The Future of Mechanical Circulatory Support

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Much has transpired in the world of mechanical circulatory support (MCS) in a very short period of time. Less than twenty years ago, the pulsatile Heartmate XVE was found to be superior to medical therapy for improving survival among patients with advanced heart failure with reduced ejection fraction (HFrEF).[1] While simplistic in design, the XVE was large, bulky, and unstable over the long-term. Innovative approaches towards device design eventually led to the introduction of continuous-flow technology, first with the axial flow Heartmate II left ventricular assist device (LVAD)[2], followed by two centrifugal-flow pumps, the Heartware VAD (HVAD)[3] and the Heartmate 3.[4] Over the last decade, healthy competition between these pumps spawned a revolution in all aspects of MCS, from refinement of pump design, drivelines and batteries, to automated modulations in speed, surgical implantation techniques, and even the concept of LVADs as a "bridge-to-recovery". Survival and quality-of-life have improved, and the rate of LVAD-associated complications has declined. Fast forward to 2021, whence one of these pumps – the Heartmate 3, has emerged victorious in this competition, with the HVAD finishing as the "runner-up". Following withdrawal of the HVAD from the global market on June 3rd, 2021, we are now left with one device – a reliable pump, with which to incorporate into our armamentarium for managing patients with advanced HFrEF.

Competition will always declare a victor, and while the Heartmate 3 will now inevitably receive increasing levels of attention and scrutiny, there remains much to be learned from the HVAD in spite of its shortcomings. The HVAD platform incorporated unique features – namely, real-time waveform analysis and logfiles, not available on other durable MCS devices, which improved patient care and general awareness of how

the cardiovascular system interacts with centrifugal-flow pumps. The flow waveform is a real-time, continuous display of pump performance, a feature that allows for an estimation of LVAD volume and pressure, analogous to ventricular pressure-volume loops, the gold-standard method of characterizing ventricular function. These measures allow clinicians to make informed decisions on management of patient factors such as fluid status, blood pressure, arrhythmias and right heart function. Conditions such as overt right heart failure and pericardial tamponade can be identified by interrogation of the waveform and logfiles. In addition to the Medtronic HVAD, the Abiomed Impella and Abbott Centrimag system also utilize waveform displays, highlighting the importance of continuous evaluation of pump performance on all MCS platforms.

The potential for investigation of patient-pump interaction is the more interesting application of the waveform. Physiologically responsive pumps are a holy grail of durable MCS therapy. While current pumps allow for greater exercise tolerance compared to the pre-implant state, recent analyses have demonstrated that patients still have features of heart failure after LVAD implantation.[5] Waveform analysis allowed physicians to appreciate that a continuous-flow LVAD, operating at a fixed speed, does not adequately perfuse the body during periods of increased demand, such as occurs during exercise. Analogous to rate-responsive pacemakers, speed-modulating LVADs can only be developed once the interaction between patient and LVAD is better understood. While the HVAD was clinically limited by inferior outcomes, particularly in regards to survival and stroke rate, it nevertheless created a role for itself in the MCS space that is not filled by the Heartmate 3. Instantaneous waveform display at the patient's bedside proved to be an invaluable asset for clinical decision-making since it

provided information regarding factors such as heart rate and arrhythmia burden, preload assessment, status of aortic valve opening and flow pulsatility. The graphical logfile display provided additional information, including diurnal variations in pump performance, flow pulsatility, suction, and even evidence of device-related complications such as gastrointestinal bleeding. As such, certain aspects of the HVAD proved invaluable to patient management and it is our hope that these attributes are incorporated as standardized features of future MCS platforms. Along those lines, the question is, where to now? The challenge for providers is to derive as much information as possible from the pump while also encouraging device engineers to push the envelope in design as newer pumps emerge.

Regardless of the device, LVAD patients – including those supported by the Heartmate 3, are limited by complications including strokes, right heart failure, gastrointestinal bleeding and device-related infections, which may occur in isolation, sequentially or simultaneously. The mechanism(s) predisposing to these complications – while not fully understood, may be related, at least in part, to a limitation of all continuous-flow pumps, namely, the lack of a physiologic pulse. The relative importance of pulsatility has long been debated amongst experts, however, the true flow profiles throughout the macro- and microcirculation of different LVAD patients largely remain unknown. Patient-specific end-organ flow profiles result from an individual's unique haemodynamic profile and are the product of contractile reserve of the native ventricle, flow through the pump itself, and interactions with the central and peripheral arteries, which may be dysfunctional (e.g. endothelial dysfunction, arterial stiffness) as part of the natural history of HFrEF.

A successful reduction in the rate of adverse events depends on the ability to better understand the degree to which an LVAD can integrate into the cardiovascular system. To this end, coordination between device manufacturers, clinical practitioners, and researchers is paramount. Device manufacturers can facilitate immediate bedside availability of pump behavior from the LVAD controller. *In-vivo* cardiovascular hemodynamics and heart-pump interactions can be provided through invasive and non-invasive means in both clinical and research settings. Patient-specific profiles of flow patterns should continue to be incorporated into bedside management to personalize care.

HVAD engineers and developers are to be congratulated for their contributions to the field of durable MCS. While this chapter in LVAD technology closes, and a new one emerges – one involving a single device sitting comfortably with no immediate competitor, we remember the irreplaceable value and lasting impression the HVAD has had on the field. At the same time, the Heartmate 3 designers are to be congratulated for earning their place at the head of the table. Moving forward, we must be careful to avoid complacency with the field in its new state, which now involves a single pump. Complacency leads to stagnation, which neither the field of MCS, nor its patients, can afford. The competition between pumps created an environment that encouraged tremendous innovation and improved outcomes. That competitive drive to excel must continue.

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