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CASE SERIES
Heart failure

Heterotopic caval valve implantation for the management of severe tricuspid regurgitation: a case series

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Background Severe tricuspid regurgitation (TR) is a complex condition that can be difficult to treat medically, and often surgical intervention is prohibited due to the high morbidity and mortality associated with this intervention. In patients who have failed maximal medical therapy and have progressive symptoms related to their severe TR, heterotopic caval valve implantation (CAVI) offers potential for symptom relief for these patients.

Case summary We present two cases of patients with severe TR with symptoms of heart failure that were refractory to medical therapy. Due to extensive comorbidities in these patient's surgical intervention was deemed unsuitable and the decision was made to proceed with heterotopic CAVI in order to try and control their symptoms. Both patients successfully underwent the procedure and had an Edwards SAPIEN 3 valve (Edwards Lifesciences, Irvine, CA, USA) implanted in the inferior vena cava/right atrium junction. In both patients, there was improvement in the postoperative haemodynamics as measured by invasive and non-invasive methods. Successful discharge was achieved in both patients with improvement in their symptoms.

Discussion Selective use of heterotopic CAVI to treat symptomatic severe TR that is refractory to medical therapy may be a viable option to improve symptoms in those patients that are unsuitable for surgical intervention.

Keywords Heart failure • Tricuspid regurgitation • Valvular heart disease • Percutaneous intervention • Caval valve implantation • case series

Learning points

- Severe tricuspid regurgitation (TR) that is refractory to medical therapy can cause significant downstream effects due to venous backflow into the hepatic and portal venous system.
- Heterotopic caval valve implantation is an emerging minimally invasive intervention that reduces caval backflow and thus reduces the symptoms associated with the downstream effects of severe TR.

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Introduction

With the advent of percutaneous interventions for structural heart disease there has been a recent focus on innovative percutaneous interventions to treat patients with significant symptomatic tricuspid regurgitation (TR) who may be unsuitable for surgical intervention.[1] Tricuspid annular dilation that frequently occurs with functional TR often precludes valve-invalve or edge-to-edge repair as treatment options. To this effect, transcatheter heterotopic caval valve implantation (CAVI) has been suggested as a possible therapy for these patients.[2] In the pathological cascade, heterotopic CAVI aims to reduce the caval backflow and hepato-renal congestion, which occurs at the later stage of severe TR. Herein, we report two patients who underwent successful heterotopic CAVI to improve the symptoms they were experiencing as a result of the downstream effects of their severe TR.

Timeline

Case 1:	
15 June	Admitted to hospital with heart failure symptoms due to severe tricuspid regurgitation (TR). Also noted to have right upper quadrant pain as a result of hepatic engorgement from her TR and also a declining renal function.
1 July	Underwent successful edge-to-edge repair of her tricuspid valve with the MitraClip™ device. A reduction in the severity of her TR was noted during the procedure.
3 July	Postprocedure echocardiogram showed two dehisced MitraClip™ devices across the tricuspid valve and persistent severe TR
11 August	Reviewed in the clinic and due to persistent symptoms, another percutaneous intervention was scheduled to try and alleviate symptoms.
26 October	Patient underwent a heterotropic caval valve implantation.
27 October	Discharged to the rehabilitation unit.
1-year follow-up	Improvement in her heart failure symptoms and also the resolution of her abdominal pain. Renal function also showed some improvement as measured by GFR.
Case 2:	
15 December	Presented to hospital with decompensated heart failure. She was dyspnoeic on minimal exertion and had associated ascites, pleural effusions, and reduced renal function. There were multiple previous similar admissions in the last 2 years with similar symptoms that required in-patient admission and intravenous diuretic therapy. Intravenous therapy was commenced on this admission and she was then transitioned to oral medications.
29 February	Discharged from the rehabilitation unit on maximal medical therapy
3 March	Re-presents to hospital with refractory heart failure symptoms. The structural heart team consulted and given the frequency of exacerbations over the last 2 years a percutaneous intervention was scheduled.
24 March	Patient underwent a heterotropic caval valve implantation to relieve the downstream effects of her severe TR.
15 April	Patient was discharged to a rehabilitation unit with improving heart failure symptoms, abdominal pain and slight improvement in her renal function as measured by GFR.

Case presentation

Case 1

A 73-year-old female presented with a history of severe symptomatic TR. She had New York Heart Association (NYHA) class IV symptoms along with significant lower limb edema and right sided abdominal pain that was attributed to hepatic venous engorgement as a result of her severe TR. The patient also had evidence of renal impairment as evidenced by a reduction in her glomerular filtration rate (GFR) which measured 40mL/min/1.73m^2 (normal range >90mL/min/1.73m^2). Despite aggressive medical therapy with diuretics her symptoms persisted, and the patient was worked-up for edge-to-edge repair of her tricuspid valve (TV) with the MitraClipTM (Abbott Inc., Chicago, IL, USA) device. She underwent this procedure with initial good success and a reduction in the severity of TR but suffered early partial clip dehiscence thus leaving her with persistent severe TR. Her symptoms once again gradually progressed despite aggressive medical therapy, and at this stage she was re-considered for surgical intervention but was deemed to have a prohibitively high surgical risk due to severe chronic obstructive pulmonary disease (COPD), recurrent aspiration pneumonias, atrial fibrillation, recent pulmonary embolism, lung adenocarcinoma status post previous right upper lobectomy, and gastric lymphoma status post gastrectomy. After a multi-disciplinary team discussion, a heterotopic CAVI procedure was proposed for this patient in order to try and improve her symptoms.

After induction of general anesthesia, a transesophageal echocardiography (TEE) was performed which confirmed the diagnosis of severe TR and also showed hepatic flow reversal and pulsatile flow in the portal vein (*Figure 1*) (*Supplementary Video 1*). The septal leaflet of the TV was flail and two MitraClips were visualized as partially attached to this leaflet from the previous MitraClip procedure (*Supplementary Video 2*). The right atrium (RA) and right ventricle (RV) were severely dilated with normal RV function. Her left ventricular function was normal and there were no other valvular

abnormalities. The right femoral vein was accessed with a 16F E-sheath and a pigtail catheter placed into the RA to measure baseline pressures which revealed elevated pressures with prominent V-waves (*Figure 2A*). Another wire was placed in the hepatic vein to allow easy identification of the hepatic vein throughout the procedure and thus help prevent its occlusion by the valve during deployment (*Figure 3A*). The The inferior vena cava (IVC) diameter was calculated to be 31 mm and with that a Palmaz 39 mm x 10 mm stent (Johnson & Johnson, Warren, NJ, USA) was sited at the RA-IVC junction in order to provide an anchor for the valve to be positioned within the IVC (*Figure 3A*). A 29 mm Edwards SAPIEN 3 valve (Edwards Lifesciences, Irvine, CA), was then deployed within the IVC stent under fluoroscopic and TEE guidance (*Figure 2B*). Post-deployment invasive hemodynamic pressures showed a reduction in the V-waves (*Figure 2B*) and echocardiography also demonstrated a notable reduction in the systemic venous backflow of blood through the hepatic vein (*Figure 4*) (*Supplementary Video 3*). After hemostasis, the patient was extubated, transferred to the post anesthesia care unit, and quickly discharged home on post-procedure day 1. On follow-up, this patient demonstrated improvement in her heart failure symptoms along with resolution of her RUQ pain and improvement in her GFR to 88mL/min/1.73m^2 (normal range >90mL/min/1.73m^2). Approximately 11 months post-procedure the patient developed an out-of-hospital cardiac arrest with return of spontaneous circulation following advanced life support. She was subsequently transferred to the hospital where she developed cardiogenic shock and sepsis. The patient and family chose to pursue comfort care measures with home hospice as opposed to invasive therapies and the patient passed away a short time later.

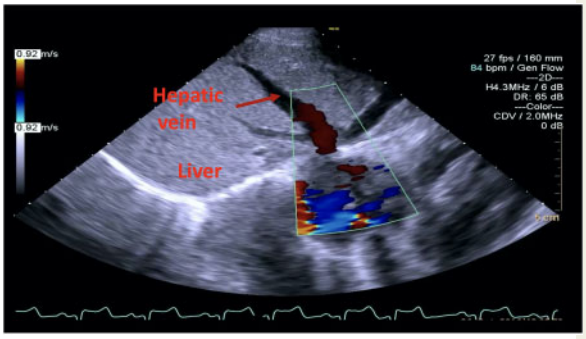

Figure 1 Subcostal image demonstrating flow from tricuspid regurgitation entering the inferior vena cava and hepatic.

Case 2

A 72-year old female with a history of Ebstein's Anomaly and consequential severe TR that was refractory to maximal medical therapy was scheduled for percutaneous heterotopic CAVI. Despite intensive diuretic therapy to optimize her volume status her heart failure symptoms progressed and had led to several prominent sequelae including ascites, bilateral pleural effusions and severe abdominal pain due to hepatic engorgement. She also demonstrated signs of renal impairment with a reduction in her renal function as measured by her GFR which was 16 mL/min/1.73m^2 (normal range >90mL/min/1.73m^2). Given the extent of her disease and other significant co-morbidities including COPD, lung cancer and lymphoma she was deemed unsuitable for surgical intervention and was thus referred for percutaneous heterotopic CAVI.

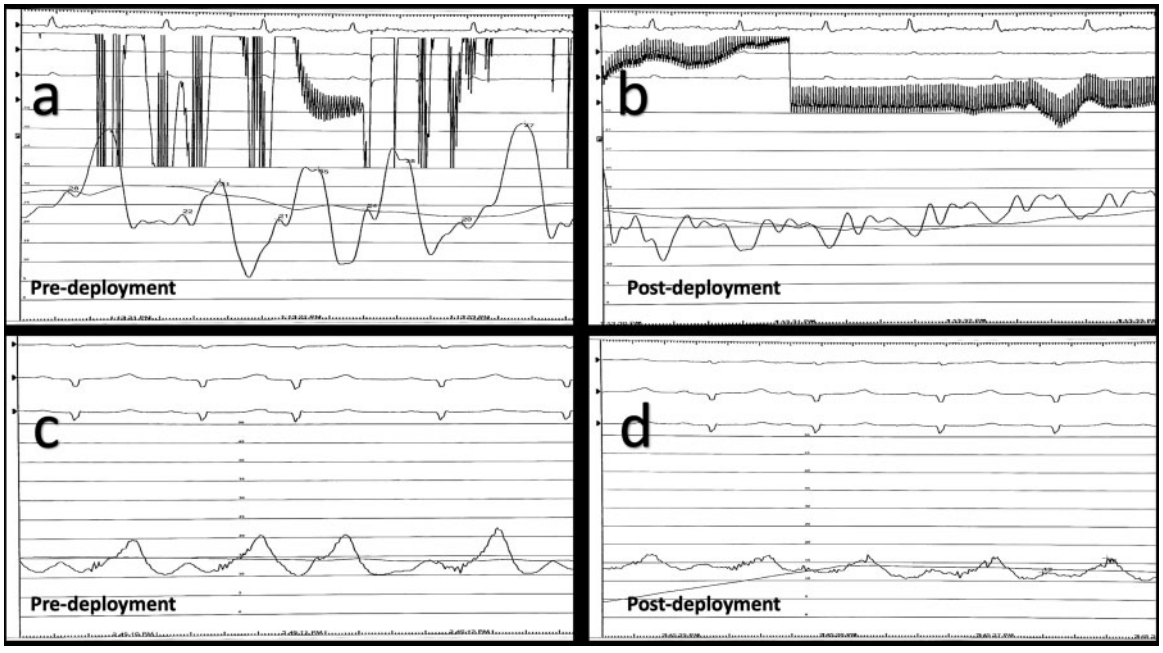

Figure 2 Invasively measured hemodynamics measured pre-CAVI and post-CAVI in both patients.

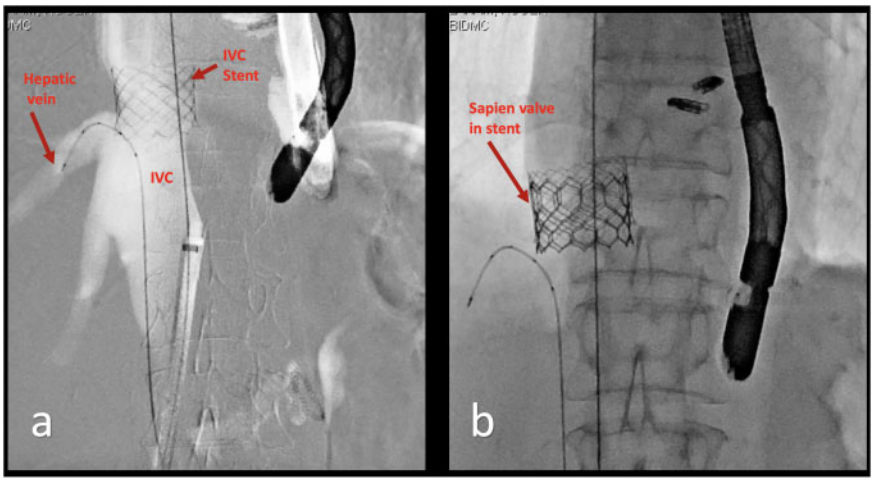

Figure 3 Fluroscopic images depicting the anchoring IVC stent being sited at the IVC/RA junction and then the 29 mm Edwards SAPIEN 3 valve deployed within the stent. Also shown is a guide wire placed in the hepatic vein so as to mark the hepatic vein take-off from the IVC and help prevent deploying the valve over the hepatic vein.

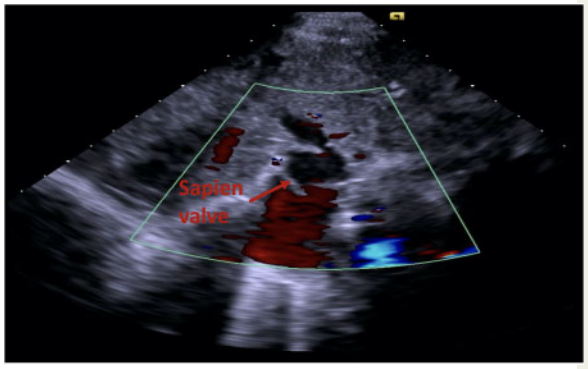

Figure 4 Subcostal image showing a competent 29 mm Edwards SAPIEN 3 valve deployed in the inferior vena cava with no regurgitation into the hepatic vein.

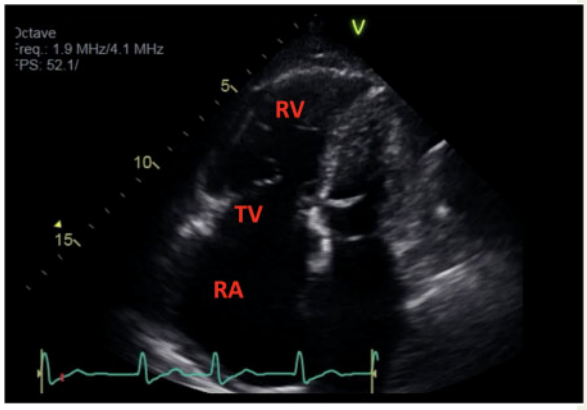

Figure 5 Apical 4 chamber view showing anterior displacement of the septal leaflet along with a significant coaptation defect between the septal and anterior/posterior tricuspid valve leaflets.

Pre-operative transthoracic echocardiogram (TTE) demonstrated a severely dilated RA, moderate RV dilation with mild free wall hypokinesis and bowing of the interventricular septum towards the left ventricle during both systole and diastole indicating RV pressure and volume overload. There was a significant coaptation defect between the septal and anterior/posterior leaflets, appearing to contribute to the majority of her TR (*Figure 5*) and precluding her from other percutaneous interventions such as edge-to-edge repair. Her mean right atrial pressure was elevated and there was significant pulsatile flow in the systemic venous system signifying venous backflow (*Figure 6* and *Supplementary Video 4*). RV function was mildly depressed in the context of her severe TR and left ventricular function was preserved with no other significant valvular lesions.

Given the patient's extensive co-morbidities, the procedure was conducted under monitored anesthesia care (MAC), along with concomitant fluoroscopic and TTE guidance. Using ultrasound, the right femoral vein was accessed, and a 16 Fr E-sheath was advanced. A wire was then advanced and placed in the inferior vena cava (IVC) and superior vena cava (SVC) as confirmed by fluoroscopy. Baseline invasive hemodynamics were measured which showed elevated right sided pressures and prominent v-waves (*Figure 2C*). Intravascular ultrasound was used to measure the caliber of the IVC which was measured at 3.2cm. In order to provide an anchor and landing zone for the undersized 29 mm Edwards SAPIEN 3 valve (Edwards Lifesciences, Irvine, CA), a 4010 Palmaz stent (Johnson & Johnson, Warren, NJ, USA) was deployed just above the hepatic vein and post-dilated. The 29 mm SAPIEN 3 valve was then advanced across the iliofemoral vein and IVC and deployed within the in-situ stent. The deployed valve protruded slightly into the right atrium but

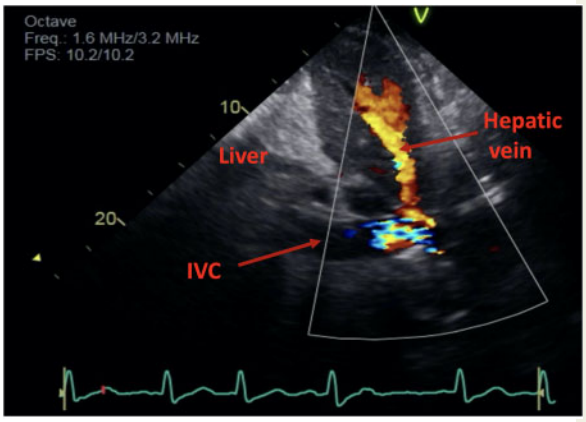

Figure 6 Subcostal image demonstrating regurgitant flow into the IVC and hepatic vein from severe tricuspid regurgitation.

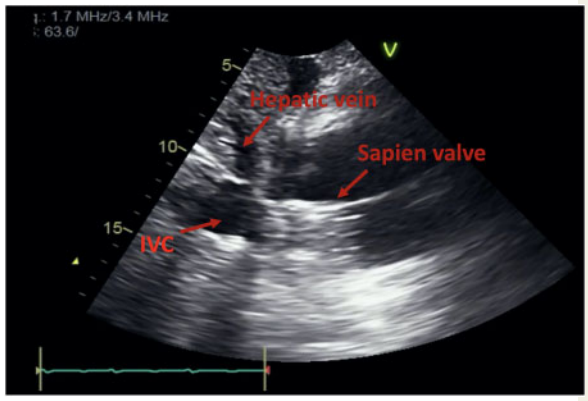

Figure 7 Subcostal image showing a deployed 29 mm Edwards SAPIEN 3 valve at the inferior vena cava and right atrium junction.

appeared stable on TTE (*Figure 7*). Post-deployment TTE showed a competent valve sitting at the IVC/RA junction with a visible reduction in hepatic venous backflow as assessed by color flow Doppler (CFD) (*Supplementary Video 5*). Invasively measured hemodynamics also demonstrated a reduction in V-waves when compared to baseline (*Figure 2D*).

Two weeks post-procedure, the patient was transferred to a rehab unit with improvement in her heart failure symptoms and also her abdominal pain. She also had some improvement in her renal function with her GFR increasing to 27 mL/min/1.73^2 (normal range >90mL/min/1.73m^2) prior to discharge. The improved renal function and symptomatic relief that the procedure afforded persisted, however, approximately nine months post-procedure, the patient experienced an aspiration pneumonia from which she unfortunately did not recover.

Discussion

Tricuspid regurgitation (TR) is a complex pathology of the right ventricle (RV) and tricuspid valve (TV) apparatus that incurs a high morbidity and mortality as well as being difficult to treat, both medically and surgically.[3,4] Medical treatment is often confined to optimizing volume status with diuretics and surgical intervention is often not feasible due to prohibitive surgical risk.[5,6] Heterotopic CAVI is a possible treatment for these patients with the aim not to address the TR but to reduce the downstream effects of the severe TR and thus improve symptoms and quality of life.

To date, there have been limited studies addressing the feasibility and outcomes related to this procedure. A recent observational multi-center registry study that evaluated 25 patients undergoing heterotopic CAVI demonstrated positive initial results.[2] This study showed a high procedural success rate with a low incidence of complications. There were also noticeable improvements in NYHA class symptoms and also in the hemodynamic profile as measured by a reduction in the mean pressures in the IVC and right atrium.

This case series adds to the emerging body of literature for this procedure in terms of it being a safe and well-tolerated procedure. Although both patients presented above had differences with regard to the underlying mechanism of their disease with the first case being the result of functional TR and second case due to primary TR in a patient with congenital heart disease, they both benefited from the procedure. This benefit was evidenced by improvement in their invasively measured hemodynamics with a reduction in the v-waves and elimination of pulsatile flow in the portal vein on echocardiography post valve deployment. Their heart failure symptoms as well as renal function improved after the procedure. Despite the aforementioned improvements, both of these patients passed away within 12 months succumbing to other comorbid disease. Indeed, in the multi-center registry study, the one-year mortality was 63%, indicating that heterotopic CAVI may be more of a palliative procedure to prevent and treat the downstream complications and symptoms associated with severe refractory TR.[2]

While heterotopic CAVI appears to offer potential benefits to patients with severe TR who are deemed unsuitable for surgical intervention, there are still multiple questions that need to be addressed in randomized controlled studies before its routine implementation can be recommended. Hemodynamic concerns following CAVI, including persistent right atrial overload, right atrial ventricularization due to a new upstream valve, and the effect of an increased right ventricular preload on the right chamber function all need to be further evaluated. Future studies will need to explore if any mortality benefit exists in the targeted patient population, or if CAVI is more of a palliative procedure to improve symptoms and quality of life in the short-term. From a technical aspect, the optimal valve to be utilized during CAVI needs to be determined. Currently, the Edwards SAPIEN 3 balloon-expandable valve that is designed for deployment in the aortic position has been the most widely utilized. However, with the increasing clinical presence of newer valves, such as the self-expandable TricValve (P & F Products & Features Vertriebs GmbH, Weßling, Germany), differences between the available valves need to be studied. In addition, a need exists to identify which patients may benefit from bi-caval valve implantation versus just IVC valve deployment, and subsequently outcomes with both of these methods of intervention will need to be examined.

Conclusion

Management of severe TR presents a dilemma for those physicians treating this cohort of patients with either medical or surgical therapy, with medical therapy often providing sub-optimal results and surgical intervention conferring unacceptable patient risk. Minimally invasive procedures such as heterotopic CAVI may provide a reduction in symptoms and improvement in the quality of life of these patients. The two patients we described here had this procedure done as a last resort for symptom relief, and in both cases, clinical improvement was evident. Although the CAVI technique is still in its infancy, this procedure may confer benefit in reducing the symptoms of the downstream effects of severe TR in select patients who have failed other therapies. Future studies should address identifying optimal patient candidates for this therapy, as well as assessing its efficacy and mortality benefit before widespread adoption of this procedure.

Lead author biography

Dr Aidan Sharkey graduated from the School of Medicine at Trinity College Dublin and undertook his residency training in Anesthesia from the College of Anesthetists of Ireland. After completion of his residency training he undertook a Cardiac Anesthesia fellowship in Canada at Toronto General Hospital and is currently an attending anesthesiologist at Beth Israel Deaconess Medical Center in Boston and an instructor of Anesthesia at Harvard Medical School. He has a keen clinical and academic interest in structural heart interventions and procedural guidance for these procedures.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patients in line with COPE guidelines.

Conflict of interest: none declared.

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