First reported dual-chamber leadless pacemaker in a patient with orthotopic heart transplant

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Introduction

Permanent pacemaker implantation is needed in approximately 5% of patients post–orthotopic heart transplant (OHT).[1–6] The primary indications for permanent pacing post-OHT include sinus node dysfunction occurring more often in the early postoperative phase (within 30 days following OHT) and atrioventricular block occurring more often in the later phase (>30 days post-OHT).[1,3,5] Early postoperative sinus node dysfunction can be related to cardiac denervation or autonomic dysfunction, surgical injury to the sinus node, sinus node ischemia, or acute rejection.[1,4,6,7] Notably, the rate of early sinus node dysfunction and the need for permanent pacemaker post-OHT has significantly decreased with the use of bicaval anastomosis compared with biatrial anastomosis.[1,4,7] Indications for permanent pacing in the later postoperative phase (>30 days post-OHT) include late sinus node dysfunction and high-grade atrioventricular block related to coronary allograft vasculopathy with nodal ischemia and chronic graft rejection.[1,4,6] Owing to the high infection risk in this immunosuppressed population, leadless pacemakers are emerging as a safe and effective alternative to conventional transvenous pacemakers in heart transplant recipients.[3,4]

There are a few case reports and case series of OHT recipients who have undergone leadless pacemaker placement for both sinus node dysfunction and atrioventricular block. Most of these patients received the Medtronic Micra™ VR single-chamber leadless pacemaker,[2,3,8] which provides VVI pacing capability. One patient received the Medtronic Micra AV single-chamber leadless pacemaker with atrial-synchronous VDD pacing via tracking of mechanical atrial contraction.[5] A recent case discussed the first OHT recipient implanted with the active fixation Abbott Aveir™ VR leadless pacemaker as part of the LEADLESS II IDE trial.[6] This retrievable device allows for single-chamber right ventricular pacing with the potential for a future upgrade to a dual-chamber leadless pacing system with an implant of a leadless Aveir in the right atrium.

We are reporting a unique case of implantation of the Abbott Aveir DR dual-chamber leadless pacemaker (Abbott, Abbott Park, IL) in a cardiac transplant recipient, with special consideration of atrial device placement and programming owing to dual P-wave phenomenon. This device was

KEY TEACHING POINTS

- This is the first reported case of implantation of the Abbott Aveir DR dual-chamber leadless pacemaker (Abbott, Abbott Park, IL) in a cardiac transplant recipient, with special consideration of atrial device placement and programming owing to the presence of dual P-wave phenomenon post–cardiac transplant.
- The Aveir can map intracardiac electrical measurements prior to device deployment to optimize device location and function and minimize repositioning attempts. In our patient, this feature was used during atrial device placement to ensure exclusive sensing and tracking of donor P waves and not recipient P waves in the setting of dual P-wave phenomenon.
- Dual-chamber leadless pacemakers provide necessary atrial pacing and atrioventricular synchrony with a lower infection risk than conventional transvenous devices, which is advantageous in immunosuppressed heart transplant recipients.
- The limitations of leadless pacemakers include the need for an experienced operator in the setting of complex cardiac anatomy, and the present inability to integrate leadless pacemakers with defibrillation or cardiac resynchronization systems.

KEYWORDS Chronotropic incompetence; Dual-chamber leadless pacemaker; Dual P-wave; Orthotopic heart transplant; Terbutaline-induced atrial fibrillation

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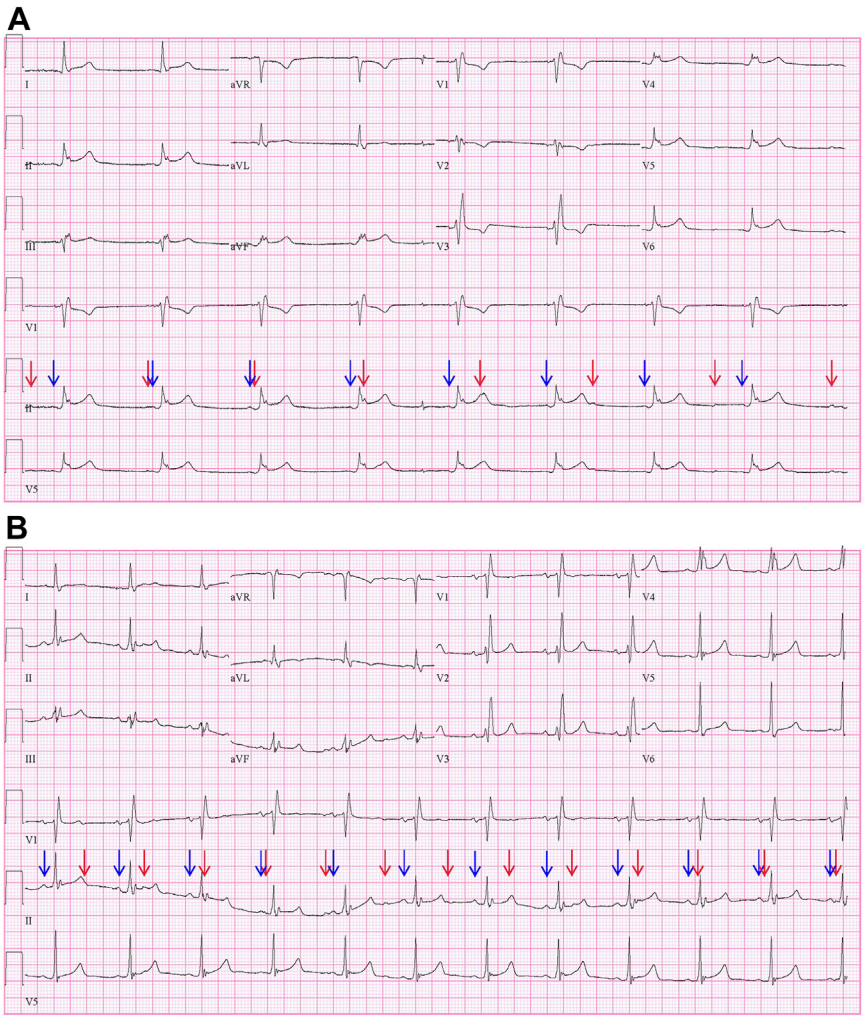

Figure 1 Electrocardiograms post–orthotopic heart transplant exhibiting dual P-wave phenomenon. **A:** Electrocardiogram on postoperative day 3 showing sinus bradycardia with right bundle branch block and dual P-wave physiology. **B:** Electrocardiogram 3 months postoperatively showing normal sinus rhythm with right bundle branch block and dual P-wave physiology. This electrocardiogram was obtained prior to pacemaker implant. Blue arrows indicate donor P waves with associated QRS complexes (intact atrioventricular conduction). Red arrows indicate recipient P waves from electrically dissociated remnant atrial tissue (no conduction to ventricles).

investigational at the time of implant as part of the Abbott Aveir Dual-Chamber Leadless i2i IDE clinical trial, conducted at Advocate Aurora St. Luke's Medical Center in Milwaukee, Wisconsin.[9]

Case report

The patient is a 43-year-old man with a history of nonischemic cardiomyopathy with reduced ejection fraction, who presented with cardiogenic shock requiring mechanical support with an intra-aortic balloon pump and pulmonary artery catheter hemodynamic monitoring. Additional past medical history included COVID pneumonia, hypertension secondary to pheochromocytoma with normalization of blood pressure after left adrenalectomy, dyslipidemia, and diabetes mellitus type II. Coronary angiogram showed significant multivessel coronary artery disease suggestive of ischemic cardiomyopathy superimposed on nonischemic cardiomyopathy, with the severity of left ventricular dysfunction out of proportion to the degree of coronary artery disease. Left ventricular ejection fraction was as low as 5%–10% on echocardiogram. He was evaluated for advanced heart failure options and underwent OHT with modified biatrial anastomosis. This surgical technique is a bicaval anastomosis with residual recipient right atrial tissue left intact. Multiple post-transplant electrocardiograms were significant for dual P waves at different sinus rates, representing dissociated atrial depolarizations originating from recipient tissue and donor atrial depolarizations that conducted to the ventricles (Figure 1A and 1B).

Post–cardiac transplant he had sinus node dysfunction with junctional escape rhythm owing to transplant ischemic injury, which resolved by postoperative day 8. After discharge he had symptomatic chronotropic incompetence with heart rates <50 beats per minute (bpm), for which he was started on terbutaline on postoperative day 22, with improvement in heart rates to 80 bpm. He developed atrial

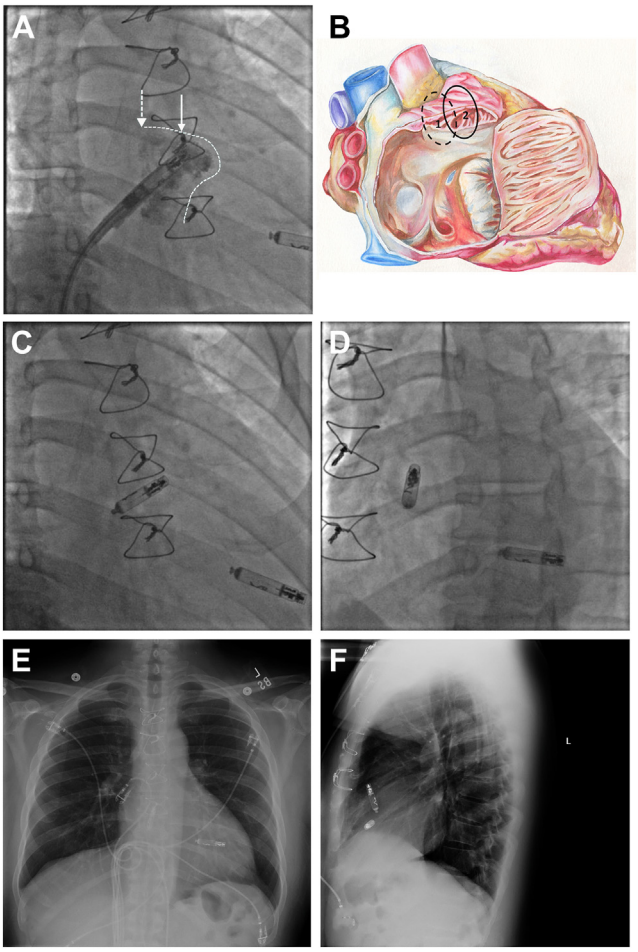

Figure 2 Radiologic images obtained during and after implantation of Abbott Aveir DR dual-chamber leadless pacemaker (Abbott, Abbott Park, IL), with associated illustration of atrial implant locations. **A:** Fluoroscopy RAO 30. Iodinated contrast injection highlights the inner border of the right atrial appendage (dashed white line). The Aveir atrial leadless pacemaker was initially deployed at the base of the right atrial appendage (*dashed white arrow*). The device was subsequently repositioned to the mid right atrial appendage (*solid white arrow*). **B:** Implant locations in the right atrium for the Aveir atrial leadless pacemaker. The atrial leadless pacemaker was initially deployed at the base of the right atrial appendage (position 1). At this location, there was equal sensing of both donor and recipient P waves. The device was repositioned to the mid right atrial appendage (position 2), with resultant increased amplitude of donor P waves and decreased amplitude of recipient P waves. This resulted in exclusive sensing and tracking of donor P waves, regardless of atrial sensitivity setting. **C, D:** Fluoroscopy RAO 30 (C) and LAO 31 (D). Final dual-chamber leadless pacemaker position post-deployment. **E, F:** Chest radiograph posteroanterior (E) and lateral (F) obtained the day after placement of Aveir DR dual-chamber leadless pacemaker. LAO = left anterior oblique; RAO = right anterior oblique.

fibrillation with terbutaline on postoperative day 25. Owing to his dependency on terbutaline for maintenance of adequate heart rates and consequent atrial arrhythmia, he was referred for permanent pacemaker placement with discontinuation of terbutaline. The option of a conventional transvenous dual-chamber pacemaker vs a dual-chamber leadless pacemaker was discussed. The leadless approach offered significant advantages for our young patient, who is on chronic immunosuppressive therapy, including decreased risk of infection, absence of chronic indwelling leads (which predispose to subclavian vein stenosis and occlusion), and the ability to retrieve the device in the future. The patient opted for a dual-chamber leadless pacemaker implant with the Aveir DR as part of a clinical research trial.

The patient presented 3 months after OHT for scheduled placement of an Aveir DR dual-chamber leadless pacemaker. After it was confirmed that the patient was well sedated, the delivery system was advanced through the right femoral venous access. First, the right ventricular leadless pacemaker was deployed uneventfully into the right ventricular apical septum. A second device was advanced into the right atrium using the same femoral access. Figure 2 illustrates a series of fluoroscopy images in which anatomical landmarks and iodinated contrast injection were used for atrial device placement. On initial placement of the atrial device into the base of the right atrial appendage (Figure 2B, position 1), mapping of the atrial electrogram before device deployment showed equal and persistent sensing of both donor and recipient P waves, as noted by 2 distinct P-wave morphologies at different rates, with only 1 morphology associated with QRS complexes. Despite adjustment of atrial sensitivity, both P waves were equally sensed at that position. The Aveir leadless pacemaker allows for electrogram mapping and device repositioning prior to active fixation to optimize device location and function. Thus, the atrial device was repositioned to the mid right atrial appendage (Figure 2B, position 2), resulting in increased amplitude of donor P waves and decreased amplitude of recipient P waves. This resulted in exclusive sensing of donor P waves, even after adjusting atrial sensitivity to the most sensitive setting (Figure 3). Intact atrioventricular conduction with atrial pacing was confirmed. After deployment and sensitivity programming, both the atrial and the ventricular leadless pacemakers were paired successfully with implant-to-implant (i2i) communication and were functioning appropriately. The final interrogation of the devices showed an atrial threshold of 2.5 V at 0.4 ms, sensing at 1.0 mV, and impedance of 320 ohms; and a ventricular threshold of 0.5 V at 0.4 ms, sensing at 9.1 mV, and impedance of 1210 ohms. The devices were programmed to DDDR at a rate of 60–120 bpm. Device interrogation on postimplant day 1 showed rapid improvement in atrial threshold of 0.25 V at 0.4 ms, sensing at 2.8 mV, and impedance of 350 ohms; and ventricular threshold of 0.25 V at 0.4 ms, sensing at 12.1 mV, and impedance of 870 ohms. There was 55% atrial pacing and 9% ventricular pacing. Ventricular-to-atrial i2i communication was 69%, and atrial-to-ventricular i2i communication was 90%. The chest radiograph showed stable device positions the day after implant (Figure 2E and 2F).

On follow-up 23 days post–pacemaker implant, the patient was doing well, without cardiac symptoms or postprocedural complications. Terbutaline had been discontinued at the time of the device implant. He had required 76% atrial pacing and 7% ventricular pacing. Ventricular-to-atrial i2i communication improved to 89% and atrial-to-ventricular i2i was 91%. Device interrogation showed stable atrial threshold of

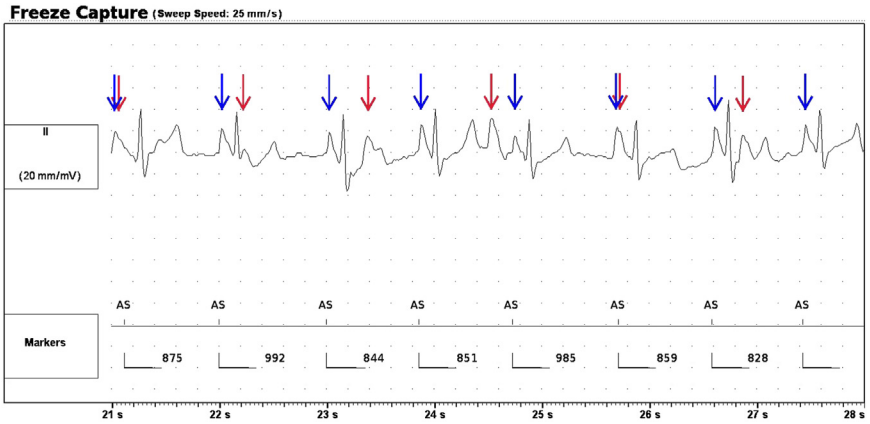

Figure 3 Intracardiac electrograms after implantation of Abbott Aveir DR dual-chamber leadless pacemaker (Abbott, Abbott Park, IL). Lead II and atrial marker channel show that after atrial leadless pacemaker repositioning, donor P waves (*blue arrows*) are sensed by the atrial leadless pacemaker, whereas recipient P waves (*red arrows*) are not sensed. AS = atrial sensed.

0.5 V at 0.4 ms, sensing at 4.1 mV, and impedance of 370 ohms; and ventricular threshold of 0.5 V at 0.4 ms, sensing at 16.9 mV, and impedance of 620 ohms.

Discussion

To our knowledge, this is the first reported case of implantation of the Abbott Aveir DR dual-chamber leadless pacemaker in a cardiac transplant recipient. It is also the first case of implantation of a leadless pacemaker post-OHT, with special consideration of atrial device placement and programming owing to the presence of dual P-wave phenomenon. Regarding traditional transvenous pacemaker lead placement, a review article by DeFilippis and colleagues[4] advises against positioning the lead in the posterolateral recipient remnant right atrial tissue, and to confirm the association between a sensed P wave and the QRS complex and/or intact atrioventricular conduction with atrial pacing. There is no discussion in the literature about programming leadless pacemakers in the setting of dual P-wave phenomenon, as this technology has been investigational until recently.

The Aveir DR leadless pacemaker is the only available leadless pacemaker with the ability to map intracardiac electrical measurements, including assessment of current of injury prior to device deployment. The present case demonstrates the advantages of this feature, which allowed us to map the right atrial appendage and localize a site at which we would have adequate discrimination between donor and recipient P waves. Thus, we were able to ensure accurate sensing and tracking of donor P waves to maintain normal atrioventricular synchrony.

Compared to conventional transvenous pacemakers, leadless pacemakers are safer (lower complication and infection rate), with comparable efficacy and battery life,[3–6,8] making these devices an alternative therapeutic option in an immunocompromised population of heart transplant recipients on chronic immunosuppressive therapy. Transvenous pacemakers have a higher risk of complications and morbidity, including infection related to transvenous leads and subcutaneous or submuscular generator pockets, pocket hematomas, tricuspid valve regurgitation, lead and insulation fractures, and the risk of transvenous lead extraction, compared to leadless pacemakers.[2,5,10] Leadless pacemakers can also be implanted with occluded upper-extremity veins or complex upper-extremity anatomy and can be considered for patients in whom there is a desire to preserve upper-extremity vascular access (eg, in chronic kidney disease with anticipated future need for hemodialysis).[2,4,5]

Disadvantages of leadless pacemakers have historically included the lack of atrioventricular synchrony with single-chamber devices and the high risk of chronic retrieval at end of service.[11] The Aveir VR leadless pacemaker with active fixation helix has enabled safe and successful chronic retrieval of this device. This leadless pacemaker also allows for intracardiac electrogram mapping prior to active fixation to optimize device placement.[12] The Aveir DR dual-chamber leadless pacemaker additionally allows for atrioventricular synchrony as well as atrial pacing. At this time, leadless pacemakers cannot be integrated with defibrillation or cardiac resynchronization systems, which are often required in a heart failure population. Additionally, leadless pacemaker implantation can be challenging, particularly in the setting of atypical cardiac anatomy. Our physician had experience implanting approximately 100 leadless pacemakers, including Micra, Aveir VR, and Aveir DR as part of a clinical trial. Implantation of leadless pacemakers by experienced and skilled operators should be considered in challenging cases.

The results of the first clinical trial using the Aveir DR have recently been published,[9] and this device was subsequently approved by the U.S. Food and Drug Administration on July 5, 2023.

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References

1. Xu Q, Xu L-H, Qu B-M, Xue Q. Experience on temporary and permanent cardiac pacing after heart transplantation. Oncotarget 2018;9:s1162–s1167.
2. Araj FG, Morlend RM, Daniels JD. Leadless pacemaker implant after heart transplant. Am J Cardiol 2019;124:455–456.
3. Rordorf R, Savastano S, Bontempi L, et al. Leadless pacing in cardiac transplant recipients: primary results of a multicenter case experience. J Electrocardiol 2020; 60:33–35.
4. DeFilippis EM, Rubin G, Farr MA, et al. Cardiac implantable electronic devices following heart transplantation. JACC Clin Electrophysiol 2020; 6:1028–1042.
5. Mistry A, Assuvinkumar S, Gador G, Somani R. Atrioventricular synchronous pacing using leadless pacemaker in a heart transplant patient. BMJ Case Rep 2021;14:e243365.
6. Trivedi R, Kleinhans A, Doshi R. A first report of an active fixation leadless pacemaker in a patient post orthotopic heart transplant. EP Lab Digest 2022;22:1–5.
7. Huang WA, Woo JP, Boyle NG. The rogue P-wave: atrial dissociation following bicaval heart transplantation. J Innov Card Rhythm Manag 2019; 10:3472–3475.
8. Martínez-Sande JL, García-Seara J, González-Melchor L, et al. Leadless pacemaker implantation in a transplanted heart. Rev Esp Cardiol (Engl Ed) 2019; 72:270–272.
9. Knops RE, Reddy VY, Ip JE, et al. A dual-chamber leadless pacemaker. N Engl J Med 2023;1–11.
10. Rubin GA, Wan EY. Leadless pacemakers after cardiac transplantation. ASAIO J 2020;66:e57.
11. Medtronic. Micra pacemakers - transcatheter pacing systems. https://www.medtronic.com/us-en/healthcare-professionals/products/cardiac-rhythm/pacemakers/micra-pacing-system.html. Accessed May 30, 2023.
12. Abbott. Why the Aveir VR Leadless Pacemaker. https://www.cardiovascular.abbott/us/en/hcp/products/cardiac-rhythm-management/pacemakers/aveir-vr-leadless-pacemaker/why.html. Accessed May 30, 2023.