ELSEVIER

The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

STATE OF ART

Comprehensive review and suggested strategies for the detection and management of aortic insufficiency in patients with a continuous-flow left ventricular assist device

Jennifer Cowger, MD, MS,[a] Vivek Rao, MD, PhD,[b] Todd Massey, MD,[c] Benjamin Sun, MD,[d] Karen May-Newman, PhD,[e] Ulrich Jorde, MD,[f,*] and Jerry D. Estep, MD[g,*]

From the [a]Department of Cardiology, St. Vincent Heart Center of Indiana, Indianapolis, Indiana; [b]Division of Cardiac Surgery, Peter Munk Cardiac Centre, Toronto, Ontario, Canada; [c]Department of Surgery, University of Rochester, Rochester, New York; [d]Department of Cardiothoracic Surgery, Abbott Northwestern Hospital, Minneapolis, Minnesota; [e]Bioengineering Program, San Diego State University, San Diego, California; [f]Division of Cardiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York; and the [g]Department of Cardiology, Houston Methodist Hospital, Houston, Texas.

With over 6,000 implants annually worldwide, continuous-flow left ventricular assist devices (CF-LVADs) have become a widely accepted treatment modality for advanced heart failure (HF).[1] Originally devised for the bridge to cardiac transplant indication with limited support times, over 40% of CF-LVADs are now implanted for destination therapy.[1] As a result, support times have progressively increased, now averaging 2 to 3 years, with individual cases exceeding 8 years. With more patients on long-term CF-LVAD support, research focus has shifted from survival to morbidity, quality of life, and a better elucidation of the altered physiology induced by continuous flow.

Aortic insufficiency (AI) is noted in 25% to 52% of patients by 1 year of CF-LVAD support, yet substantial debate continues regarding etiology, clinical significance, need and feasibility of AI prevention, as well as management of AI.[2–6] With longer durations of CF-LVAD support, the prevalence of AI in the CF-LVAD population is anticipated to increase. Accordingly, this group of cardiologists and surgeons representing multiple large-volume mechanical circulatory support programs formed a working group with the primary aim to summarize published data and to provide strategies for the assessment, prevention and management of AI.

AI during LVAD support

The development of AI after CF-LVAD implant has been well documented.[2–6] Cowger et al studied 166 CF-LVAD patients supported for a median 461 days and found the development of moderate AI in 36 patients at a median 273 days after LVAD implant.[4] The cumulative incidence of at least moderate AI during CF-LVAD support was estimated to be 33% by 2 years.[4] Similarly, Jorde et al followed 232 patients for a median 252 days and estimated a 30% cumulative incidence of at least moderate AI development by 3 years of support.[5] Patients on longer durations of LVAD support tend to demonstrate worse AI than those with short support times, suggesting AI development is both time-dependent and progressive with longer support durations.[3–5]

Several theories exist for the pathophysiologic development of AI during LVAD support, including degeneration of the valve,[7–11] aortic sinus dilation[2–4] and increased transvalvular gradients during states of high LVAD support.[12,13] These theories have been well summarized by John et al.[13] In brief, aortic valve (AV) fusion secondary to fibrinous degeneration arising from the root aspect of the coronary

*Dr. Estep and Dr. Jorde contributed equally as senior authors.

Reprint requests: Jennifer Cowger, MD, Department of Cardiology, St. Vincent Heart Center of Indiana, 8333 Naab Road, #400, Indianapolis, IN 46260. Telephone: +317-338-6666. Fax: +317-338-6066.

E-mail address: jennifercowger@gmail.com

1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2014.09.045

cusps has been noted in pathologic valve specimens of patients supported on both pulsatile and CF-LVADs.[7–11] In patients on substantial LVAD support, pressure generation during isovolumic contraction fails to exceed aortic pressures and the AV remains closed. In the AV degeneration "disuse theory," valves that remain closed during a majority of ventricular systoles are subject to static flow and thrombus formation on the ventricular aspect of the aortic valve.[8,9] Thrombus organization is then hypothesized to promote leaflet fusion.[9] Alterations in blood flow dynamics and aortic pressures also likely contribute to valve degeneration and AI development. Fluid studies by May-Newman et al of proximal aortic cannulation in the CF-LVAD configuration demonstrated high-velocity retrograde flow hitting the root side of the aortic valve.[12,13] High shear stress can lead to AV damage and aortic sinus dilation through smooth muscle cell apoptosis,[14] whereas high retrograde pressures can lead to valve malcoaptation during both diastole and systole, all promoting AI.[3,12,13]

Pre- and intra-operative assessment of the CF-LVAD candidate AV competence

A thorough assessment of the structure and integrity of the AV in the pre-operative period using transthoracic (TTE) and/or transesophageal (TEE) echocardiography is essential for surgical planning. Structural assessment should focus on valve morphology (tricuspid vs bicuspid) and structural alterations (e.g., calcific or previous infectious degeneration) that may impact long-term valve competency. Many valvular lesions may be reasonably tolerated during short durations of CF-LVAD support. However, for those patients in whom prolonged CF-LVAD support can be expected, ample attention must be given to underlying valve pathology with the expectation that AV disease in CF-LVAD supported patients often progresses at a faster rate than that of non-supported patients.

The American Society of Echocardiography (ASE) guidelines for measuring and categorizing AI severity should be followed.[15] The process of grading AI requires a comprehensive examination using a combination of established signs and measurements obtained by Doppler echocardiography, as shown in Table 1. AI measurements apply equally to TTE and TEE. The presence of at least mild to moderate AI is defined by a continuous wave pressure half-time <500 ms, a vena contracta width ≥ 0.3 cm or a jet-width/left ventricular outflow tract (LVOT) ratio $>25\%$. In addition, visualization of holo-diastolic flow reversal in the transverse arch and/or descending aorta with pulse-wave Doppler is suggestive of at least moderate aortic insufficiency.

Table 1 Qualitative and Quantitative Parameters Useful for Grading AI

	Mild	Moderate	Severe
Structural parameters			
LA size	Normal[a]	Normal or dilated	Usually dilated[b]
Aortic leaflets	Normal or abnormal	Normal or abnormal	Abnormal/flail or wide coaptation defect
Doppler parameters			
Jet width in LVOT (color flow)[c]	Small in central jets	Intermediate	Large in central jets; variable in eccentric jets
Jet density (CW)	Incomplete or faint	Dense	Dense
Jet deceleration rate (CW; PHT, ms)[d]	Slow >500	Medium 500–200	Steep <200
Diastolic flow reversal in descending aorta (PW)	Brief early diastolic reversal	Intermediate	Prominent holo-diastolic reversal
Quantitative parameters[e]			
VC width (cm)[c]	<0.3	0.3–0.6	>0.6
Jet width/LVOT width (%)[c]	<25	25–45 mild–moderate, 46–64 moderate–severe	≥65
Jet CSA/LVOT CSA (%)[c]	<5	5–20 mild–moderate, 21–59 moderate–severe	≥60
R Vol (ml/beat)	<30	30–44 mild–moderate, 45–59 moderate–severe	≥60
RF (%)	<30	30–39 mild–moderate, 40–49 moderate–severe	≥50
EROA (cm^2)	<0.1	0.1–0.19 mild–moderate, 0.2–0.29 mod–severe	≥0.30

Adapted from Zoghbi et al.[15] AI, aortic insufficiency; CSA, cross-sectional area; CW, continuous-wave Doppler; EROA, effective regurgitant area; LA, left atrium; LV, left ventricle; LVOT, left ventricle outflow tract; PHT, pressure half time; PW, pulsed-wave Doppler; R Vol, regurgitant volume; RF, regurgitant fraction; VC, vena contracta.

[a]Unless there are other reasons for LV dilation. Normal 2D measurement: LV minor axis ≤ 2.8 cm/m^2, LV end-diastolic volume <82 ml/m^2.

[b]Exception would be acute AI, in which chambers have not had time to dilate.

[c]At Nyquist limit of 50 to 60 cm/s.

[d]PHT is shortened with increasing diastolic LV pressure and vasodilator therapy and may be lengthened in chronic adaptation to severe AI.

[e]Quantitative parameters can sub-classify the moderate AI group into mild-to-moderate and moderate-to-severe AI.