Vulnerable Brain and Ventricular Assist Devices

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See related article, p 2702.

In the past 50 years, we have learnt to transition mechanical circulatory support devices, such as durable left ventricular assist systems (LVAS), from crisis intervention life-saving devices to the contemporary era of using such therapy in prolonging meaningful life in patients with advanced heart failure.1 Despite generational shifts in engineering of such devices, from large pulsatile mechanisms to smaller continuous flow devices, the complications related to neurologic adverse effects have not improved substantially.2,3 Hemorrhagic and ischemic strokes continue to occur, with a frequency greater than that observed in patients with advanced heart failure.4 This complication has limited the expansion of such devices to patients with less severe stages of illness, and the quest to understand these devastating events and to prevent them is ongoing.

Most studies of neurological complications with LVAS have found a strong correlation between elevated mean arterial blood pressure, anti-coagulation levels, and systemic infection.5–5 Ischemic strokes can occur because of thrombi that pass from the heart through the device and into the brain or could develop in unique locations, such as the aortic surface of the valves within the sinus of Valsalva, the carotid bulb, and in some cases septic emboli as a result of infections.6–9 The role of cardiovascular disease comorbidities in stroke risk and mortality associated with LVAS has not been well established. Systemic inflammation is a strong arbiter of vascular disease, and the state of implantation of LVAS induces such a pattern, arguably predisposing to strokes, although this association has been difficult to define.9,10

In this issue of the journal, Parikh et al11 evaluate real-world data using claims information, from 3 distinct regions of the United States (West [California], South [Florida], and Northeast [New York]), in a cohort of 1813 patients with durable LVAS. The authors demonstrated an incidence of stroke of 8.7% per patient-year, with ischemic strokes outpacing bleeds (5.5% versus 3.1%). Curiously, women were more likely than men to incur a stroke risk (hazard ratio, 1.6), particularly that of hemorrhagic stroke (hazard ratio, 2.2). One limitation of this data is that the time period used mixes contemporary devices (continuous flow LVAS) with those of historical interest (pulsatile LVAS). The older devices were larger and had a lower incidence of thrombosis, and therefore, anti-coagulation targets were different compared with today’s devices. Yet, the general incidence of neurological complications, principally stroke, has not decreased in the contemporary era. This must posit, therefore, that the underlying reasons for strokes may be changing as a function of device era, with causative factors that may have more to do with vascular biology than simply anti-coagulation strategies.

Other studies have reached similar conclusions. In an investigation of 100 patients with the HeartMate II LVAS (St Jude Medical, Inc) as either a bridge to transplant (n=65) or destination therapy (n=35), strokes occurred in 12 patients (12.0%): 4 embolic and 8 hemorrhagic.12 Patients with strokes had a significantly higher incidence of diabetes mellitus, history of pre-implant stroke, and aortic cross-clamping with cardiopulmonary arrest during their device implant as well as anti-coagulation targets. Importantly, the 30-day mortality is high at 25%.12 Clinical trials and registry series have pointed to the high incidence of debilitating strokes in patients with LVAS, especially in women, and differences between devices are apparent, with a high incidence encountered with the HeartWare left ventricular assist device (HVAD; HeartWare, Framingham, MA).5,13,14 A study found that subclinical strokes are common if serial monitoring is performed at predefined time points. Thus, it is clear that the brain remains a highly vulnerable organ even as the heart is well supported with LVAS.15

The causes of strokes with newer LVADS are unclear and could relate to (1) clots that pass through the device (as with atrial fibrillation in patients with a device or with clots that form within the device or in the proximate ventricle), (2) vascular changes as a result of nonpulsatile flow (we know that reduced pulse pressure with the newer devices increases vascular fragility, so even lower levels of blood pressure can cause vascular loss of integrity), and (3) rheological causes (new devices create an acquired von Willebrand syndrome and can predispose to bleeding).16,17

Debilitating stroke is a disastrous situation that diminishes the gains from application of LVAS therapy and occurs with enough frequency and is intertwined with other complications of LVAS, that it is a major concern, especially in older patients who are receiving these devices as lifetime therapy without the option of a transplant.18,19 Often, the diagnosis leads us to have to shut off these devices for compassionate reasons because the quality of life is immeasurably reduced.20

Because the occurrence of stroke is largely unpredictable in an individual and comorbidities are common, we must focus our efforts on performing a thorough evaluation for the risk of stroke pre-implantation of these devices, establish optimal surveillance guidelines in follow-up after implant, and ensure good blood pressure control and use of antiplatelet therapy.
Avoidance of hemorrhagic strokes by tightening control of anticoagulation and evaluating those with thrombophilia should be carefully done to avoid ischemic strokes. In patients who do not open their aortic valves on LVAS therapy and demonstrate low peripheral pulse pressure, we should consider surveillance to pick up clot formation at sites such as the proximal aorta and the carotid bulb. We need to do more studies that help us understand neurovascular blood flow characteristics with LVADs and the impact on vascular integrity and research how best to follow these patients in an effort to decrease this devastating occurrence. Until we learn more of this complication, tackle it more effectively, LVAS application to broader populations of advanced heart failure will remain greatly encumbered.

Disclosures

Dr Mehra reports relevant conflicts as follows: Consultant for Thoratec (now St Jude Medical, Inc), HeartWare, Medtronic, Johnson and Johnson (Janssen), and Tea Pharmaceuticals. He is also Editor-in-Chief of the Journal of Heart and Lung Transplantation. The other authors report no conflicts.

References


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