridged to transplant with a VAD at 30 days, 1, 3, and 5 years. Interestingly, the survival benefit seen in those who went directly to transplant or who were bridged with VAD support was lost after censoring for the first 4 months after transplant.

- Peng E, Kirk R, Wrightson N, et al. An extended role of continuous flow device in pediatric mechanical circulatory support. *Ann Thorac Surg* 2016. Aug; 102(2): 620-7.

In this study, the authors describe the single center experience with the implantation of the HeartWare HVAD in 12 patients. The median age was 7.1 years, with 4 patients between 3-5 years, 4 were 6-10 years, and 4 were 10-17 years. The median weight was 31.2 kg, but ranged from 13.5 kg to 100 kg. Most patients had a diagnosis of cardiomyopathy and were implanted at INTERMACs level 1. Seven patients received LVAD support and 5 received BiVAD support. The mean length of support was 150 days (range 16 to 638 days). There was no early (30 day) mortality. Sixty-seven percent went on to receive a transplant, 8.3% had recovery of function with HVAD explantation, and 17% remained on VAD support. While HVAD support in children has been previously reported, this series describes the feasibility of HVAD use in younger children (median age of 7 with 33% of patients aged 5 years or less).

### **Catheterization Cardiovascular Interventions**

- Webb MK, Wang J, Riegel MS, et al. Initial experience with the pediatric Impella device: A feasibility study in a porcine model. *Catheter Cardiovasc Interv* 2016 May 24.

In this article, the authors describe the feasibility of a modified device based on the current Impella 2.5 platform, which was created in hopes of providing minimally invasive circulatory support for children. A porcine model was used which has similar sized carotid arteries and left ventricles as children with BSA < 1 m<sup>2</sup> and weights between 10-20 kg. Successful implantation was achieved in 10 animals for a duration of 4 hours with no mitral or aortic artery injury.

### **Congenital Heart Disease**

- Acheampong B, Johnson JN, Stulak JM, et al. Postcardiotomy ECMO support after high-risk operations in adult congenital heart disease

Many surviving congenital heart disease patients require further operations related to their primary defects or for acquired cardiovascular disease, which can be associated with higher morbidity and mortality given the complex anatomy and multiple previous sternotomies. The authors describe a single institution experience of 2264 ACHD patients of whom 24 (1.1%) required ECMO support. Patient ages ranged from 22-75 years (mean 41 years) and included 58% males. Cardiac diagnosis included pulmonary atresia with intact ventricular septum, tetralogy of Fallot, Ebstein anomaly, cc-TGA, septal defects, and other. Mean systemic ventricular systolic function was 47% and a majority of the patients were NYHA class III/IV heart failure. ACHD patients on long-term VAD support or IABP alone were excluded.

Post-operatively, 42% of patients were placed on ECMO alone, while the remainder were attempted on an IABP which was subsequently followed by ECMO. Mean duration of support was 8.4 days (0.8-35.4 days). Common morbidities included coagulopathy (60%), renal failure (56%), and arrhythmia (48%). Overall, survival to hospital discharge was 46%, which is similar to previously reported by ELSO data for adults with cardiac disease.

### **Artificial Organs:**

- Wei X, Sanchez PG, Liu Y, et al. Extracorporeal respiratory support with a miniature integrated pediatric pump-lung device in an acute ovine respiratory failure model. *Artif Organs*. 2016. Apr 18

The authors describe the use of a newly developed miniature portable integrated pediatric pump-lung device in 6 adult sheep. After induction of respiratory failure with IV anesthesia and low minute ventilation, the PediPL device was able to reverse respiratory failure, with an O<sub>2</sub> transfer of 86.8 mL/min and CO<sub>2</sub> removal of 139.1 mL/min. The authors conclude that the PediPL has the potential to treat hypoxia and hypercarbia, while offering a compact size making it more portable and well suited for emergency situations.