Title

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Hemodynamic Manifestations of Concomitant Radiation-Induced Tricuspid Regurgitation and Pericardial Constriction Undergoing Transcatheter Tricuspid Valve Repair

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A 67-year-old female with a history of left breast angiosarcoma at the age of 30 treated with chemotherapy and radiation presented with worsening dyspnea, orthopnea, abdominal distension, and weight loss for approximately 1 year. Her chemoradiation regimen consisted of doxorubicin (unknown doses), cyclophosphamide, and high-dose chest radiation (estimated at 120 Gy). Her recovery course was complicated by osteoradionecrosis of the left anterior chest with recurrent pleural effusions, requiring multiple reconstructive chest operations. She had known tricuspid valve regurgitation on prior outside echocardiograms.

In cardio-oncology clinic, her physical exam was notable for elevated jugular venous pressure and Kussmaul's sign. Her chest exam was significant for a missing sternum with overlying skin grafts. The cardiac exam was notable for a faint I/VI holosystolic murmur along the right upper sternal border. Laboratory findings were notable for BNP (brain natriuretic peptide) of 724 pg/mL. The patient was urgently admitted for shock with altered mental status, hypothermia, and hypotension. Due to progressive kidney injury and increasing pressor requirements, she was initiated on venoarterial extracorporeal membrane oxygenation.

On admission, a transthoracic echocardiogram demonstrated severe tricuspid regurgitation (TR), preserved left ventricular ejection fraction, and possible constrictive physiology with the findings of a septal bounce, ventricular septal shift, and expiratory diastolic hepatic vein flow reversal (Figure 1).

Due to her tenuous clinical status and comorbidities, particularly lacking a functional chest, she was deemed a prohibitive risk for surgical tricuspid valve repair/replacement and advanced heart failure therapies, including heart transplantation and ventricular assist devices. Off-label tricuspid transcatheter edge-to-edge valve repair (TEER) with a Mitraclip (Abbott, Abbott Park, IL) in the tricuspid valve position was considered. The timing of TEER was also debated, as to whether to take place while on ECMO support, or after weaning—if successful. There was concern for potential hemodynamic worsening with TEER, either due to worsening right ventricle function (increased afterload due to acute TR reduction) or an increase in left ventricular preload (due to increased forward flow). These potential consequences led to concerns about the inability to wean the patient off ECMO if TEER was attempted while on optimal support (Figure 2).

Key Words: cardiomyopathies ■ catheterization ■ constrictive pericarditis ■ hemodynamics ■ radiotherapy ■ shock, cardiogenic ■ tricuspid valve insufficiency

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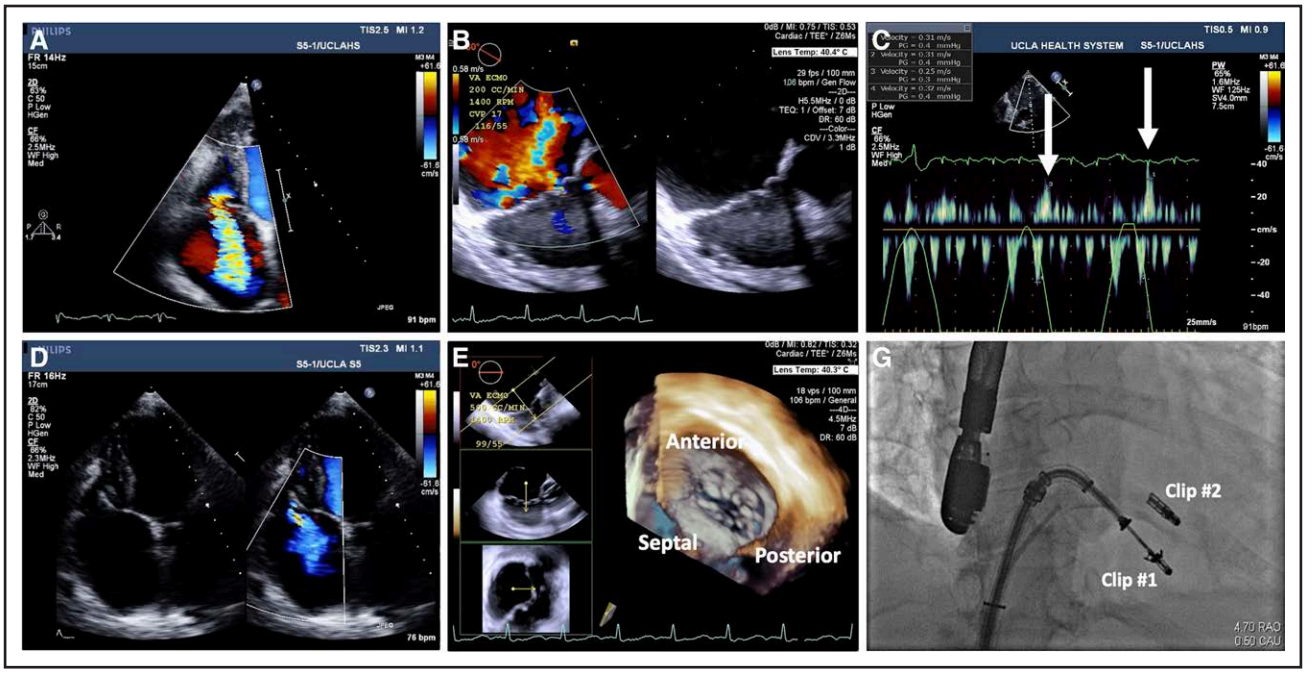

Figure 1. Multimodality imaging of cancer treatment associated valvulopathy and transcatheter tricuspid valve repair.

A, Two-dimensional (2D) transthoracic echocardiogram (TTE) 4-chamber apical view of the tricuspid valve pretranscatheter edge-to-edge valve repair (TEER). Severe tricuspid regurgitation is noted. **B**, 2D transesophageal echocardiogram (TEE) mid-esophageal view of the tricuspid valve on venoarterial extracorporeal membrane oxygenation support. Views with and without color Doppler are juxtaposed, demonstrating severe tricuspid regurgitation. **C**, Continuous wave doppler in the hepatic veins, demonstrating systolic flow reversal noted pre-TEER, consistent with severe tricuspid regurgitation. Significant hepatic expiratory flow reversal in diastole (arrows) is suggestive of possible concomitant constrictive physiology. **D**, Four-chamber apical TTE views of the tricuspid valve post-TEER placement. A significant reduction of tricuspid regurgitation with mild residual tricuspid regurgitation is noted. **E**, Three-dimensional TEE view of the tricuspid valve before the placement of 2 clips. **F**, Cardiac fluoroscopy, anteroposterior view, demonstrating transesophageal echocardiography–guided TEER with the placement of 2 clips (labeled) between the posterior and septal leaflets of the tricuspid valve.

Thus, the decision was made to wean off circulatory support and reassess her ability to tolerate medical therapy. The patient was hemodynamically stabilized and underwent ECMO decannulation on hospital day 22. However, she developed progressive right heart failure and worsening renal failure despite escalating diuretic and vasopressor doses. The decision was therefore made to proceed with TEER.

Cardiac hemodynamics were obtained pre- and post-TEER. Peri-procedurally, no significant fluid or transfusions were administered. Pre-TEER hemodynamics revealed simultaneous near equalization of right atrial and ventricular systolic and end-diastolic pressures consistent with severe TR (Figure 3). Two clips were placed between the posterior and septal tricuspid leaflets with residual mild TR (Video S1). Intraprocedural transesophageal echocardiography provided close monitoring of the right ventricle function before delivery of each clip to ensure that the right ventricle function could tolerate any subsequent increased afterload. Post-TEER, there was an elevation of right-sided pressures and pulmonary capillary wedge pressure, which was not expected (Table). This suggests the potential unmasking of an underlying constrictive physiology versus a noncompliant right atrium with restrictive physiology that was difficult to diagnose in the setting of concomitant TR.

Post-procedure, the patient's renal function improved, and she was eventually discharged on furosemide 40 mg twice daily. A post-TEER transthoracic echocardiogram demonstrated improved TR (Figure 1). She was discharged on hospital day 32 with a subsequent functional class of New York Heart Association Class II. Serial TTEs post-discharge demonstrated persistent hepatic expiratory diastolic flow reversal and ventricular septal shift, and cardiac magnetic resonance imaging performed 10 months later demonstrated pericardial thickening of 4 mm and abnormal diastolic septal motion (Video S2), all suggestive of residual pericardial constriction.[1,2] She continues to be clinically stable on oral diuretics 5 years since her hospitalization, with no heart failure–related hospitalizations.

This case highlights the hemodynamic challenges in addressing long-term sequelae of cancer-associated

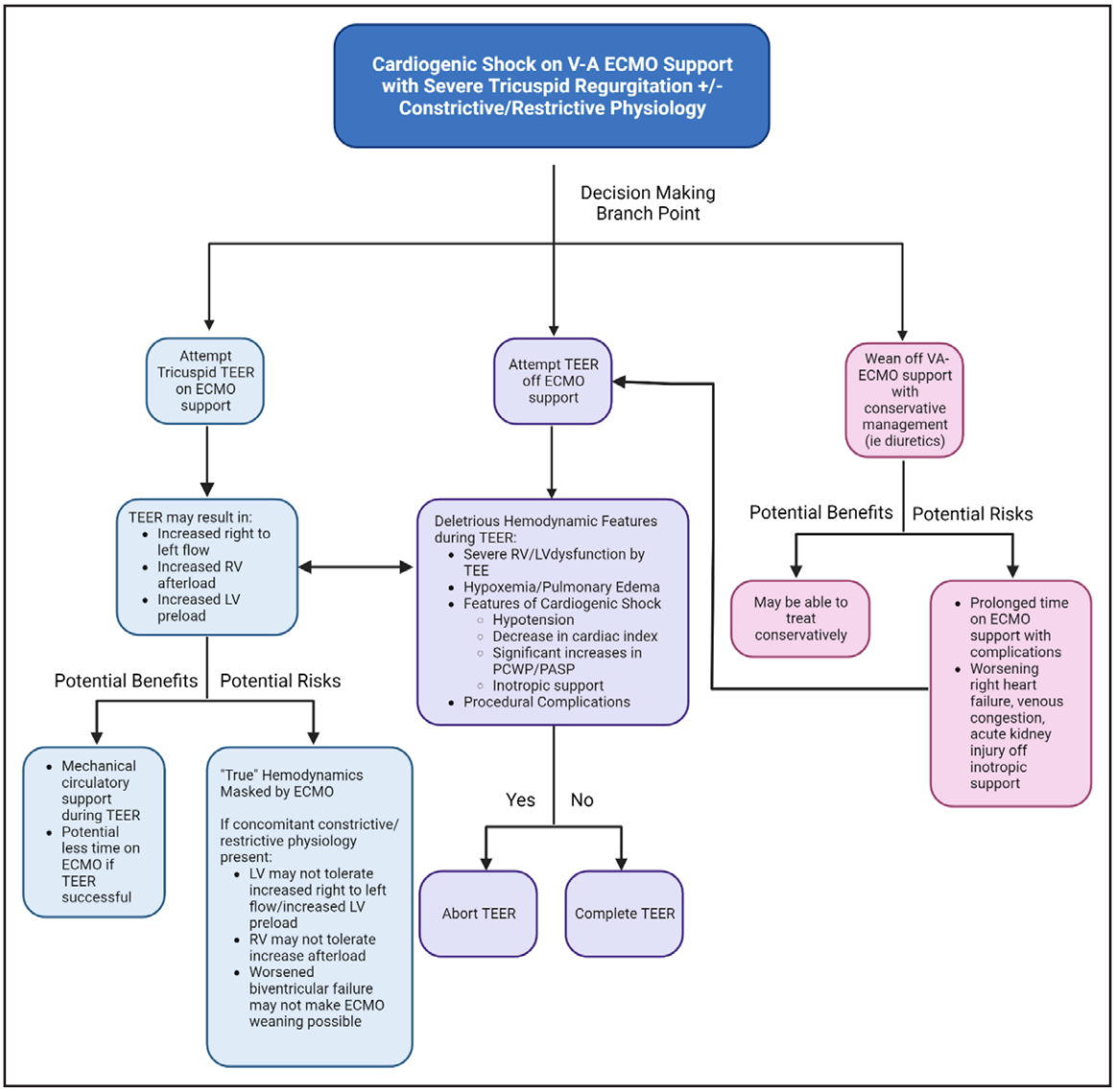

Figure 2. Decision-making pathway regarding the timing of possible tricuspid valve transcatheter edge-to-edge repair (TEER) while the patient was on mechanical circulatory support.
Risks and benefits of TEER intervention while on or off extracorporeal membrane oxygenation (ECMO) are presented. Ultimately, the decision was made to attempt to wean off ECMO support, which was successful and manage conservatively with diuretics; however, due to worsening right-sided failure and acute kidney injury, the decision was made to proceed with TEER. Features of deleterious hemodynamic features peri-procedurally that would determine whether to abort or continue TEER are listed. LV indicates left ventricular; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; RV, right ventricular; TEE, transesophageal echocardiogram; TEER, transcatheter edge-to-edge repair; and V-A ECMO, venoarterial extracorporeal membrane oxygenation. Created by www.biorender.com.

therapy, which can manifest as radiation-associated valvulopathy and pericardial disease. It is now advised that radiation treatment survivors undergo serial cardiac imaging to screen for late effects.[3] However, even with advanced imaging modalities and invasive diagnostic techniques, evaluating for pericardial constriction in the setting of severe TR can be difficult to ascertain, and careful combined noninvasive and invasive hemodynamic assessment is critical for an accurate diagnosis.[1,2,4] This case also highlights the critical importance of a multidisciplinary Heart Team approach—with Cardio-Oncology input—in addressing advanced valvular and cardiac disease in the cancer survivor patient, along with the novel off-label use of edge-edge TEER techniques, which continue to be investigated with great interest.[5–7]

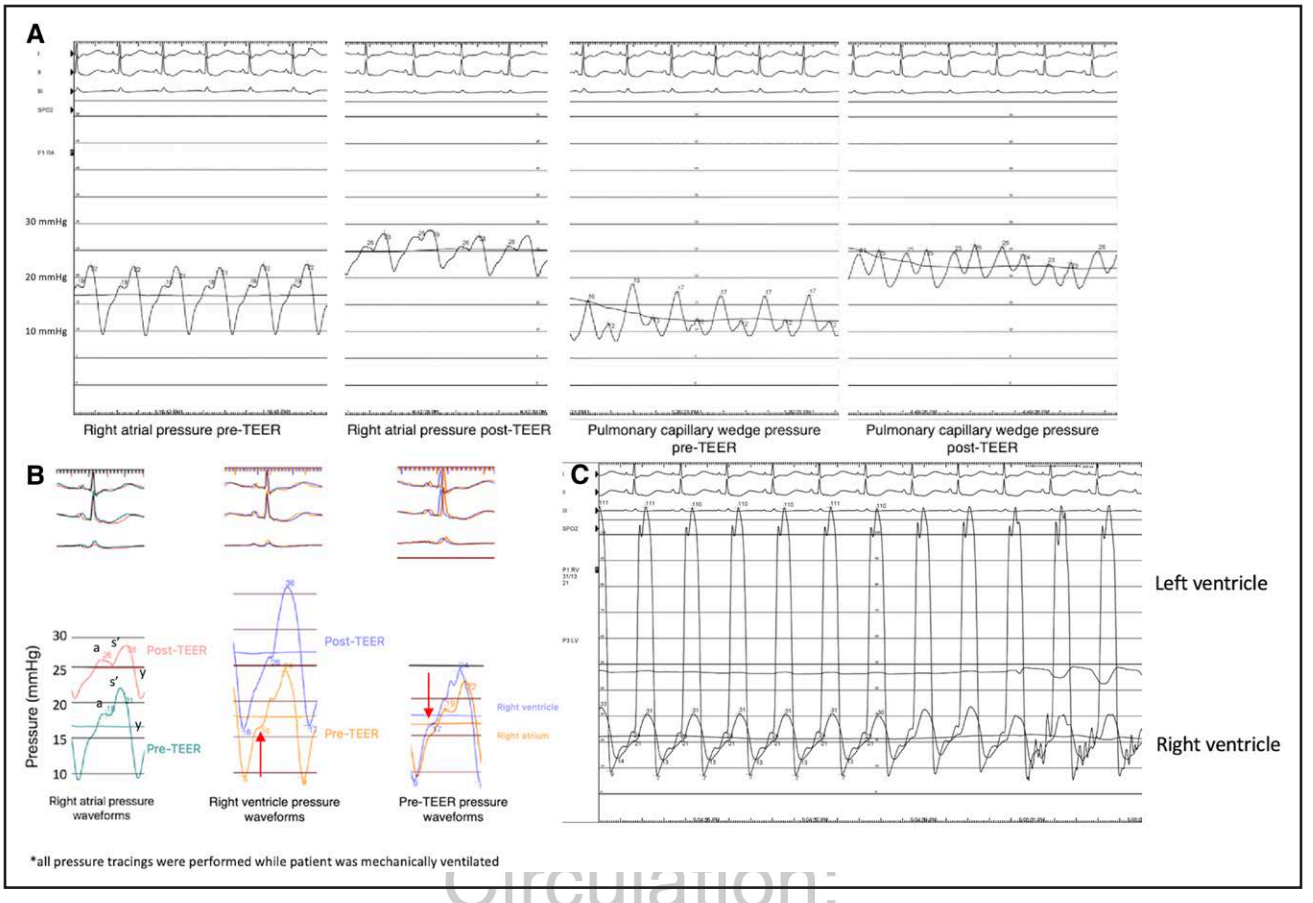

Figure 3. Invasive hemodynamics pre- and post–transcatheter edge-to-edge valve repair (TEER).
A, Right heart catheterization pressure wave form tracings from the right atrium (RA) pre- and post-TEER. A prominent systolic ("s," or c-v) wave is noted with a steep y descent due to severe tricuspid regurgitation (TR) causing early atrial filling from regurgitation (s wave) followed by early ventricular filling (y descent). Pre-TEER RA pressure tracing is seen in the **left** panel with a mean RA pressure of 18 mm Hg. RA pressure tracings after successful placement of the second clip show an increased RA mean pressure at 25 mm Hg. Post-TEER, there is normalization of the v wave occurring later after ventricular systole, corresponding with closure of the tricuspid valve. While the anticipated hemodynamic effect is that the mean right atrial pressure decreases post-TEER, it increases with diastolic equalization with the other chambers–which is a finding that, along with supporting echocardiographic and magnetic resonance imaging findings, supports the concomitant physiology of pericardial constriction. Pre-TEER pulmonary capillary wedge pressure (PCWP) also sees an increase of mean pressure 12 to 22 mm Hg post-TEER. **B**, Superimposed right heart catheterization waveforms pre- and post-TEER in the RA and right ventricle (RV). The **left** tracing demonstrates the rise in mean right atrial pressures post-TEER, and delay of the s' wave and less prominent y descents–hemodynamic consequences of improved TR but also with increased right atrial afterload. The **middle** tracing demonstrates superimposed RV waveform tracings pre- and post-TEER. Post-TEER the RV systolic and end-diastolic pressure increases as a consequence of increased RV afterload. The **right** tracing demonstrates superimposed RA and RV waveforms pre-TEER, demonstrating near systolic equalization of the RA and RV pressures–manifest by the s' wave of the RA waveform–near end-diastolic equalization of RA and RV pressures, and the "dip and plateau" appearance of the RV pressure (arrow), which can be seen in both severe TR and pericardial constriction. **C**, Simultaneous left ventricle (**top** tracing) and right ventricle (**bottom** tracing) post-TEER. LV and RV end-diastolic pressures near equalization is noted. The presence of discordance on simultaneous left and right ventricular end-diastolic measurements were difficult to ascertain due to the patient's mechanically ventilated state.

Table. Invasive Hemodynamic Measurements Pre- and Post-TEER

Cardiac hemodynamics	Pre-TV repair, mm Hg	Post-TV repair, mm Hg
Right atrial pressure (A/V/M/EDP)	18/22/17/18	26/28/25/26
Right ventricular pressure (S/EDP)	24/21	36/26
Pulmonary artery pressure (S/EDP/M)	25/20/22	34/27/26
Pulmonary capillary wedge pressure (A/V/M/EDP)	17/12/13/18	25/26/23/26
Left ventricular end-diastolic pressure	19	25
Cardiac output (TD)	3.5 L/min	3.4 L/min
Cardiac index (TD)	2.2 L/min per m^2	2.1 L/min per m^2

A/V/M/EDP indicates a-wave/v-wave/mean/end-diastolic pressure; S/EDP, systolic/end-diastolic pressure; TD, thermodilution; and TV, tricuspid valve.

ARTICLE INFORMATION

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Supplemental Material

Videos S1 and S2

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