The study by Greenberg et al published in this issue of *Circulation* details the results of the randomized clinical trial known as the Multicenter trial of the Orqis Medical Cancion system for the ENhanced Treatment of heart failure Unresponsive to Medical therapy (MOMENTUM). The Orqis device is a new entry into the field of temporary mechanical circulatory support for severe heart failure. The authors point to the growing number of patients with this condition and the very high in-hospital and short-term mortalities that are typically associated with conventional medical or surgical therapy. Thus, new simple methods of providing temporary circulatory support to allow identification of individuals with reversible dysfunction to improve, while adequately supporting the circulation to prevent multorgan failure and the high likelihood of death in those without improvement in cardiac function, would be a significant advance in management of this population.

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Conducting clinical trials on patients who are this ill with very advanced heart failure is, understandably, very difficult, owing to the presence of multiple comorbidities with adverse events that are, potentially, not a direct result of the therapy being evaluated. The cohort of 168 patients enrolled in the MOMENTUM trial were typical of this population, with low blood pressure and cardiac output as well as impaired renal function despite intravenous inotrope and/or vasodilator therapy. The trial randomized patients to optimal medical therapy with or without addition of the continuous aortic flow augmentation device. The primary composite end point was a reduction in pulmonary capillary wedge pressure (PCWP) and days alive out of hospital at 35 days post support. A modest goal of the study was that the device could provide an improvement in cardiac index of at least 1 L/min over baseline.

Unfortunately, this low level of support does not seem to provide adequate benefit; the trial was stopped early because of an inability to meet the primary end point, and a significant increase in bleeding was associated with use of the device. Although the authors report a significant improvement in cardiac index with the device over medical therapy alone, during the 8 periods of assessment the device was identical to medical therapy in 4 of the periods, superior to medical therapy alone by >0.1 L/min 4 times, and only at the final time point (96 hours) did the difference reach 0.3 L/min. This is clearly too little support to make a meaningful improvement in these very ill patients. Use of an invasive device that provides only a modest benefit must be associated with minimal risk, and that was not the case in this study, as significant bleeding was observed in the patients on whom the device was used. One of the shortcomings of this study is that the data were compared using grouped means rather than being broken out by paired analysis for each patient, which would better assess the percentage of patients who improved significantly and allow for subsequent multivariable analysis to potentially identify risk factors associated with good and bad outcomes to enhance future patient selection criteria for the future.

One of the problems observed with most of the early iterations of temporary continuous flow and centrifugal pumps has been thrombosis. It is unclear whether the low outputs produced by this device will require relatively high levels of anticoagulation (with attendant increased bleeding) to prevent thrombosis. The authors do not comment on the cause of pump dysfunction that is reported in 6 patients, and specifically, whether this was a result of pump thrombosis. Heparin-induced thrombocytopenia is being reported with increased prevalence, and it is also unclear whether this was present in any of these patients.

One of the more interesting aspects of the data is the significant decrease in systemic vascular resistance in those patients supported with the device, despite very modest increases in cardiac index and stroke volume. The exact mechanism by which this device improves cardiac performance is still unclear, but the concept of ventricular-vascular coupling has been suggested as one of the primary mechanisms. Perhaps continuous aortic flow augmentation is sufficient to cause the reduction in systemic vascular resistance, but this, in turn, did not lead to further improvements in cardiac index.

Where does this device then fit in the spectrum of temporary mechanical assist devices that are now in clinical trials? The percutaneous devices include the Tandem Heart (Cardiac Assist Inc, Pittsburgh, Pa), which is a centrifugal-flow device that is placed percutaneously via the femoral vein, but requires transeptal puncture across the atrial septum (a competence that is vanishing in the current era) to decompress the left ventricle and return flow in a retrograde fashion into the aorta, to provide up to 5 L/min of flow. It has been used for other indications, but for heart failure it has been
largely a salvage strategy, with many patients having suffered cardiac arrest or having been in shock at the time of implantation, and only a moderate number of patients having been supported to date at a small number of institutions. Another device, which has the largest number of implants, is the Abio-Med device (Abiomed Inc, Danvers, Mass). It provides 3 to 5 L/min of flow, and has been used often after cardiotomy. Another newer device is the Impella device, which is perhaps the smallest and easiest pump to insert percutaneously via the femoral artery, and is advanced retrograde across the aortic valve with only 1 to 2 cm of catheter extension into the ventricular chamber. Although easy to insert, the small continuous flow pump can achieve a maximum of only 2.5 L/min of flow augmentation. A larger model can generate 5 L/min of flow but is designed for open-chest surgical implantation. Pumps are available that require surgical implantation, including the Centramag centrifugal device. It can generate up to 5 to 6 L/min of flow, and can support either the right or left ventricle or, often, both ventricles. Good outcomes have been reported with use of this pump as a bridge-to-a-bridge type of procedure, meaning, for resuscitation of patients in critical shock who are at high risk for insertion of a more definitive long-term ventricular assist device. A final device, which has similar output to the Orqis device, is the Circulite pump (Circulite Corp, Saddle Brook, NJ), which has been placed in only a very few patients thus far. It is not designed for use in critically ill patients, because it can provide only ~2 L/min of flow augmentation. It is a small device that is also designed for transcutaneous implantation via the right subclavian vein, with the drainage catheter advanced across the intrapericardial septum into the left atrium. Clinical trials, however, are being conducted only in stable outpatients with heart failure and not in critically ill patients, owing to the limited flow provided. The ideal pump for patients with advanced heart failure or shock needs to be relatively easy to implant, be associated with limited morbidity (eg, bleeding), and provide enough augmentation of the circulation to reverse the congestion and impaired organ function that are characteristic of this condition. The amount of flow required to adequately resuscitate and support an individual patient varies by the severity of ventricular dysfunction, the output of the native heart, and body size of the patient. The lessons learned from the MOMENTUM trial suggest that a minimum amount of support exists that is required for patients with this level of heart failure, and this amount is likely to be at least 2.5 to 3.0 L/min. Whether smaller pumps such as the Orqis and Circulite devices will have a role in the treatment of patients with less-severe heart failure remains to be proven. Clearly, this is an area that warrants much more investigation and support for larger prospective clinical trials. As noted, conducting trials in this population is challenging. Randomization to a control group in a clinical trial will be essential to prove the true value of a device, but a crossover design must be incorporated into the trial to provide patients the chance for survival should medical therapy alone prove inadequate.

Disclosures

Dr Miller has received research support from Thoratec for a study of the drug clenbuterol and has received honoraria for talks related to myocardial recovery and clenbuterol.

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