Reviews:

**Novel echocardiographic parameters of aortic insufficiency in continuous-flow left ventricular assist devices and clinical outcomes**

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Aortic insufficiency (AI) frequently develops *de novo* in patients supported with continuous-flow left ventricular assist devices (CF-LVAD). More than 1 in 4 patients will develop at least mild to moderate AI within 1 year after LVAD implantation although a recent report from Bhagra et al. suggest possible lower rates among patients supported with HeartWare HVAD. Despite the high disease prevalence, there remains considerable debate in the MCS community about the true clinical significance of AI. Jorde et al found that a third of patients who developed symptomatic moderate or greater AI required urgent transplantation or aortic valve intervention. Conversely, Cowger et al. and Holley et al. found that AI in patients supported with CF-LVAD did not affect long term mortality.

Recently, Grinstein et al. reported that two novel echocardiographic parameters for grading AI severity, the peak systolic-diastolic (S/D) velocity ratio of the LVAD outflow cannula and the diastolic acceleration of the LVAD outflow cannula more accurately reflected regurgitant fraction and filling pressures in patients who develop AI on CF-LVAD support. Moreover, traditional echocardiographic parameters were shown to underestimate AI severity questioning the validity of some of the prior outcome studies that exclusively used traditional AI parameters. To better understand the clinical significance of AI in CF-LVAD patients, Grinstein and colleagues explored the heart failure admission rate as well as rates of aortic valve intervention, urgent transplantation or death (combined endpoint) following the development of AI both using traditional AI parameters as well as the novel AI parameters, S/D ratio and diastolic acceleration of the LVAD outflow cannula.

In this study, 57 consecutive CF-LVAD patients had their AI graded by the traditional AI parameter, vena contracta and/or qualitative assessment as well as the novel AI parameters, S/D ratio and diastolic acceleration of the LVAD outflow cannula. Heart failure hospitalizations and rates of aortic valve intervention, urgent transplant or death were then followed over an 8 month period. Similar to the work by Cowger et al. and Holley et al., when AI was graded by traditional methods, there was no difference in the rates of the combined endpoint between those patients with moderate or greater AI and those with less than moderate AI (1.50 vs. 1.18 events/person, p =0.46). When the patients had their AI severity reclassified using the novel AI parameters, 32% of patients who were previously classified as trace or mild AI were reclassified to moderate or greater AI. AI classification using the novel parameters better risk stratified patients with significantly more events occurring on those with moderate or greater AI compared to those with less moderate AI (1.57 vs. 0.13 events/person, p =0.002). Similarly, traditional AI parameters (p = 0.343) failed to risk stratify the need for aortic valve
intervention, urgent transplantation or death whereas the novel AI parameters (p = 0.024) were better able to predict these hard endpoints.

These findings questions the validity of prior outcome studies that utilized traditional echocardiographic parameters to examine the clinical significance of AI in patients supported with CF-LVADs . It remains to be seen if more timely interventions on the aortic valve using the novel AI parameters to assess AI severity will improve clinical outcomes.

Outcomes after stroke complicating left ventricular assist device

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Stroke following continuous flow left ventricular assist device implantation (CF-LVAD) occurs in up to 28.7% of patients and leads to significant functional impairment and death. Furthermore, a devastating stroke can often preclude otherwise suitable candidates for subsequent cardiac transplantation. Prior studies examining the clinical consequences of strokes following CF-LVAD have largely been retrospective and have failed to reliably adjudicate ischemic from hemorrhagic strokes, clouding our knowledge on this topic. Many of the prior studies examining the clinical consequences of stroke in CF-LVAD patients have focused on mortality as a clinical endpoint but a devastating stroke can lead to profound functional impairment and thus, prior studies may underestimate the true clinical impact of this disorder.

In this study, Willey et al. examined the clinical impact of a stroke in a cohort of 301 patients (266 HMII and 35 HVAD) implanted with a CF-LVAD at Columbia University Medical Center (CUMC) between January 1, 2008 and April 1, 2015. At CUMC patients with a suspected stroke routinely are examined in real time by a vascular neurologist followed by an assessment which includes a full neurologic exam, NIHSS score and classification of stroke as either an ischemic stroke (IS), IS with hemorrhagic conversion or intracerebral hemorrhage (ICH). Stroke occurred in 40 patients during the follow up period. Eight patients had an ICH (4 HMII and 4 HVAD), and 32 patients had an IS (26 HMII and 6 HVAD). In hospital mortality was 50% for patients who had an ICH with higher NIHSS scores at presentation predicting subsequent mortality (18.8±13.7 vs 1.8±1.7, p =0.049). In-hospital mortality was 28% following an IS with initial functional impairment as reflected by the NIHSS score again predicting mortality (16.2±10.8 vs 7.0±7.6, p =0.111). 5 patients with an IS underwent intra-arterial embolectomy and none required a craniotomy. Among the 23 patients who survived an IS, 12 patients (52%) subsequently underwent successful cardiac transplantation with an additional 1 patient who remained active on the transplant list at the time of publication. None of the patients who ultimately were transplanted experienced a repeat neurologic event after transplantation. Using an NIHSS cutoff of less than 7 predicted survival to hospital discharge with a sensitivity of 77% and specificity of 76% (AUC 0.775).

This study suggests that stroke following CF-LVAD implantation can present with a myriad of clinical presentations but in appropriately managed and selected patients, does not necessarily need to preclude transplantation in otherwise acceptable patients. Additional studies examining which prognostic variable, in addition to NIHSS score, are needed to better predict who is likely to have meaningful recovery following a stroke in CF-LVAD patients.

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