

## Using left ventricular assist devices in advanced heart failure patients

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### ABSTRACT

Advanced Heart Failure (AHF) is a complex syndrome that affects the physiology of the heart to maintain efficient blood circulation resulting in multiorgan failure and, eventually, death. Left Ventricular Assist Devices (LVADs) have become the cornerstone therapy for AHF patients, both as a bridge to transplantation and as a decisive therapy. Recently the results of the MOMENTUM 3 Trial were published. The trial compared HeartMate 3 LVAD with HeartMate II LVAD in a randomized trial in The Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3). Of 366 patients, 190 were assigned to the centrifugal-flow pump group (HeartMate 3) and 176 to the axial-flow (HeartMate II) pump group. In the intention-to-treat population, the primary end point occurred in 151 patients (79.5%) in the centrifugal-flow pump group, as compared with 106 (60.2%) in the axial-flow pump group ( $P < 0.001$  for noninferiority). Reoperation for pump malfunction was less frequent in the centrifugal-flow pump group than in the axial-flow pump group ( $P < 0.001$ ). The results of the MOMENTUM 3 Trial are a big achievement in the cardiovascular world. Any improvement in LVADs that reduces the risk of stroke, perhaps the most feared complication of these devices, would be meaningful. Besides, given the observed lower rate of pump thrombosis and reoperation for pump malfunction, it already seems likely that the HeartMate 3 will supplant the HeartMate II in clinical practice. In addition, the risks that are associated with reoperation undoubtedly counterbalanced any unintentional bias in performing that intervention.

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Advanced Heart Failure (AHF) is a complex syndrome that impedes the ability of the heart to maintain efficient blood circulation, resulting in multiorgan failure and eventual death. For this set of patients, medical therapy is preferred; however, patients who do not respond to medical therapy or surgical intervention, or who are not candidates for heart transplantation may benefit from placement of a left ventricular assist device (LVAD). This device can also be used as a bridge to heart transplantation or used as a final therapeutic modality; it serves as a cornerstone therapy for AHF patients [1,2]. LVADs provide assistance to patients with AHF by improving circulatory mechanics. These are small pumps that usually assist the damaged left ventricle and may be situated inside or outside the body. In the past few years, LVADs have been used primarily as a 'bridge-to-transplant' for patients on a transplant waiting list. In the recent years, however, there has been an increasing interest in using LVADs as a permanent therapy.

Previously, LVADs developed were pulsatile in nature; however, the newest devices have continuous flow and are internally implanted. As such, they are

more durable, smaller and less invasive [2–5]. Extensive data are available to suggest that LVADs help improve hemodynamics of the left ventricle by augmenting cardiac output and improving overall functionality of the heart [6]. As a result, LVADs strengthen peripheral circulation, alleviate end-organ dysfunction, reduce heart failure symptoms, and improve quality of life [7,8]. In the past few years, development of continuous-flow LVAD, including HeartMate II and the HeartWare, is a major breakthrough in the management of AHF. The HeartMate 3 is a new LVAD that was approved by the Food and Drug Administration for clinical use in August 2017. Its new design features, as compared with the HeartMate II, include centrifugal flow, a magnetically levitated rotor with no mechanical bearings, wide blood-flow passages, and an artificial pulse mode.

Recently, the results of the MOMENTUM 3 Trial were published. The trial compared HeartMate 3 LVAD with HeartMate II LVAD in a randomized, non-blinded trial in The Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3) [9]. Of 366 patients,

190 were assigned to the centrifugal-flow pump group and 176 to the axial-flow pump group. The primary end point, a composite of survival free of disabling stroke or reoperation to remove or replace a malfunctioning device, occurred significantly more often among patients who received the HeartMate 3 (centrifugal-flow) than among those who received the HeartMate II (axial-flow) [9]. In the intention-to-treat population, the primary end point occurred in 151 patients (79.5%) in the centrifugal flow pump group, as compared with 106 (60.2%) in the axial-flow pump group [ $P < 0.001$  for noninferiority]; [ $P < 0.001$  for superiority]) [9]. This improvement in outcome was due to a lower rate of reoperation for pump malfunction. Reoperation for pump malfunction was less frequent in the centrifugal-flow pump group than in the axial-flow pump group ( $P < 0.001$ ) [9]. However, there were no significant differences in the rates of disabling stroke or death. The rates of death and disabling stroke were similar in the two groups, but the overall rate of stroke was lower in the HeartMate 3 group than in the HeartMate II group (10.1% vs. 19.2%;  $P = 0.02$ ) [9]. Patients were regarded as having a 'disabling stroke' if their National Institutes of Health Stroke Scale (NIHSS) score was greater than 5 [10]. The NIHSS was used as it is a useful scale for quantifying neurological injuries and predicting outcomes after stroke when performed in a consistent manner [10,11].

The results of the MOMENTUM 3 Trial are a big achievement in the cardiovascular world. Any improvement in LVADs that reduces the risk of stroke, perhaps the most feared complication of these devices, would be meaningful. However, caution is needed in the interpretation of these data. Disabling stroke, but not nondisabling stroke, was a component of the primary end point, and the rate of disabling stroke was not significantly lower with the HeartMate 3 than with the HeartMate II. Furthermore, it is unclear whether the lower rate of nondisabling stroke was independent of the lower rate of pump thrombosis or reoperation. At any rate, vigilance for unexpected complications with the HeartMate 3 should be maintained. Nevertheless, given the observed lower rate of pump thrombosis and reoperation for pump malfunction, it already seems likely that the HeartMate 3 will supplant the HeartMate II in clinical practice. Furthermore, the individual narratives describing the episodes of thrombosis with the HeartMate II were consistent with this complication of the LVAD. In addition, the risks that are associated with reoperation undoubtedly counterbalanced any unintentional bias in performing that intervention. Overall, these findings appear to be robust.

In the past few decades, research into the management of AHF patients with LVAD has increased

tremendously. Hemodynamic evaluation during stable conditions and in response to speed change with ramp tests remains a relatively understudied and underutilized tool in the management of LVAD patients. Investigation into the long-term benefits of ramp tests on survival, AHF readmission, and other comorbidities is warranted. Hence, hemodynamic assessment is a vital component of the clinical assessment of patients on LVD support. In particular, echocardiographic and hemodynamic ramp tests provide us with a useful tool to optimize hemodynamics in this population. Hemodynamic optimization may prove to be a crucial strategy in improving clinical outcomes during LVAD support.

In conclusion, a fully magnetically levitated centrifugal-flow pump was superior to a mechanical-bearing axial-flow pump with regard to survival free from disabling stroke or re-operation to replace or remove a malfunctioning device in patients with AHF, demonstrating a reduction in re-hospitalizations, hospital days spent during re-hospitalizations, and a significant cost-savings following discharge [9]. However, while advances in technologies have helped elucidate many aspects of these diseases, many questions remain unanswered. With continued research, we can expect more cost-effective and beneficial drug therapies to be developed in the near future. Further research is needed to clarify the role of these agents in AHF patients. It is anticipated that the results of these trials will influence the content of international guidelines.

### Disclosure statement

No potential conflict of interest was reported by the author.

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