Is Pulsatile Blood Flow No Longer Essential?

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The heart’s natural provision of pulsatile blood flow has been regarded as an essential requirement for normal organ function, especially critical organs such as the kidney, liver, and brain. However, in this issue of Circulation, Russell and colleagues have demonstrated that this tenet of medicine is no longer accurate. Their study examined the long-term impact of nonpulsatile blood flow as provided by a new generation of so-called continuous-flow left ventricular assist devices (LVADs), in this case the Heartmate II LVAD (Thoratec Corp, Pleasanton, Calif), on end-organ function in patients with refractory heart failure awaiting a heart transplant. These pumps draw blood from the left ventricle via a drainage cannula placed in the LV apex on a continuous basis and propel the blood by a rotary pump back into the circulation in a nonphasic flow pattern through a return cannula connected to the aorta. The major findings of the Heartmate II clinical trial, including both the primary cohort and a larger number of patients enrolled in the continuous-access protocol, have previously been reported.

This study examined the biochemical markers of hepatic and kidney function over a 6-month period after implantation of the Heartmate II LVAD in a cohort of 309 patients who were enrolled in the Heartmate II trial. These patients all had severe heart failure at the time of enrollment in the trial and required intravenous inotrope support (25% were on 2 inotropes), and nearly half had an intraaortic balloon pump in place. The goal of the study was to demonstrate whether nonpulsatile blood flow was associated with worsening end-organ function. The patients were separated into those with normal and those with abnormal end-organ function at the time of implantation. The data were analyzed by comparing the baseline values with the results at the end of the 6-month follow-up period, which seems adequate to detect any adverse effects of the new generation of nonpulsatile, continuous-flow devices on end-organ function.

The study showed that rather than causing worsening function, nonpulsatile blood flow was associated with a highly significant improvement in all the serum markers of organ function measured (blood urea nitrogen, serum creatinine, aspartate aminotransferase, and bilirubin) in those with reduced organ function preoperatively and remained unchanged in those with normal function at baseline. These results are as good as or better than reported in similar patients supported with LVADs that generate pulsatile blood flow. There were also no changes observed in neurocognitive function in a small subset of study patients who underwent a battery of tests of neurocognitive function at baseline and at the 6-month follow up. The assessment of a potential adverse impact on neurocognitive function is a difficult task in patients receiving an LVAD because they are also at risk for adverse effects of cardiopulmonary bypass alone. The fact that there was no difference in this study suggests that there is no demonstrable adverse impact from nonpulsatile blood flow on neurocognitive function.

Should these observations be considered a total surprise? Clearly, patients placed on cardiopulmonary bypass for open heart surgery have a period of nonpulsatile flow. This has been associated with a worsening of renal function in some patients, typically those with abnormal renal function or significant hemodynamic impairment at the time of operation. There have also been reports of impaired mental function after cardiopulmonary bypass. In fact, the belief that major organ function is dependent on pulsatile blood flow has often led clinicians to use an intraaortic balloon pump in patients with reduced perfusion, in part to maintain pulsatile blood flow and to augment diastolic or coronary perfusion pressure. The kidney, however, seems more dependent on mean arterial pressure than pulsatile flow because a normal heart rhythm (and pulse) does not preclude impairment in renal function in patients with low mean arterial pressure in conditions such as septic shock with low diastolic and therefore mean arterial pressure.

The transition from a pulsatile to a nonpulsatile design of LVADs was not predicated on the belief that continuous flow would provide better support, but on the need to move to that design to allow a miniaturization of the pump for both patient comfort and a reduced risk of drive-line and/or pocket-related infection. The initial experiments were done in calves in which biventricular continuous-flow devices were implanted at birth. These animals demonstrated normal growth, development, and organ function. This finding led to pilot clinical trials that showed no adverse impact on organ function and set the stage for this large clinical trial, which has confirmed the initial observations and those of other small series noted by Russell et al.

What adverse effects resulting from nonpulsatile blood flow could be missed by focusing only on end-organ function? One interesting side effect reported with the continuous-flow pumps is an increase in gastrointestinal bleeding that is due primarily to arteriovenous malformations located most commonly in the first part of the jejunum and stomach. The cause of this associated problem is unclear, but a similar
problem of gastrointestinal bleeding and arteriovenous malformations, more typically in the colon as an acquired form of von Willebrand syndrome, has been reported in patients with the calcific form of significant aortic stenosis found in elderly patients. Although there is clearly normal pulsatile blood flow in this condition, it is often associated with a very narrow pulse pressure in the advanced phase. Most patients supported with a continuous-flow pump have nearly complete unloading of the ventricle and inadequate preload to open the aortic valve with electrical and mechanical systole and therefore have no palpable pulses. Interestingly, some clinicians have observed a reduction in bleeding with a reduction in the speed of the device to a level that increases LV dimension and volume and allows the aortic valve to open and generate pulsatile flow, palpable pulses, and a normal pulse pressure. Whether setting the pump to allow the aortic valve to open on a more regular basis will alter the risk of arteriovenous malformations and associated bleeding is unclear.

The article by Russell et al is an important contribution to the field and confirms that the nonpulsatile blood flow generated by the new generation of rotary pumps has no adverse effects on end-organ function. This observation is consistent with the significant improvement in survival, the reduction in adverse events, and the improved functional capacity associated with this new design. The lack of adverse effects on organ function will allow further miniaturization of these pumps and increased adoption of their use.

Disclosures
Dr Miller was a principal investigator in the Heartmate II trial but had not seen these data before review of the article and had no role in the analysis of the data or the preparation of the article.

References

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