Case Report

Left Ventricular Assist Device Support for Fabry Cardiomyopathy: A Case Series

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ABSTRACT

Patients with restrictive cardiomyopathy due to Fabry disease are often deemed ineligible for left ventricular assist device (LVAD) support due to the risk of suction events with a small LV cavity. We describe the first case series of LVAD support for Fabry disease. LVAD therapy can improve survival, quality of life, and provide clinical stability to start enzyme replacement therapy. Precautions at the time of surgery include rapid treatment of fever to avoid Fabry crises, involvement of a multidisciplinary team, and early initiation of rehabilitation. We describe LVAD support for both bridging and destination therapy.

RÉSUMÉ

Les patients qui ont une cardiomyopathie restrictive due à la maladie de Fabry sont souvent considérés non admissibles aux dispositifs d'assistance ventriculaire gauche (DAVG) en raison du risque de succion lié à la petite cavité VG. Nous décrivons la première série de cas liée aux DAVG en présence de la maladie de Fabry. La thérapie par DAVG peut contribuer à l'amélioration de la survie, de la qualité de vie et offrir une stabilité clinique pour débiter l'enzymothérapie de substitution. Parmi les précautions à prendre au moment de l'intervention chirurgicale figurent le traitement rapide de la fièvre pour éviter les crises de Fabry, la participation de l'équipe multidisciplinaire et la mise en place précoce de la réadaptation. Nous décrivons l'utilisation du DAVG à titre de pont jusqu'à la transplantation et à titre de thérapie définitive.

Background

Patients with restrictive cardiomyopathy (RCM) due to Fabry disease (FD) are often deemed ineligible for left ventricular assist device (LVAD) support due to the risk of suction events with a small LV cavity. We describe the first case series of LVAD support for FD to demonstrate that LVADs are an option for select patients with FD.

Case 1

A 70-year-old man with RCM and a recent diagnosis of FD presented to hospital in cardiogenic shock. Diagnoses include hypertrophic cardiomyopathy with basal septal hypertrophy on magnetic resonance imaging 19 years prior, which was recently determined to be FD based on decreased alpha-galactosidase enzyme activity (< 1 nmol/mL/hour) and a pathogenic variant in the GLA gene, and a secondary prevention intra-cardiac defibrillator for ventricular tachycardia storm. Baseline creatinine was 128 μ mol/L, brain natriuretic peptide (BNP) 1169 ng/L, and brain computed tomography normal. Physical examination showed cold extremities, blood pressure 86/62 mm Hg, heart rate 70 per minute (ventricular pacing), and distended jugular veins. Laboratory testing showed sodium 131 mmol/L, creatinine 299 μ mol/L, lactate 2.3 mmol/L, high-sensitivity troponin I 355 ng/L, BNP 2743 ng/L, ALT 50 U/L, bilirubin 58 μ mol/L, and albumin 33 g/L. Transthoracic

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Ethics Statement: This manuscript is in adherence with the relevant ethical guidelines.

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See page 203 for disclosure information.

Novel Teaching Points

- FD is a lysosomal storage disease that can result in restrictive cardiomyopathy.
- Patients with restrictive cardiomyopathies are often deemed ineligible for LVAD support due to the risk of suction events with a small LV cavity size.
- LVAD support can improve survival, improve quality of life, and provide clinical stability to start enzyme replacement therapy in select patients with FD.
- These select patients often share features of dilated cardiomyopathy including LV dilation and/or LV systolic dysfunction, suggesting a mixed phenotype that may develop in end-stage RCM.
- LVAD support is safe and effective as both bridging and DT in select patients with FD.

echocardiography showed mild LV dilation (left ventricular end-diastolic volume, indexed [LVEDVi] 88 mL/m², LVED dimensions [LVEDD] 63 mm), moderate LV systolic dysfunction (left ventricular ejection fraction 35%) with restrictive filling, mild-to-moderate right ventricular (RV) dilation and dysfunction, moderate-to-severe mitral and tricuspid regurgitation, and moderate aortic regurgitation (Video 1 , view video online). Right heart catheterization showed the following pressures: right atrial 10 mm Hg, RV 30/8 mm Hg, pulmonary artery (PA) 29/20 (mean 24) mm Hg, and wedge 17 mm Hg. Indirect Fick cardiac output was 4.5 L/min (2.3 L/min m²) while administering moderate doses of milrinone and nitroprusside.

The patient had persistent cardiogenic shock, multiorgan dysfunction (creatinine 340 µmol/L, alanine transaminase 227 U/L), and ventricular arrhythmias despite antiarrhythmic therapy. Enzyme replacement therapy (ERT) for FD was considered of little benefit due to the late stage of Fabry cardiomyopathy (Fig. 1). Therefore, he was assessed for advanced therapies. The patient was ineligible for heart

transplantation due to severe peripheral artery disease and a newly identified cecal adenoma.

A HeartMate 3 LVAD (Illinois) was implanted as destination therapy (DT) to improve survival (Video 2 , view video online). At the time of implant, an aortic valve repair with a central coaptation (Park's) stitch and a tricuspid valve repair (60 mm Simplici-T annuloplasty band) were performed. The myocardial tissue was thick and edematous. Given the potential friability of the myocardium, a "cut and sew" technique was employed enabling the ventriculotomy to be explored for potential thrombus/obstruction and to facilitate full-thickness myocardial sutures to secure the apical sewing cuff. The patient subsequently underwent endoscopic resection of the cecal adenoma and was discharged home 3 weeks later. At 8 months of follow-up, he is now receiving ERT for noncardiac disease and remains well, with NYHA Functional Class II symptoms and no emergency department visits or hospitalizations.

Case 2

A 51-year-old man with gene-positive FD resulting in RCM presented with recurrent heart failure hospitalizations and cardiogenic shock. Diagnoses include longstanding FD with RCM (basal anterolateral and inferolateral hypertrophy, posterior wall scar, primary prevention intracardiac defibrillator), end-stage kidney disease requiring hemodialysis, acroparesthesias, hearing loss, and extensive white matter changes of the brain consistent with chronic small vessel ischemia. These symptoms stabilized while on ERT with agalsidase alfa with urinary Gb3 monitoring for 14 years. Physical examination showed cold extremities, blood pressure 106/78 mm Hg, heart rate 70 per minute (ventricular paced), and distended jugular veins. Laboratory testing showed sodium 138 mmol/L, creatinine 528 (intermittent hemodialysis) µmol/L, lactate 0.9 mmol/L, BNP 2717 ng/L, international normalized ratio 1.4, alanine transferase 24 U/L, bilirubin 14 µmol/L, and albumin 39 g/L. Transthoracic echocardiogram showed severe LV dilation (LVEDVi 128 mL/m², LVEDD

Figure 1. Histologic appearance of the myocardial apical (LVAD) core specimen from patient 1. (A) Haematoxylin and eosin stain; myocytes demonstrate marked vacuolated appearance (septated clearings within the cytoplasm), as well as large nuclei; scale bar 200 µm. (B) Modified Movat's pentachrome stain; myocytes are highlighted in red, again with marked vacuolization, and interstitial fibrosis is highlighted in yellow; scale bar 200 µm. (C) Electron microscopy demonstrating numerous lamellar bodies, a known and characteristic ultrastructural pattern of degeneration in Fabry's disease; scale bar 500 nm. LVAD, left ventricular assist device.

Figure 2. Photograph of the gross heart explant specimen from patient 2, demonstrating the placement of the left ventricular assist device (LVAD) into the septal side of the apex of the left ventricle. **Scale bar** 1 cm. HeartMate II LVAD (Abbott, Abbott Park, IL) reproduced with permission of Abbott, Illinois.

63 mm) and dysfunction (left ventricular ejection fraction 24%), a moderately dilated RV with moderate-to-severe dysfunction, moderate calcific aortic stenosis, and severe mitral and tricuspid regurgitation (Video 3 view video online). Right heart catheterization showed the following pressures: right atrial 17 mm Hg, PA 64/40 (mean 50) mm Hg, and pulmonary artery wedge pressure 31 mm Hg while administering moderate dose of dobutamine. The transpulmonary gradient was 19 mm Hg, Fick cardiac output 2.98 L/min, and Fick cardiac index 1.62 L/min m². The patient required advanced heart failure therapy. Precapillary pulmonary hypertension contraindicated heart transplantation. Therefore, he received a HeartMate II LVAD (Illinois) as a bridge-to-candidacy.

After 3 months of LVAD support, his pulmonary pressures normalized and he received a heart transplant. At explantation, the LVAD was inserted into the septal aspect of the left ventricular apex (Fig. 2) and there was marked ventricular wall hypertrophy (Supplemental Fig. S1). Thrombus was also identified within the LVAD. The patient was discharged after 8 days, received a kidney transplant at 1 year, and remains well at 3 years after heart transplant.

Discussion

LVADs improve survival and quality of life for select patients with advanced heart failure. However, they are generally avoided in patients with FD and RCM because of the risk of

RV failure as well as the risk of suction events and inflow cannula obstruction with a small LV cavity size. As a result, only 2% of LVAD recipients have RCM or hypertrophic cardiomyopathy.¹ Indeed, patients with RCM were excluded in the most recent randomized trial of LVAD support.²

We describe 2 patients with FD who were ineligible for heart transplantation. The first received a DT LVAD to improve survival, improve quality of life, and provide clinical stability to start ERT. The second patient received a bridge-to-candidacy LVAD for pulmonary hypertension and later received a heart transplant and sequential kidney transplant. Carefully selected patients with FD may benefit from LVAD and/or heart transplantation, despite FD with multisystem involvement being a longstanding contraindication. In the absence of specific criteria for LVAD support in FD, we extrapolate criteria from the RCM population. Larger LV end-diastolic and end-systolic dimensions are associated with improved survival.³ These select patients often share features of dilated cardiomyopathy including LV dilation and/or LV systolic dysfunction, suggesting a mixed phenotype that may develop in end-stage RCM. Conversely, an LV end-diastolic diameter ≤ 46 mm is associated with increased mortality after LVAD implantation.³ We avoid LVAD support for FD in patients with severe and irreversible multisystem involvement. Precautions at the time of surgery include rapid treatment of fever to avoid Fabry crises, involvement of a multidisciplinary team, and early initiation of rehabilitation. To our knowledge, this is the first case series of LVAD support for FD.

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Disclosures

V.R. is a consultant to Medtronic and Abbott, and serves on the North American Surgical Advisory board of Medtronic. The rest of the authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjcopen.ca/> and at <https://doi.org/10.1016/j.cjco.2020.09.024>.