

Forward “MOMENTUM” in left ventricular assist systems: advanced engineering meets biology

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Alvarez J, Rao V. HeartMate 3—a “Step” in the right direction. *J Thorac Dis* 2017;9:E457-60;

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The abandonment of need for pulsatile flow in favor of the unnatural physiology of continuous flow circulation with current left ventricular assist systems (LVAS) led to the widespread application of these devices in the patients with advanced heart failure refractory to medical therapy (1). Troublesome consequences, related to hemocompatibility related adverse effects (the clinical consequences of interaction between the device and blood interface) began to surface once long-term support was realized (2). While bleeding was recognized as *fait accompli* due to the need for chronic anticoagulation, curiously, gastrointestinal bleeding and epistaxis were noted with alarming frequency, subsequently associated with loss of high molecular weight multimers of Von Willebrand factor (a biomarker of this high shear circulation) and potential consequences of circulating micro-particles (a manifestation of premature destruction of blood cells) as well as expression of growth factors (3). The HeartMate 3 has demonstrated early signs of amelioration of some of these biomarkers, particularly abnormal Von Willebrand factor and absence of hemolysis of circulating cells (4). Yet, bleeding complications persist and show an age dependency, especially in those above 65 years of age (5). Rounding out hemocompatibility related

complications are thromboembolic events exemplified by strokes and de-novo pump thrombosis. Strangely, strokes occur with high frequency and correlate with multiple factors that include the type of device (the HeartWare HVAD has the highest risk of accompanying stroke rates), advancing age, and uncommon manifestations such as spontaneous aortic valve and carotid bulb thrombosis (6). Vascular integrity issues and septic emboli have also been implicated as causative factors. Indeed, such an outcome remains a significant deterrent to broadening the application of LVAS to a lesser sick heart failure population or to reliably investigate the potential for hemodynamically facilitated recovery in earlier disease stages (7). In MOMENTUM 3, we were able to demonstrate a signal to lesser non-disabling strokes, but the numbers of disabling strokes were similar between devices (8).

Clearly, the most reliable clinical benefit with the HeartMate 3 is seen in the observed absence of suspected or established de-novo pump thrombosis. Interestingly, the sheer consistency of this observation across the spectrum of first in human experience data, the MOMENTUM 3 randomized trial, ongoing real world registries and single center studies is reassuring. Yet, we should not become

complacent with this observation. Although the de-novo development of pump thrombosis is abrogated by the engineering inherent in the HeartMate 3 LVAS, there remains potential for ingestion of material (thrombus, calcium, marantic or septic vegetation) that could paradoxically take advantage of the wide gaps in the pump (and pass into the circulation leading to a peripheral event including large stroke) or obstruct the pump function. Thus, despite the laudatory observations of absent pump thrombosis, vigilance and longer follow-up (both patient numbers and length of implant) is warranted. Another important point that we wish to make is to not relax the need for optimal anticoagulation targeting the INR to 2–3. While the temptation to employ less intense anticoagulation to HeartMate 3 recipients may exist, we strongly argue that until proper safety experiences are completed, this strategy must be avoided. A trial testing low intensity anticoagulation targeting the INR between 1.5–1.9 with the HeartMate 3 is currently underway in its safety phase in Europe (9). This may form the rationale for an even larger clinical trial and such a staged approach is vital to not fall prey to an untimely and fallacious clinical change. Similarly, aspirin therapy is required in the regimen of anti-thrombotic therapy for this pump. The use may be meritorious not just for prevention of pump thrombosis, but to tackle other thromboembolic complications as well (8).

The HeartMate 3 experience, currently the largest of any LVAS, has completed enrollment of its entire primary MOMENTUM 3 trial cohort (n=1,028) as well as a 500-patient continued access protocol in the US. A second 500 patient extended continued access protocol is now underway in the United States, targeted to enroll long-term recipients. Worldwide, the experience with implants now is close to 1,200–1,500 pumps and it is likely that this novel LVAS will become the predicate device for use in vulnerable patients. Yet, we must not forget that other complications such as worsening of the unsupported right ventricle and drive-line associated infections will continue to plague this field (10). Similarly, as Alvarez and Rao point out, aortic valve insufficiency is an increasingly recognized problem that requires further characterization. Each of these attributes either diminish the quality of life experienced with the LVAS or reduce the potential for underlying disease modification or attenuation of disease progression. We look to the large experience with the HeartMate 3 to inform us regarding management strategies to enhance quality of life and we suggest that the short-term outcomes of the MOMENTUM 3 study need confirmation of durability

in its long-term follow up phase and the development of a robust event related experience. In either case, we believe that the engineering alterations in the HeartMate 3 interact more favorably with the advanced heart failure patient biology than has been observed with older currently available continuous flow pumps. The field will now renew a focus on moving towards smarter physiological support by innovative management strategies to further optimize LVAS function with exercise to enhance the patient experience. We are reminded of the poignant comment by Sir Winston Churchill “*Without tradition, art is a flock of sheep without a shepherd. Without innovation, it is a corpse.*” In this case, the rich tradition of current LVAS and the innovation accorded by the HeartMate 3 is fulfilling and provides for a surge of enthusiasm in the field.

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Footnote

Conflicts of Interest: Drs. JC Cleveland, DJ Goldstein, N Uriel and MR Mehra serve as National Principal Investigators for MOMENTUM 3. Dr. MR Mehra is chair of the presentations and publications committee of the trial. All authors or their institutions have received research and or consulting support from Abbott, for participation in the trial. Dr. MR Mehra also declares consulting or research fees from Medtronic, Stealth Biotherapeutics, Portola, Teva, Johnson and Johnson (Janssen). Additionally, he is editor in chief of the Journal of Heart and Lung Transplantation. This work in no way endorses the views of neither the journal nor its parent society, the International Society for Heart and Lung Transplantation.

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