Beyond the Wires: A Case of Leadless Pacemaker–Mediated Tricuspid Regurgitation

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INTRODUCTION

Significant tricuspid regurgitation (TR) is associated with unfavorable outcomes irrespective of etiology, concurrent structural heart disease, or pulmonary hypertension.[1-5] With the emergence of transcatheter therapies as potential therapeutic options in this high-risk population, the tricuspid valve (TV) anatomy and pathophysiology are being evaluated more thoroughly than ever before. Cardiac device–induced TR is common and is associated with incremental morbidity and mortality.[6-8] The primary interventional approach in these situations is lead extraction followed by alternative modalities of pacing, including the leadless pacemaker (LP) systems. Leadless pacemakers were shown to be a safe and effective alternative pacing mode, with a growing acceptance and utilization in the medical community. With greater use, it is apparent that LPs can cause unwanted and occasionally meaningful clinical adverse effects.[9,10] We report the case of a patient with severe and progressively symptomatic TR after an LP implant and review the current literature and gaps in knowledge.

CASE PRESENTATION

A 59-year-old female patient was referred to the local valve clinic from the renal transplantation team regarding the presence of symptomatic severe TR. Her medical history is significant for paroxysmal atrial fibrillation, systemic hypertension, and end-stage renal disease, status post–renal transplant with subsequent graft failure and reinitiation of intermittent hemodialysis. In 2017, a transvenous permanent pacemaker (PPM) was placed for sick sinus syndrome, with a preprocedural echocardiogram showing mild to moderate TR with structurally normal size and function of right-sided chambers, no significant cardiac structural abnormalities, and estimated pulmonary pressures < 40 mm Hg. In 2018, the patient had infective endocarditis related to the pacemaker system, which required lead extraction and antibiotics. Post–lead extraction echocardiogram demonstrated similar findings to the echo done in 2017 with mild to moderate TR (Figure 1, Video 1). A few weeks later after resolution of infective endocarditis, an LP was placed due to the persistence of symptomatic bradycardia. She subsequently developed progressive dyspnea on exertion (New York Heart Association II-III) and abdominal distension that persisted despite maximally tolerated diuresis and fluid removal by hemodialysis. On physical exam, the patient's blood pressure was 90/63 mm Hg, heart rate was 61 bpm, respiratory rate was 18 rpm, oxygen saturation was 93% on room air, and she was afebrile. A grade 2/6 holosystolic murmur on the lower left sternal border was noted, along with increased jugular venous pressure, cv-waves on the jugular venous pulse assessment, pedal edema, and ascites. Laboratory tests showed no major abnormalities other than abnormal renal function. A transthoracic echocardiogram noted an isolated significant increase in severity of TR with evidence of TV leaflet tethering (Figures 2 and 3, Videos 2 and 3). The TV annulus measured 34 mm. No clear evidence of TV trauma after PPM lead extraction was detected. Given the timing of onset after lead extraction, the patient was referred for transesophageal echocardiogram to further define the underlying mechanism of regurgitation.

The transesophageal echocardiogram confirmed the degree of TR (Figures 4-6, Video 4) with the primary mechanism of apical tethering of the leaflets with a central coaptation gap. The largest coaptation gap was central, with a 3-5 mm gap relative to the septal leaflet, and no secondary leaflet trauma was detected (Figures 7-9, Videos 5-7). The LP was visualized in the right ventricle (RV) distal to the largest coaptation gap interacting with the subvalvular apparatus (Figure 8, Video 6). Notably, in keeping with the progressive increase of TR severity, systolic flow reversal in the hepatic veins became evident and prominent throughout follow-up (Figure 9).

VIDEO HIGHLIGHTS

Video 1: Transthoracic echocardiogram after lead extraction and prior to LP insertion showing mild to moderate TR in an apical four-chamber view.
Video 2: Transthoracic echocardiogram after LP insertion showing severe TR in a focused RV apical view.
Video 3: Transthoracic echocardiogram after LP insertion showing severe TR in an RV inflow view.
Video 4: Biplane imaging of the TV showing the large regurgitation jet from a deep transesophageal view.
Video 5: Midesophageal view showing the tethered valve leaflets and the malcoaptation. The septal leaflet is more prominently restricted.
Video 6: Biplane imaging from a midesophageal view showing the tethered leaflets, particularly the septal leaflet, and the LP entangled and pulling the subvalvular apparatus.
Video 7: Single-beat three-dimensional data set showing malcoaptation of the TV.

View the video content online at www.cvcasejournal.com.

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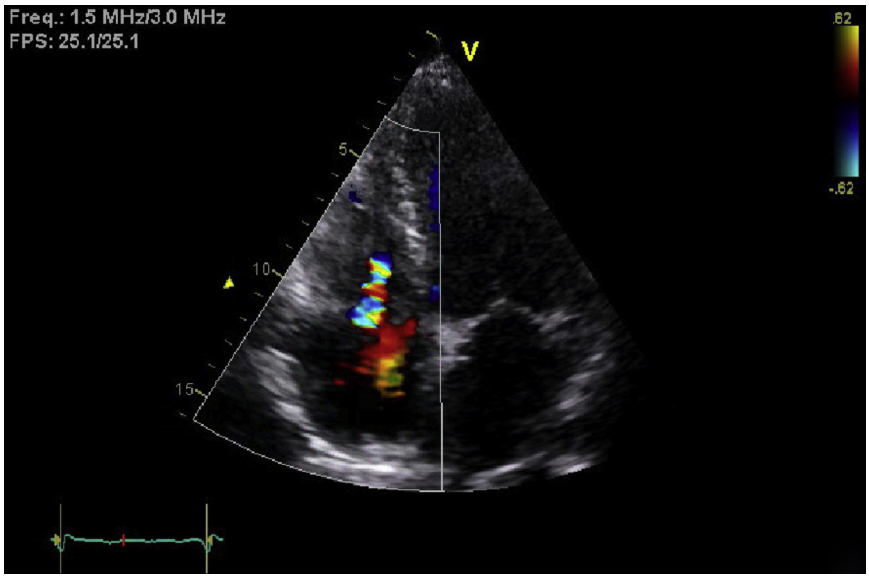

Figure 1 Transthoracic echocardiogram after lead extraction and prior to LP insertion showing mild to moderate TR in an apical four-chamber view.

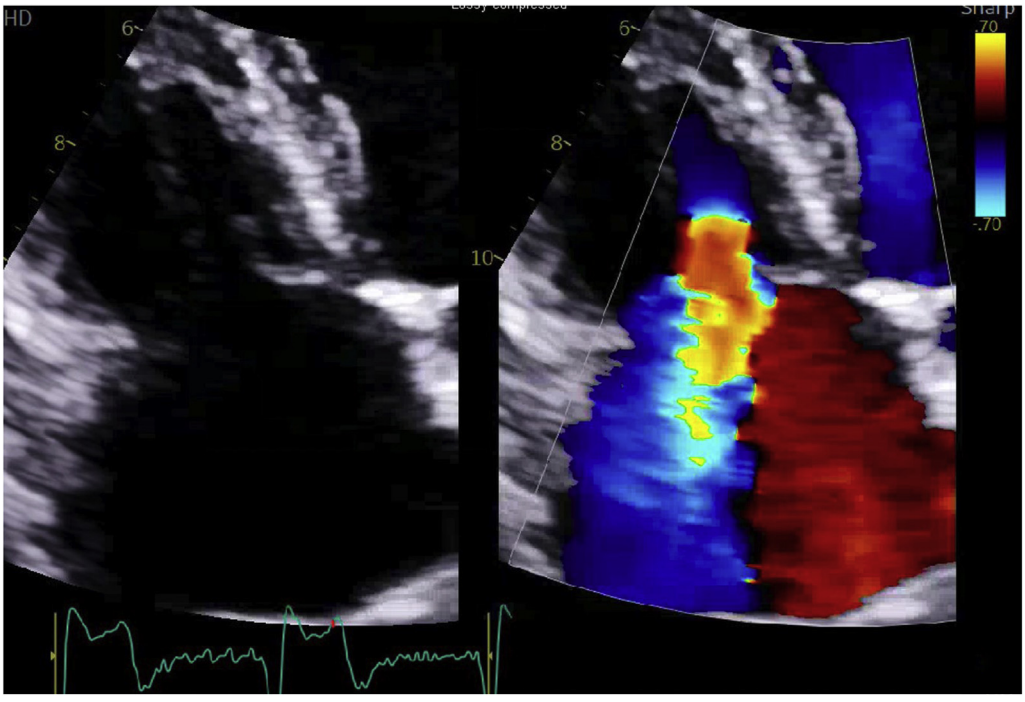

Figure 2 Transthoracic echocardiogram after LP insertion showing severe TR on a focused RV apical view.

Intervention of the TR is currently being evaluated as it is deemed to be a major barrier to proceeding with a second renal transplant for this relatively young patient. In preparation for this, right heart catheterization has been completed, and a mean pulmonary artery pressure of 16 mm Hg, pulmonary capillary wedge pressure of 8 mm Hg, pulmonary vascular resistance of 1.7 Woods units, and Fick cardiac output and index of 4.8 and 2.8, respectively, have been noted. The right heart catheterization data are consistent with the pacemaker as the primary TR mechanism and current volume optimization. No obstructive coronary disease was present on coronary angiography. The high risk and controversial benefits of TV interventions coupled with the patient's own surgical risk (Euroscore II was calculated at 7.1% for in-hospital mortality) make her unlikely to be a good surgical candidate. Hence, given the favorable TV anatomy, a strong consideration to pursue a catheter-based leaflet intervention (edge-to-edge repair) will be favored rather than attempting to extract this three-year-old

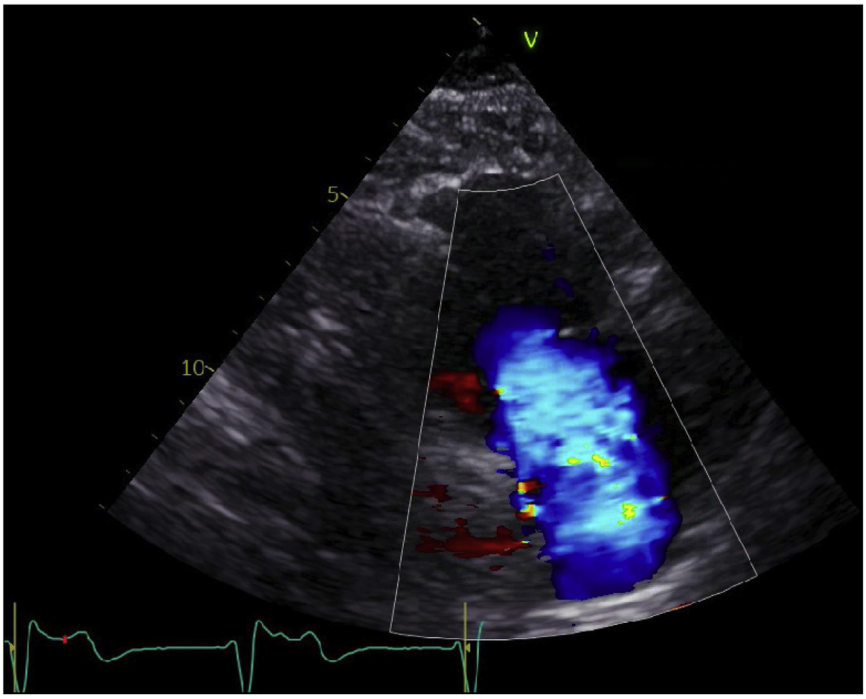

Figure 3 Transthoracic echocardiogram after LP insertion showing severe TR on an RV inflow view.

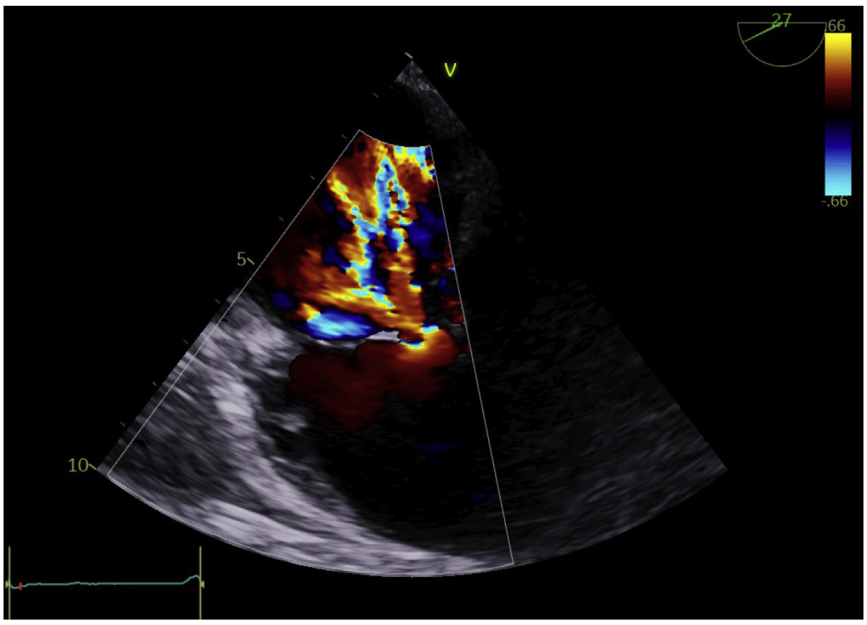

Figure 4 Transesophageal deep esophageal RV focused view showing a broad tricuspid regurgitant jet.

device in this pacemaker-dependent patient and risk further TV injury.

DISCUSSION

Whether in isolation or accompanying left heart disease or pulmonary hypertension, significant degrees of TR have been shown to worsen quality of life and decrease short- and long-term survival.[1-5] Contemporary studies show that PPMs and implantable cardioverter-defibrillators (ICDs) can cause a nonnegligible rate of significant TR (greater than or equal to moderate) in up to 5% of overall cases, with an evident increase in heart failure hospitalization and mortality rates.[6-8,11] These devices can affect TV function by one or more mechanisms, including perforation or impingement of one or more leaflets, lead entanglement into the subvalvular apparatus, RV dyssynchrony, and cardiac device–related endocarditis with associated direct infectious damage to the valvular structure or leaflet flail/avulsion after lead extraction (Table 1). While LPs theoretically avoid multiple of

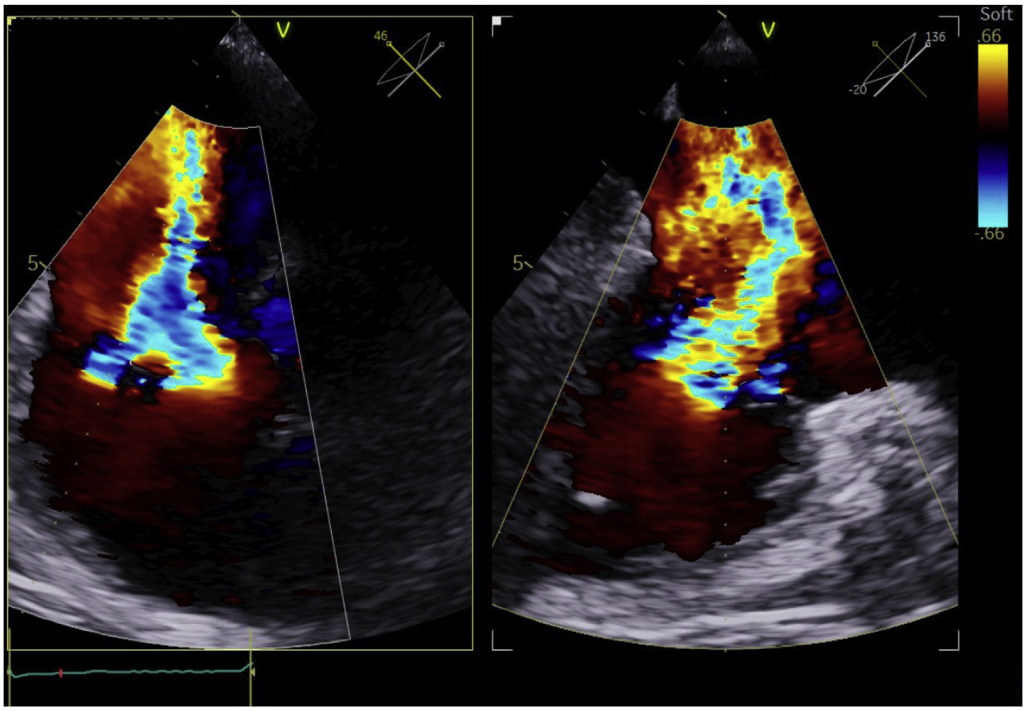

Figure 5 Biplane imaging from a deep esophageal view showing the severe TR.

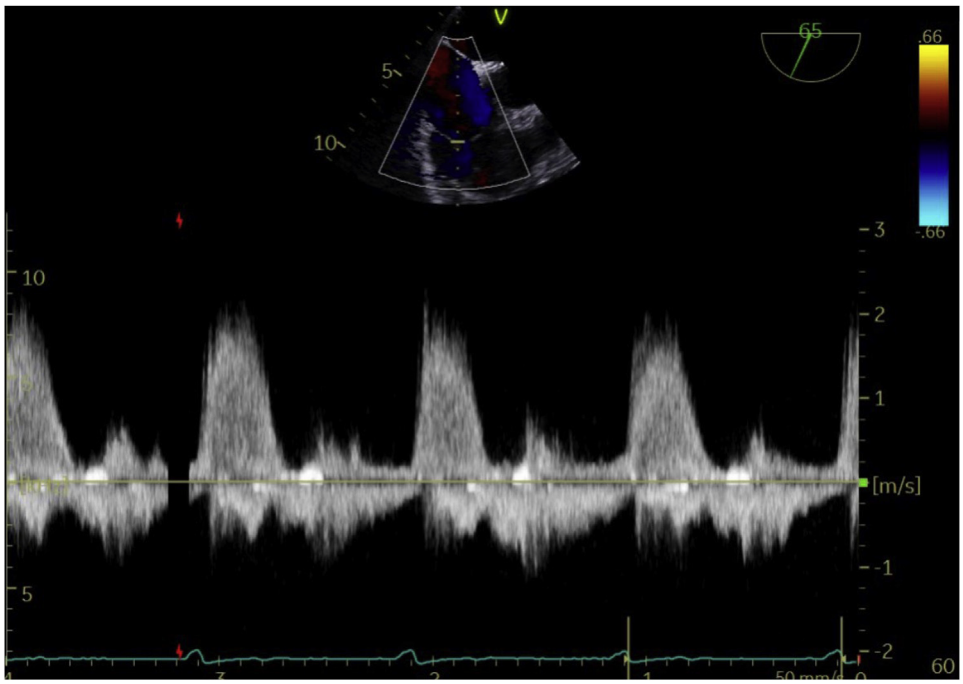

Figure 6 Continuous-wave Doppler of the TV showing a very dense profile and early peaking regurgitant jet consistent with severe TR.

these potential device-mediated TR causes, the pacemaker interaction with the complex TV subvalvular apparatus remains. The data on significant LP-induced TR are limited. In one of the first reports specifically addressing this issue, a French study assessing 23 consecutive patients showed that in patients chronically implanted with LPs there were no significant changes in heart structure and function observed, especially concerning the RV and TV. Only one patient developed significantly increased TV regurgitation, without abnormal leaflet motion, suggesting a non-device-mediated mechanism.[12] More recently, Beurskens *et al*[13] showed that after LP implant, 43% of patients have worsening degrees of TR at 1 year compared with baseline, with a twofold increase in the rates of moderate to severe TR. When compared with a dual-chamber transvenous control group, the LP group had similar rates of changes in TR. Consistent with our case,

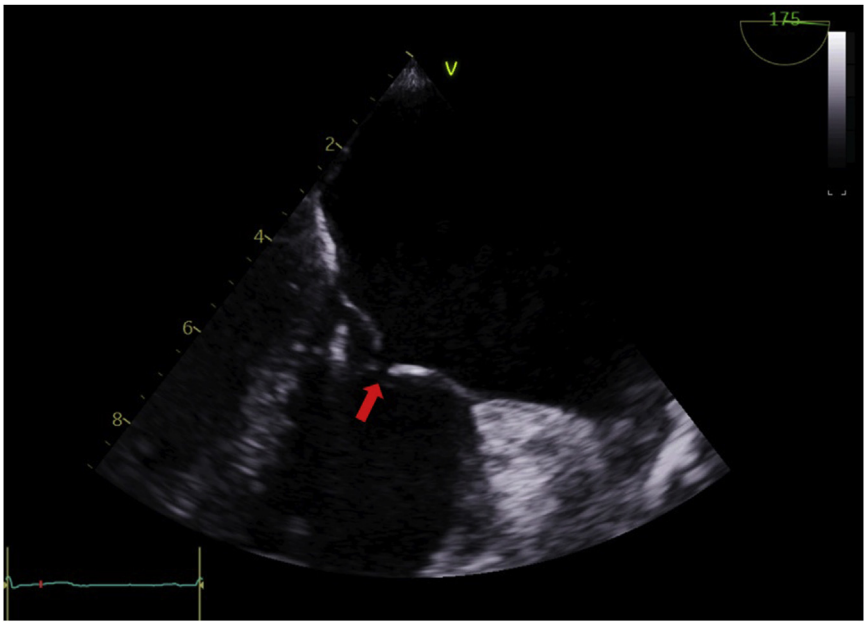

Figure 7 Transesophageal echocardiogram in deep esophageal view demonstrating tethering of the TV leaflets with malcoaptation (*red arrow*).

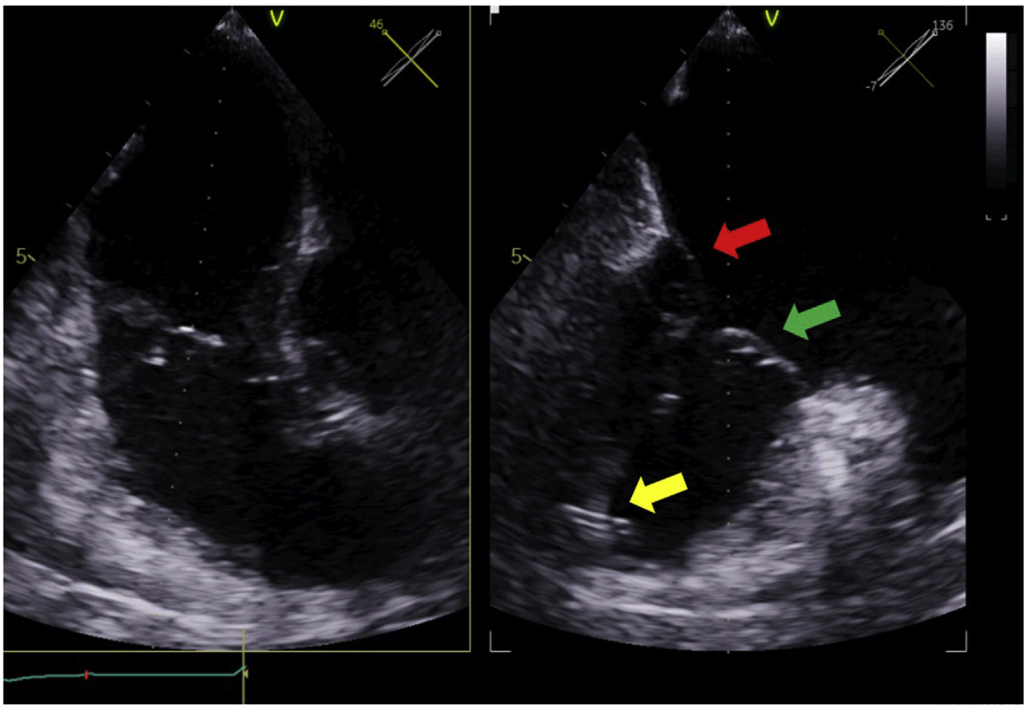

Figure 8 Transesophageal echocardiogram with biplane imaging across the TV (RV inflow-outflow view at 45°) from a deep esophageal view showing the LP in the RV apex (*yellow arrow*). The LP is shown to be interacting with the subvalvular apparatus, with consequent papillary muscle and chordae tendinae restriction; leaflet tethering of the septal leaflet is shown by the *red arrow*, and leaflet tethering of the anterior leaflet is shown by the *green arrow*.

the authors suggest that the likely mechanism for triggering or worsening TR in these individuals is the interference with the subvalvular apparatus, with a more septal device position increasing the risk of worsening TR by five-fold.[13] One factor of these discordant incidences of TR may be secondary to underdiagnosis. As with conventional lead-based PPMs, if systematic imaging surveillance is not completed, the often longer latency of signs and symptoms associated with significant TR likely results in underestimation of its prevalence after device insertion.[7] These patients often also present late in the clinical course of TR when significant right-sided remodeling has occurred, making

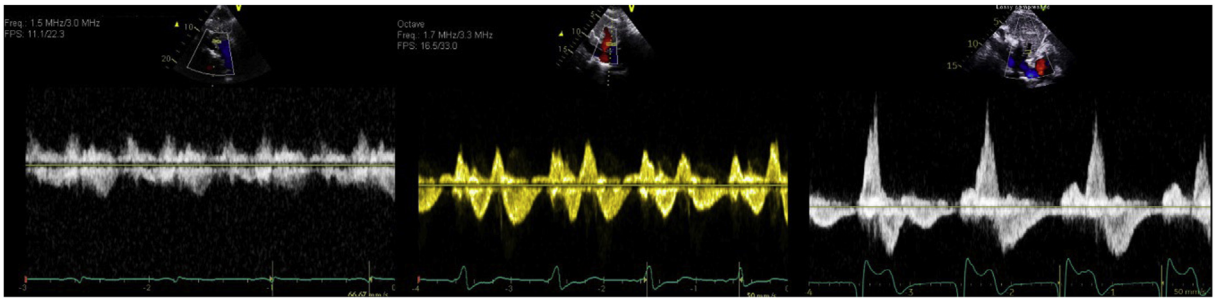

Figure 9 From left to right, image 1 shows no evident systolic flow reversal in the hepatic veins prior to LP implant; images 2 and 3 shows systolic reversal after LP implant on subsequent transthoracic echocardiograms done in 2019 and 2021, respectively.

Table 1 Mechanisms of PPM and ICD-related TR

Mechanism	Echocardiographic features*	Suggested definitive treatment†
Leaflet perforation by direct lead damage	Focal leaflet tissue disruption with color Doppler flow across the defect; regurgitant jet can be central or eccentric.	Surgical or percutaneous valve replacement
Leaflet impingement	Direct interaction of the PPM or ICD lead pushing the leaflet away from its original position with consequent restricted motion in systole; regurgitant jet is usually eccentric.	Lead repositioning or extraction, with or without associated valve repair or replacement (surgical or percutaneous)
Lead entanglement into the subvalvular apparatus‡	Tethered leaflets with restricted systolic motion of one or more leaflets; regurgitant jet can be central or eccentric.	Lead repositioning or extraction, with or without associated valve repair or replacement (surgical or percutaneous)
RV dyssynchrony	RV or biventricular dilatation and systolic dysfunction; markedly abnormal septal motion; predominantly an early-mid systolic TR jet; regurgitant jet is usually central; intraventricular dyssynchrony; associated atrioventricular and/or interventricular dyssynchrony can be noted.	Cardiac resynchronization therapy or lead repositioning (including His bundle), with or without valve repair or replacement (surgical or percutaneous)
Cardiac device–related endocarditis	Vegetations on PPM leads extending to the TV; primary leaflet involvement with destruction; pulmonary hypertension, RV dilatation and dysfunction if associated pulmonary embolism; regurgitant jet can be central or eccentric.	Antimicrobials plus full PPM system extraction, with or without associated valve repair or replacement (surgical or percutaneous)
Leaflet and/or subvalvular apparatus damage after lead extraction	Leaflet prolapse, flail or avulsion; chordal and/or papillary muscle partial or complete rupture; regurgitant jet can be central or eccentric.	Valve repair or replacement (surgical or percutaneous)

*Three-dimensional echocardiography is a useful adjunct tool for better understanding of the mechanism of TR, anatomy of the valve, and surrounding structures as well as treatment planning and guidance.
†Irrespective of the mechanism, whenever a patient is no longer considered suitable for an RV lead-based PPM system, alternative pacing methods can be considered.
‡This can also be caused by LPs, in which case isolated valve repair or replacement (surgical or percutaneous) is likely the first-line therapeutic option.

the detection of device-mediated TR as the primary mechanism a challenge. Therefore, despite the reassuring data on the efficacy and safety of LPs from the pivotal trials, conflicting data exist to suggest that the proportion of individuals that will develop significant TR is not negligible and needs attention. Beyond LPs, this case also highlights the complex interaction of cardiac devices and TV function. The focus of the echocardiographic assessment for TR in the context of cardiac devices is often on the leaflet–lead direct interaction while not considering the complex and more difficult to define subvalvular–device relationship. This also likely leads to further underestimation of the importance of all cardiac devices as a major causal factor of significant TR. Overall, this subset of patients that present with clinically

significant TR post-LP is a complex and challenging group, and this case highlights the importance of a systematic approach to routine echocardiography before and after device insertion and a comprehensive interrogation of the pacemaker-TV interaction to fully define, understand, and manage this important patient population.

CONCLUSION

Leadless pacemaker–related TR is likely an underrecognized entity in clinical practice. Nevertheless, it can cause significant degrees of TR, with relevant clinical and probable prognostic implications. After a meticulous clinical assessment and temporal ascertainment of events, echocardiography is key for assessing TV apparatus anatomy as well as TR severity and mechanism. The scarcity of data in this particular group of patients highlights the need for additional information on prevalence/incidence, risk factors, anatomy, diagnostic features, and prognosis. It is now paramount that reliable and robust reports addressing these gaps are pursued since LPs are being increasingly used.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2021.06.003.

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