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CASE REPORT
Heart failure

Percutaneous mitral and tricuspid edge-to-edge repair as a bridge therapy to heart transplantation in advanced heart failure secondary to human immunodeficiency virus: a case report

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Background Patients with end-stage heart failure (HF) and severe pulmonary hypertension (PH) are not eligible for heart transplant due to high mortality risk. Percutaneous interventions as edge-to-edge repair of the mitral/tricuspid valves are a safe and effective therapy as a bridge for transplantation in patients who have contraindications to heart transplantations (HTs).

Case summary A 44-year-old man with a previous diagnosis of infection by human immunodeficiency virus (HIV) was admitted at the emergency room for exertional dyspnoea. He was diagnosed with a decompensated heart failure with reduced ejection fraction (HFrEF), severe mitral and tricuspid regurgitation, and high probability of PH. He presented poor response to guided medical treatment, even after implantable cardiac resynchronization therapy defibrillator (CRT-D). He was listed for a cardiac transplant, but after right catheterization, he was not an ideal candidate for transplantation, so it was decided to undergo percutaneous mitral and tricuspid edge-to-edge repair as a bridge to transplantation. The post-operative course was uneventful, with significant improvement in New York Heart Association functional class. The patient underwent a successful heart transplant 10 months after the procedure.

Discussion In patients with advanced HF due to HIV, HT is an adequate treatment option. When there are functional mitral and tricuspid regurgitation and severe PH, despite optimal treatment according to current guidelines, percutaneous mitral and tricuspid repair therapy appears to be safe and effective for control of severe PH as a bridge measure for cardiac transplantation.

Keywords Case report • Advanced heart failure • Mitral regurgitation • Tricuspid regurgitation • Heart transplant • HIV

ESC curriculum 4.3 Mitral regurgitation • 4.5 Tricuspid regurgitation • 6.2 Heart failure with reduced ejection fraction

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Learning points

- The mitral and tricuspid repair in advanced heart failure is an adequate strategy option as a bridge therapy until a heart becomes available or their clinical status and the pulmonary hypertension improved enough to become eligible for transplantation.
- In patients with human immunodeficiency virus, adequate antiretroviral therapy is necessary to achieve a negative viral load before heart transplantation.

Introduction

The widespread use of combination antiretroviral therapy (ART) has improved survival and reduced opportunistic infections in people with human immunodeficiency virus (HIV).[1] However, individuals with HIV have higher rates of cardiovascular disease, including ischaemic heart disease, pulmonary hypertension (PH), and heart failure (HF).[2] Mitral regurgitation (MR) and tricuspid regurgitation (TR) is commonly found in advanced heart failure (AHF) patients, leading to a lower quality of life and predicting poor survival.[3,4] While established medical and interventional therapies are recommended for AHF, refractory symptoms and frequent hospitalizations persist.[5] Heart transplantation (HT) is the ultimate treatment for end-stage HF,[6] but PH and significant regurgitation can hinder eligibility.[7] Combined percutaneous treatment of the mitral and tricuspid valves has demonstrated improved PH and functional class, potentially making patients eligible for transplantation.[8]

Summary figure

Date	Events
August 2019	44-year-old male with a history of human immunodeficiency virus (HIV) infection (A1) and deteriorated functional class to New York Heart Association (NYHA) III.
September 2019	Progresses to advanced heart failure (AHF) with dilated cardiomyopathy, severe mitral regurgitation (MR), and severe tricuspid regurgitation (TR).
October 2019	Ischaemic aetiology, Chagas disease aetiology, toxin use, and other causes were ruled out, establishing HIV as the primary aetiology.
November 2019	Maintains NYHA III–IV functional class despite optimal medical treatment for 3 months; an implantable cardiac resynchronization therapy defibrillator (CRT-D) was implanted according to international guidelines.
December 2020	Evolves with a poor response and frequent hospitalizations due to decompensation despite outpatient inotropic therapy, being protocolized for heart transplantation (HT).
January 2021	Right heart catheterization showed severe pulmonary hypertension (PH) contraindicating transplantation at that time.
February 2021	The decision was made to perform percutaneous edge-to-edge repair of the MR and TR as a bridge therapy to HT.
July 2021	Follow-up echocardiography showed pulmonary systolic arterial pressure (PSAP) of 42 mmHg, mean pulmonary artery pressure (mPAP) of 26 mmHg, cardiac output (CO) of 3.1 L/min, cardiac index (CI) of 1.8 L/min/m^2, *E*/*e*′ ratio of 4, mild MR, and moderate TR.
December 2021	The viral load was undetectable, and the CD4 lymphocyte count reached 876 cells/mm^3 with antiretroviral therapy (ART). A heart transplant was performed without complications during the transplant and post-operative period.
June 2022	The 6-month outpatient follow-up showed an improvement in functional class to NYHA I, PSAP of 29 mmHg, and mPAP of 17 mmHg, with no data indicating graft rejection.

Continued

Clinical case

A 44-year-old male with long-standing HIV infection, poor adherence to ART, and a history of successfully treated pulmonary tuberculosis was diagnosed with HF. The patient had a reduced left ventricular ejection fraction (LVEF) 18%, MR, and TR, as indicated by specific echocardiographic parameters. These parameters included a central and holosystolic jet, mitral ring 42 mm, vena contracta width 9 mm, a velocity of 4.4 m/s, effective regurgitant orifice area (EROA) 0.4 cm^2, regurgitant volume 55 mL, dilated left ventricle with a diastolic diameter of 52 mm, an indexed end-diastolic volume (EDV) of 75 mL/m^2, and an EROA/EDV ratio of 0.53. The tricuspid valve was structurally normal with a velocity of 3.1 m/s, a maximum gradient of 38 mmHg, and an eccentric jet with a 16 mm vena contracta. A significant coaptation deficit was observed [in three-dimensional (3D) colour] between the septal and anterior leaflets (see Supplementary material online, *Video S7*) (*Figure 1*). Ischaemic, Chagasic, and other common causes of HF were ruled out, leading to the conclusion that HIV infection was the underlying cause of myocardial dysfunction.

Human immunodeficiency virus and HF treatment were initiated according to guidelines, but the patient exhibited a poor response. Three months later, cardiac resynchronization therapy defibrillator (CRT-D) placement was performed; however, symptoms and frequent hospitalizations persisted. The heart transplant protocol was initiated, and right catheterization revealed combined post- and pre-capillary PH, with a CO of 2.5 L/min, PSAP of 68 mmHg, mPAP of 48 mmHg, pulmonary artery wedge pressure (PAWP) of 22 mmHg, and pulmonary vascular resistance (PVR) of 5 WU (*Table 1*), which decreased to 3 WU and mPAP to 28 mmHg after a vasodilator challenge, making HT contraindicated at that time. Despite receiving levosimendan for persistent NYHA functional class III–IV and adhering to guideline-directed medical therapy, the patient's symptoms did not improve. In a meeting with the heart team, it was decided to perform edge-to-edge repair of the mitral and tricuspid valves to reduce PH and improve functional class. Using a femoral venous approach, a transseptal puncture was performed (*Figure 2A*), and a clip was placed on the mitral valve in segments A2–P2 (*Figure 2B and C*) (see Supplementary material online, *Video 2*)

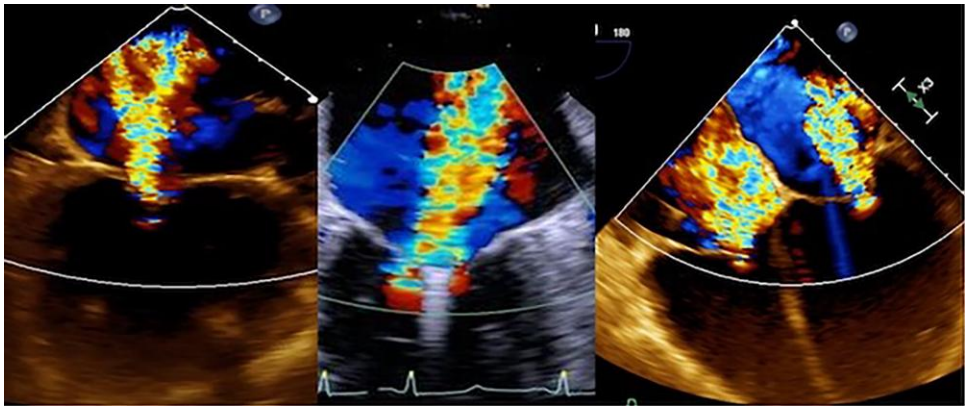

Figure 1 Transoesophageal echocardiogram showing severe mitral and tricuspid regurgitation. Four-chamber view: severe mitral regurgitation, Doppler colour showing a 9 mm vena contracta. Severe tricuspid regurgitation jet with Doppler colour showing a 16 mm vena contracta.

Table 1 Clinical and echocardiographic parameters, before and after mitral and tricuspid percutaneous repair

	Pre-procedure		Post-procedure	
	Mitral	**Tricuspid**	**Mitral**	**Tricuspid**
Vena contracta with	10	9	2	4
Regurgitant volume (mL)	55	—	—	—
Effective regurgitant orifice (cm^2)	0.4	—	—	—
LVEF		18		22
PSAP		69		42
mPAP		45		26
E/e′		18		4
NYHA		III–IV		II
VO2 (mL/kg/min)		10		16

LVEF, left ventricular ejection fraction; PSAP, pulmonary systolic artery pressure; mPAP, mean pulmonary artery pressure; NYHA, New York Heart Association; VO2, oxygen consumption.

without complications. During the same intervention, the first clip placed on the tricuspid valve detached the anterior valve, necessitating the placement of a second clip in the same location (*Figure 2E*). After this manoeuver, stability of both devices was confirmed (see Supplementary material online, *Videos 3 and 4*).

The patient's post-operative recovery was uneventful, and the follow-up echocardiogram showed no gradients in the valves, along with a significant reduction in regurgitation parameters (*Figure 3* and *Table 1*) (see Supplementary material online, *Videos 4 and 5*). There was an improvement in functional class (NYHA II, VO2 16%). A 6-month echocardiographic follow-up assessment revealed a PSAP of 42 mmHg, mPAP of 26 mmHg, a TR velocity of 2.8 m/s, CO 3.1 L/min, CI 1.8 L/min/m^2, *E*/e′ ratio 4, and LVEF of 22%. The mitral clip remained in place, displaying eccentric regurgitation and mild MR (vena contracta of 3 mm). The tricuspid clip also remained in place, showing moderate TR associated with the right ventricular implantable cardioverter defibrillator (RV-ICD) wire and presenting a central regurgitation jet (vena contracta of 4 mm). Viral load was undetectable, and CD4 lymphocytes reached 876 cells/mm^3 with ART. Based on these clinical and echocardiographic findings, the patient became eligible for a heart transplant. After 8 months of edge-to-edge repair of the mitral and tricuspid valves, a successful heart transplant was performed using an HIV-negative donor, with an aortic clamping time of 1 h and 14 min (*Figure 4*). Immunosuppressive therapy (basiliximab, methylprednisolone, and mycophenolic acid) was initiated 24 h after the surgical procedure. The patient's recovery progressed favourably, leading to discharge on the 10th day of hospitalization. In collaboration with the infectious disease service, the ART was adjusted, prescribing tenofovir/emtricitabine plus dolutegravir. At the 6-month follow-up, the patient was in NYHA functional class I, the echocardiogram showed a PSAP of 29 mmHg, mPAP of 17 mmHg, normal systolic function of the left and right ventricles, and no valvular abnormalities present.

Discussion

The association between HIV and heart failure with reduced ejection fraction (HFrEF) remains significant in the era of ART.[2] Human immunodeficiency virus cardiomyopathy can result from various factors, including viral toxicity, autoimmune response, myocarditis secondary to infections, HIV medications, nutritional deficiencies, and coronary artery disease.[2] A study found that HIV-infected individuals with a viral load of at least 500 copies/mL and a CD4 cell count below 200 cells/mm^3 had an increased risk of HFrEF.[9]

Mitral regurgitation is commonly observed in patients with AHF.[3] Consequently, functional TR and PH typically occur as a consequence of left heart disease (LHD).[10] The presence of PH in LHD is associated with higher morbidity and mortality.[10] Elevated PVR has been identified as a risk factor for mortality after HT due to the increased risk of right ventricular failure.[10,11]

Transcatheter valve technologies have shown promise in improving PH in patients with LHD valve disease MR.[7] In a population treated with the MitraClip procedure, 34% of patients experienced a sustained reduction in PH, enabling some of them to be eligible for HT.[7] However, up to 50% of patients undergoing mitral valve surgery for functional MR also have moderate or severe TR.[10] Residual TR following surgical or percutaneous treatment of left-sided valvular heart disease is associated with poor outcomes.[10]

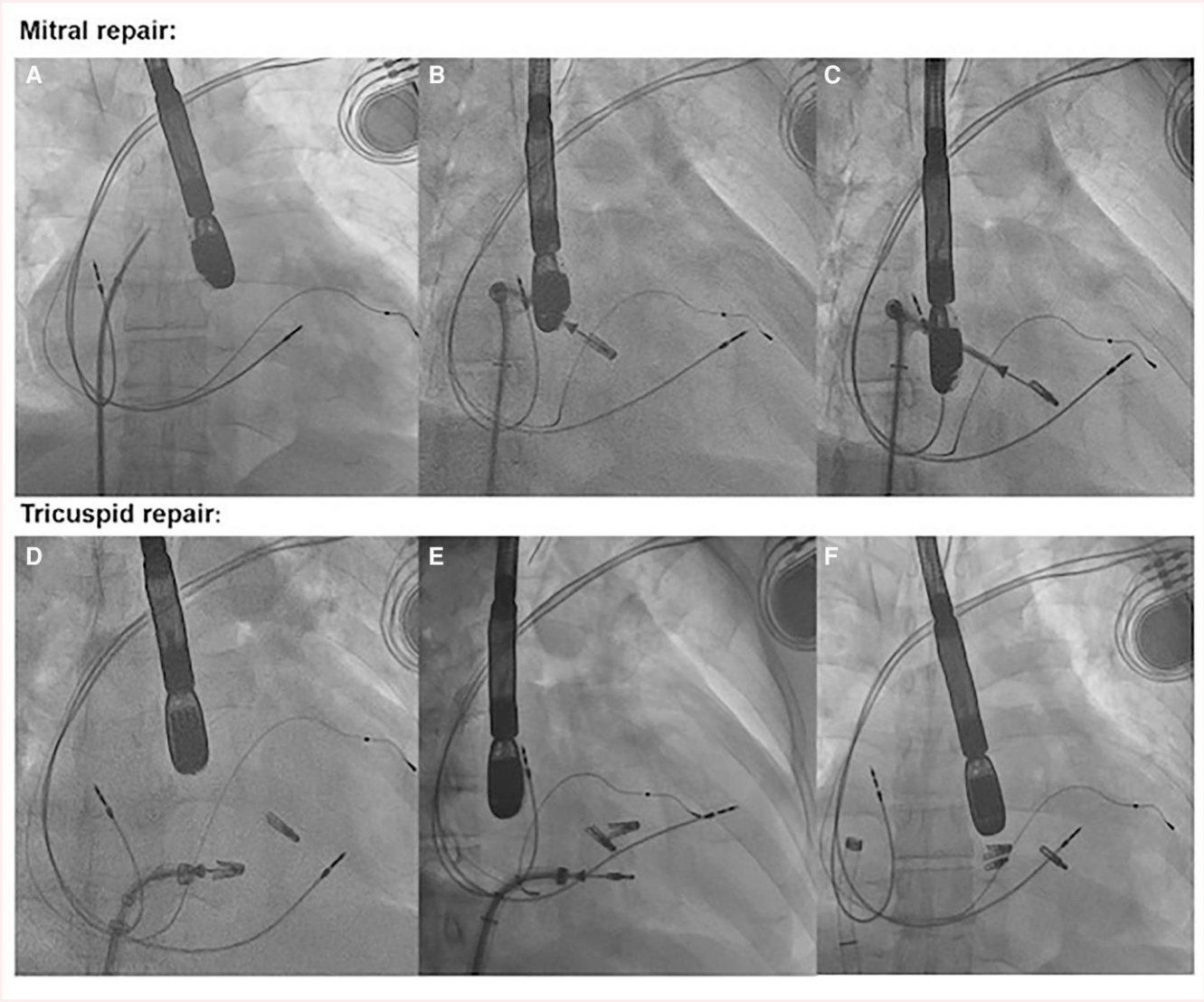

Figure 2 Mitral and tricuspid repair. (*A*) Posterior and superior transseptal puncture. (*B*) Anterior and posterior leaflet coaptation in segments A2–P2. (*C*) Release of the device, with adequate capture of both valves. (*D*) Placement of the MitraClip system towards the tricuspid valve, at the level of the anterior and septal leaflet; the first clip is placed. (*E*) After the release, detachment of the anterior valve was observed, so a second clip is placed in the same place. (*F*) The stability of both devices is confirmed. Final tricuspid clip placement, with mild residual insufficiency and an average transvalvular gradient of 1.3 mmHg (see Supplementary material online, *Video 6*).

Correcting MR is beneficial only if it independently contributes to disease progression rather than serving as a marker of terminal ventricular dysfunction. The MitraBridge registry evaluated the use of the MitraClip procedure as a bridge-to-transplant strategy in AHF patients with significant secondary MR. The results demonstrated that the selective use of MitraClip was safe and effective, with a high success rate and no deaths within 30 days. Many patients experienced clinical improvement and a reduction in adverse events, leading to eligibility for transplantation in some cases. These findings support the viability of MitraClip as an option for patients with AHF and significant MR, particularly when treatment options are limited. Despite not meeting the COAPT trial criteria, these patients showed significant improvements compared with those in the MITRA-FR trial.[7]

Severe TR in patients with mitral valve disease is associated with reduced survival, worsened HF symptoms, and frequent hospitalizations. Additionally, severe TR is particularly an independent predictor of mortality.[12] Although transcatheter repair of the mitral valve can improve the severity of TR in some patients, the existing studies are heterogeneous, and its beneficial clinical impact is not well-established.[8] Percutaneous repair of severe TR as an additional therapy led to an increase in effective systolic volume of the right ventricle and, consequently, forward pulmonary blood flow. This allows for an improvement in effective systolic volume of the left ventricle in patients with combined mitral and TR treatment, if the right-sided circulation is capable of supplying this additional stroke volume.[8,12,13]

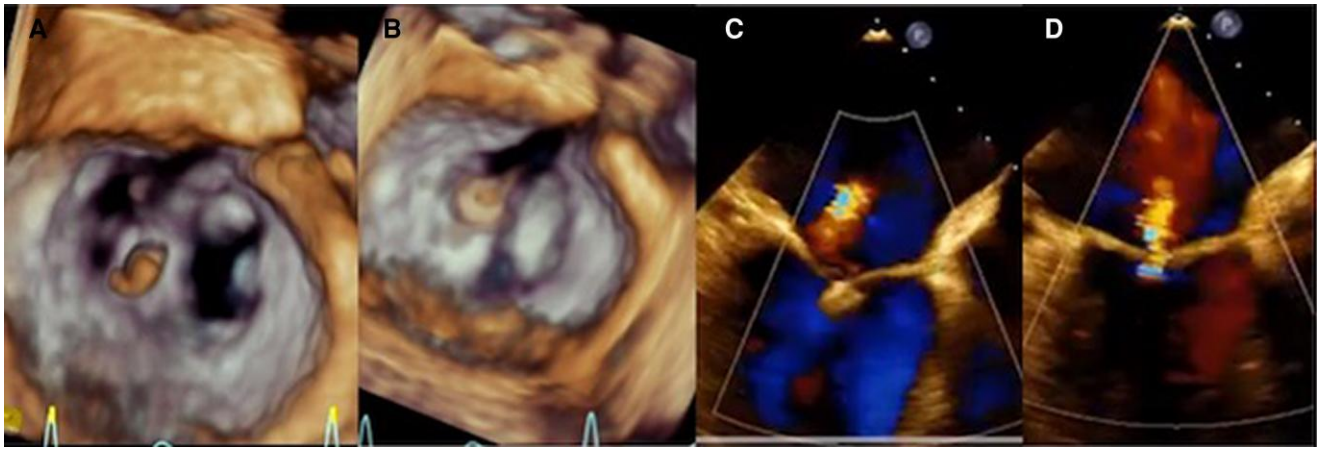

Figure 3 Transoesophageal and 3D echocardiogram, post-procedure. (*A*) 3D image showing proper placement of the mitral clip. (*B*) Proper placement of the tricuspid clips. (*C* and *D*) Reduction of mitral and tricuspid regurgitation, respectively.

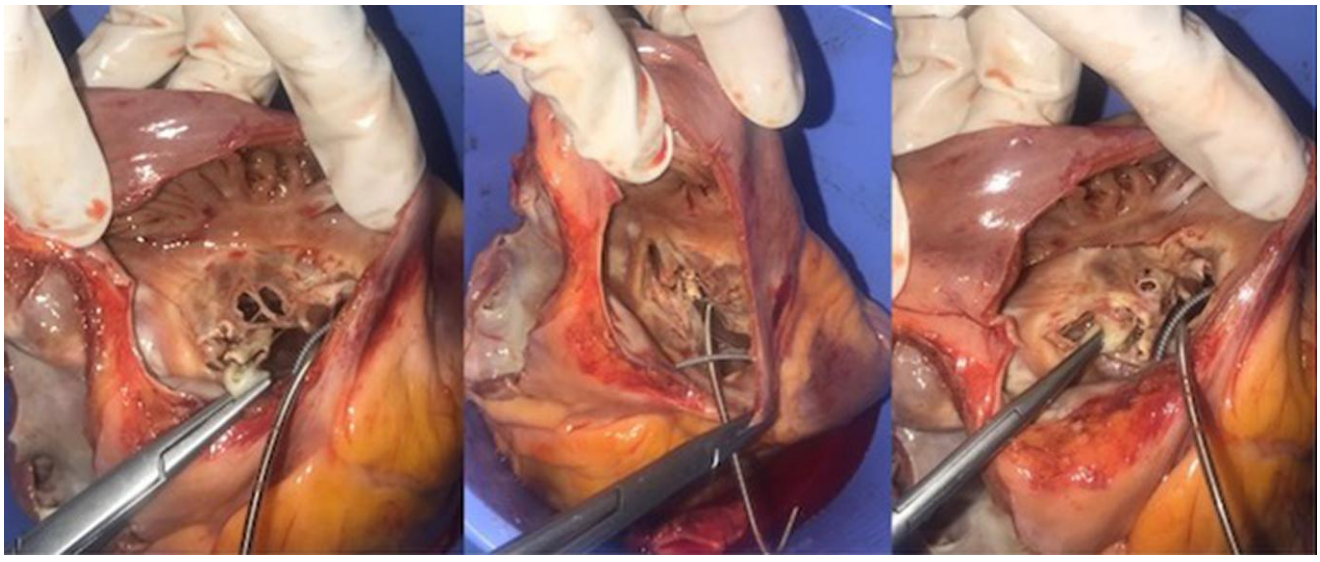

Figure 4 Native heart, where the ventricular electrode and the presence of the tricuspid and mitral clips are observed. Histopathological report describes a myocardium with interstitial fibrosis, myocytes showing degenerative changes characterized by increased nuclear size, vacuolated cytoplasm, focal necrosis, and a moderate chronic infiltrate composed of lymphocytes and macrophages in the interstitium.

In patients with HIV and AHF, HT has been performed successfully; currently, the criteria for HT in HIV-positive patients are cell count within the normal range, stable highly active antiretroviral therapy (HAART) regimen for >1 year, and undetectable HIV viral load.[14]

According to the literature, this is the first case of heart failure secondary to HIV in Latin America that underwent combined percutaneous treatment for the treatment of heart failure and reduction of PH as a bridge therapy to HT.

Patients with AHF refractory to treatment should consider HT; however, severe PH is one of the main contraindications; therefore, combined percutaneous repair of MR and TR can be performed to improve the clinical status, PH, and eligibility for transplantation. In HIV-infected patients with an undetectable viral load and a normal CD4 lymphocyte count, HT can be performed without any contraindications. Randomized observational studies are needed to evaluate combined mitral and tricuspid therapy before HT.

Lead author biography

Dr Aquino is a Cardiologist who graduated in 2022 at the National Medical Center November 20, Mexico City, Mexico. He is currently a cardiology interventional fellow. His main areas of interest include structural heart interventions.

Supplementary material

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

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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