

EDITORIAL COMMENT

Changing the Carburetor Without Changing the Plugs



The Intersection of Stock Car Racing With Mechanically Assisted Circulation*

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This Editorial Comment is dedicated to those “*who think the last four words of the national anthem are ‘Gentlemen, start your engines’*” (Jeff Foxworthy) (1).

Summer in the South is filled with sweltering heat, the sweet smell of magnolias, lazy summer weekends, and afternoons at the racetrack watching well-tuned automobiles run at breakneck speeds in such proximity that a driver with an extended arm could easily touch an adjacent car. Although many view stock car racing as a testosterone-infused, estrogen-tolerated sport composed primarily of men who attempt to relive youthful aspiration, I have developed a deep appreciation for the complex man-machine interplay that results in winning a race. The competitive advantage in stock car racing goes to the team that most effectively integrates a skilled driver, the best car setup, fuel strategy, teamwork in the pits, and subtle engine nuances that provide a little more speed than the competition. It is only in the optimization of these components that the car achieves maximal performance.

Over the past decade, mechanically assisted circulation has earned an accepted position in the treatment of advanced heart failure. The limitations of medical and electrical therapies to improve

survival and symptoms in Stage D heart failure with reduced ejection fraction (HFrEF) coupled with a shortage of suitable donors and a growing heart failure population has fueled exponential growth in left ventricular assist device (LVAD) implantation (2). Registry and clinical trial data have demonstrated that patients requiring inotropic support live longer, with better quality of life and submaximal exercise performance, when treated with LVAD than would be predicted with ongoing medical therapy (2,3). Contemporary LVADs have a rotary design that moves blood continuously through the pump and typically empty the left ventricle sufficiently to minimize aortic valve opening. As a result, pulse pressure is minimized and often undetectable using noninvasive techniques. However, despite near normalization of central hemodynamics with LVAD, exercise performance does not return to the level of healthy, age-matched controls, and continuous flow (CF) LVAD patients have a persistent risk of vascular adverse events, including mucosal bleeding and stroke, suggesting lingering abnormalities in vascular regulation.

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In this issue of *JACC: Heart Failure*, Witman et al. (4) provide important insights into the importance of reduced pulse pressure and potential mechanisms that explain the disconnect among improved central hemodynamics, suboptimal functional improvements, and vascular complications in CFLVAD patients. The authors used flow-mediated vasodilation to evaluate peripheral vascular function in 68 subjects distributed across 4 distinct cohorts:

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normal controls, New York Heart Association functional class II HFrEF, New York Heart Association functional class III to IV HFrEF, and patients on a CFLVAD. They hypothesize that pulsatility would decrease across the heart failure continuum with the lowest detectable pulsatility in the CFLVAD cohort and that pulsatility reduction would be correlated with progressively abnormal vascular physiology. This interesting model addresses the role of pulse pressure in vascular health and has the potential to provide insights about residual functional limitations and vascular complications associated with current LVAD technology.

The control group was selected to have no known cardiovascular disease and was not taking prescription medications. The majority of HFrEF patients had underlying ischemic heart disease, severe ventricular dysfunction, and were more likely to have abnormal glycemic control. The patient groups had lower mean cholesterol values, although nearly 70% were taking a statin at the time of the study. Baseline brachial artery diameter, flow velocity, and shear rates were similar across the study cohorts. A progressive decline in pulsatility was observed in the heart failure patients (control > HFrEF II > HFrEF III-IV > CFLVAD). The prototypical vasodilatory response to transient arterial occlusion was progressively attenuated as heart failure advanced and was most abnormal in the CFLVAD cohort. The investigators also demonstrate that the extent of normal vasodilatory response to arterial occlusion was dependent on the degree of pulsatility.

This study has several intriguing implications. Peripheral vascular adaptations to heart failure may plausibly be implicated in abnormal exercise response, muscle metabolism, and end-organ function. Leveraging the novel circulatory characteristics of CFLVADs and creating a human model of progressive pulse pressure reduction, the investigators of this study have identified pulse pressure as an important mediator of vascular dysfunction in chronic heart failure. In addition, perhaps a portion of the observed vascular adverse events that occur in CFLVAD patients are related to alterations in normal vasoregulation. For example, mucosal arteriovenous malformations are a common cause of post-operative bleeding in CFLVAD patients, and it has been postulated that chronic mucosal ischemia plays a role. It is plausible that abnormal vasoregulation of splanchnic resistance arterioles plays a role in that phenomenon. Hemorrhagic stroke is a devastating vascular

complication associated with CFLVAD support that has been linked to systemic hypertension with mean arterial blood pressure >90 mm Hg, a level that would not typically be concerning in non-VAD patients (5). Loss of appropriate cerebral vasoregulation may also be implicated in hemorrhagic stroke.

This study has a few noteworthy limitations. First, study patients had a burden of comorbid conditions, including hypertension, hyperglycemia, and hyperlipidemia, that predispose to atherosclerosis and abnormal vasoregulation. Second, and perhaps more important, patients were maintained on prescribed medications at the time of the study, including medications that may have altered the vasoregulated response. Third, there is an assumption that device-supported patients had normal central hemodynamics at the time of this study, although this was not proven in the context of this trial. Finally, there is no definitive linkage of altered vascular response to clinical events or exercise performance in this patient cohort, leaving only inference about the clinical implications.

Winning at the race track is in many ways similar to achieving clinical benefit with mechanically assisted circulation. Success is a highly dependent on a complex interplay of factors, some of which can be controlled and others that cannot. It requires integration of man and machine, a constant reassessment of components, and new approaches to old challenges. We have reached a point in mechanically assisted circulation where the new devices reliably pump blood for prolonged periods of time. We are left with the onerous task of understanding the impact of minimally pulsatile flow on long-term outcomes, particularly those affecting the vasculature. Junior Johnson, one of the more famous stock car racers in history, once said, "If you ain't cheatin,' you ain't tryin'" (6). In fact, Mr. Johnson was notorious for making minor illegal alterations in his car so the inspectors would stop looking and not find the more egregious changes. Similarly, we need to search for subtle and overt biological and physiological changes associated with CFLVAD that might serve as targets to minimize risk and assist supported patients reach peak performance.

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