Commentary

Mechanical circulatory support for the failing functional single ventricle

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The advent of surgical palliation for functional single ventricle (FSV) heart defects was an impressive feat for pediatric cardiovascular surgery and medicine just a few decades ago. Parents were given hope for what would have been uniformly fatal congenital heart disease, and today, substantial survival is expected by both families and care providers for neonates with many types of FSV defects. However, decades have since past and these very same patients who were successfully palliated are now facing despair themselves as they encounter significant cardiovascular issues. These issues can be classified as Fontan failure (as evidenced by protein losing enteropathy and plastic bronchitis) and contractile failure (systolic or diastolic) of their single ventricle.

Heart transplantation is accepted as the definitive therapy for failing FSV patients and can be speculated to be the "fourth stage" of FSV palliation (1). Needless to say, heart transplantation is a very scarce resource with far too few donor organs available to meet the need of all FSV and non FSV patients. FSV patients may have high levels of preexisting panel reactive antibodies (PRA), and these antibodies further shrink the eligible donor pool thereby increasing the waitlist time. Furthermore the enthusiasm for transplanting failing adult FSV patients is decreased among adult and pediatric heart transplant surgeons because of the increased risk, as compared to the standard risk adult heart transplant waitlist patient.

As a consequence, the use of mechanical circulatory support (MCS) for failing FSV patients as a bridge to heart transplantation is being explored. A recently published report by Arnaoutakis and colleagues reviews the Children's Hospital of Philadelphia MCS experience in failing FSV patients. In this small case series, they report the use of four different types of MCS devices (HeartWare HVAD, Thoratec Paracorporeal ventricular assist device, Berlin Heart Excor ventricular assist device and Syncardia Total Artificial Heart) in 5 failing FSV patients (1 bidirectional Glenn and 4 Fontan patients) as a bridge to heart transplantation from January 2006 to December 2014. The reasons for FSV circulatory failure were not defined in this report, but appeared to be the result of ventricular dysfunction. The average age at the time of MCS was 12±8 years. The median duration of MCS support was 59 days. Although two patients suffered early deaths, the three patients that survived to heart transplantation were ambulatory with normal end-organ function at the time of transplantation. These three patients were still alive at an average follow-up of 9±14 months. Two patients suffered stroke and one suffered a subdural hemorrhage. All patients had an infectious complication (not defined) and one required dialysis. Of the three patients that underwent heart transplantation, two of them had the presence of PRA. One of these patients had a negative crossmatch while the other (with 91% class I PRA and 100% class II PRA) had a T

and B cell positive crossmatch; the authors remarked that the latter patient suffered an episode of antibody mediated rejection but was alive at last (unspecified length) follow-up. These authors conclude that MCS can be successfully used in failing FSV patients as a bridge to heart transplantation.

Experience with MCS in failing FSV patients has been reported by other teams, mostly in the form of case reports (2-13). While these case reports describe successful efforts, undoubtedly we can speculate that there are numerous unsuccessful attempts that have not been reported. In a prior unbiased review of the EXCOR Investigational Device Exemption study database, Weinstein and colleagues reported that FSV patients supported with the Berlin Excor ventricular assist device fared much worse than patients with two ventricles supported with the same device (13). In the FSV cohort, results for ventricular assist device support after the stage I procedure were quite dismal (only 1 out of 9 survived).

Collectively, these results indicate that MCS can indeed successfully bridge FSV patients to heart transplantation. However, the results are certainly inferior to those seen in the current and much larger adult MCS experience (14-16). Clearly, there is great room for improvement in supporting failing FSV patients with MCS. One area of potential improvement is MCS device design optimization. As can be seen from the published MCS for failing FSV experience referenced above, many devices have been utilized with none yielding clearly superior results. It is not known what aspects of MCS device design should be specifically optimized for the failing FSV. World-wide participation in registries is needed to compile all attempts at MCS bridge to transplant for failing FSV patients so that we all can learn from successes, failures, and the impact of different devices, thus moving the field forward at a more rapid pace (17).

An important concept of MCS for the failing Fontan patient with relatively preserved ventricular function is cavopulmonary assist (18). This entails the implantation of a ventricular assist device in the Fontan circulation to propel blood into the pulmonary arteries and does not provide any other support to the systemic ventricle outside of improving preload. However ventricular assist devices are unlike native ventricles in that they can function at very low preload levels, thus potentially actively pulling pulmonary blood through the lungs. Thus we feel that all ventricular assist devices placed to support or bypass the FSV can help with the failing Fontan circulation as well as the failing FSV with poor systolic function. Again, besides that of a prospective clinical trial, data from a detailed registry of MCS in failing FSV may yield insight into the best location of a MCS device within the FSV circulation.

Placing two ventricular assist devices (one as cavopulmonary support and the other for systemic ventricular support) has also been utilized (19). This approach converts the Fontan circulation into that of a biventricular one, but is a more extensive procedure. Arnaoutakis and colleagues report the use of the Syncardia Total Artificial Heart, which is another method of converting to a Fontan circulation to a totally assisted biventricular circulation. The patient in their series that received this device appeared to be well-supported without end-organ dysfunction and eventually survived heart transplantation. Before widespread adoption of the total artificial heart, better techniques of creating separate atrial cuffs from the common atrium usually found in FSV patients will need to be developed.

Another important issue that can be raised by the report by Arnaoutakis and colleagues is that of preexisting alloantibodies present in failing FSV patients. These patients likely develop alloantibodies as a result of prior exposures from blood products transfusions and implanted allogeneic tissue in contact with the blood stream. It is well recognized that the presence of alloantibodies prior to heart transplantation leads to significantly worse outcomes (20). Thus failing FSV patients with very high levels of allosensitization are in an especially dire situation: MCS might be able to rescue them but the time on the waitlist will be exceedingly long since the donor pool with acceptable antigens would be extremely small. This issue is a segue into another important question: Should MCS be used as destination therapy for adult failing FSV patients? Obviously, there is no easy solution to this emerging epidemic of failing FSV patients. However, the fields of both pediatric and adult cardiovascular medicine will have to wrestle with this difficult problem, of which MCS may be part of the solution.

In conclusion, the report by Arnaoutakis and colleagues draws attention to the challenges of treating failing FSV patients with MCS. It reinforces the urgent need to optimize and develop new treatment strategies to address the failing FSV. Overcoming the hurdles of FSV in early childhood has been a dramatic success. Overcoming the hurdles of the failing FSV later in life is and will be the next challenge for the current and future generations of pediatric and adult cardiovascular practitioners.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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