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A novel tricuspid flow optimiser for severe tricuspid regurgitation (TRiFlO)

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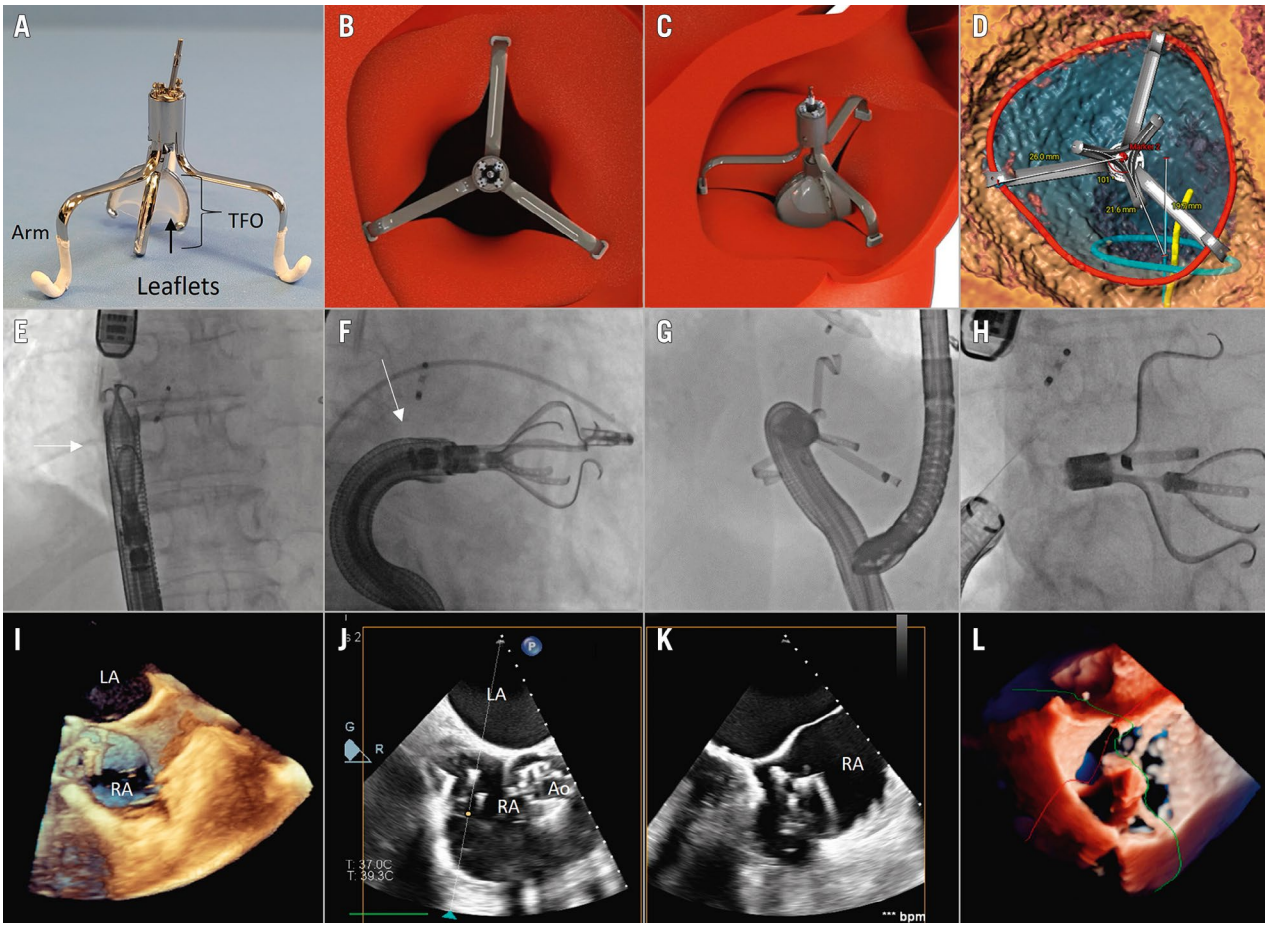

Figure 1. *Novel transcatheter tricuspid valve therapy with the Tricuspid Flow Optimizer (TRiFlO) device. The TRiFlO device consists of three arms positioned in the commissural scallops of the tricuspid valve (TV) and a central tricuspid flow optimiser (TFO) targeting the regurgitant orifice (A). The TFO mini-valve polymeric leaflets close in diastole (B), open in systole (C) and coapt with native leaflets, in order to regulate blood flow effectively and reduce tricuspid regurgitation. The procedure requires dedicated CT scan planning and simulation before the intervention (D). For transcatheter implantation, once the 37 Fr steerable catheter (white arrow) enters the right atrium (E, I), the device must be oriented coaxial and coplanar to the tricuspid valve (F, J, K). A lateral deflection of the steerable catheter is necessary to compensate the offset of the inferior vena cava ostium relative to the TV plane (G). Once the anchors are secured to the commissural scallops, the position of the TFO mini-valve is optimised to achieve the best native device leaflet coaptation, and then released (H, L). Dedicated transoesophageal echocardiographic views are required for guiding the procedural steps. Ao: aorta; CT: computed tomography; LA: left atrium; RA: right atrium*

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Severe tricuspid regurgitation (TR), leading to a cascade of pathophysiological changes, significantly impacts quality of life, increases hospitalisation rates, and reduces survival if left untreated[1]. Increased systemic venous congestion from volume overload reduces cardiac output, leading to right-sided heart failure. This also causes right ventricle (RV) dilation and dysfunction, exacerbating ventricular interdependence and resulting in systolic and diastolic dysfunction of the left ventricle (LV) along with pulmonary congestion. These effects can lead to irreversible multiorgan damage, highlighting the importance of timely intervention[1,2].

Current medical therapies primarily focus on alleviating systemic congestion, providing only palliative effects. This highlights the need for more effective interventional therapies that address the underlying structural issues of the tricuspid valve (TV) and right heart chambers. Given the complex anatomy of the TV and the intricate pathophysiology of RV dysfunction, selecting the appropriate patient and device for intervention is challenging[2,3]. The ideal transcatheter TV device should not only restore physiological TV function through laminar flow but also minimise interaction with the RV and native TV leaflets, accommodate anatomical variations, and promote positive RV adaptation following TR treatment. Additionally, it should have a low rate of bleeding complications and the ability to be repositioned, recaptured, and retrieved if necessary.

We present the results of the first Italian compassionate experience with the TRicuspid Flow Optimizer (TRiFlO [Triflo Cardiovascular]) in three patients with symptomatic torrential TR and in New York Heart Association (NYHA) Class ≥III, despite optimal medical therapy. The median left ventricular ejection fraction was 50% (range 42-51). All patients were ineligible for surgery or current transcatheter therapies, but they fulfilled the anatomical feasibility criteria for TRiFlO[4]. All three patients received approval from the regional ethics committee, which carefully assessed the clinical indications, contraindications to currently available devices, and the necessity for compassionate use. Final authorisation was subsequently granted by the Italian Ministry of Health. The median age was 81 years (range 71-86), and all patients presented multiple comorbidities. The TR aetiology was primary in the first two patients, while prevalently atrial secondary in the third **(Moving image 1A-Moving image 1C)**.

The device characteristics and the procedure have already been described **(Moving image 2)**[5]. Briefly, the device consists of three arms, anchoring the TV commissures, and a central tricuspid flow optimiser (TFO) targeting the effective regurgitant orifice area. The procedures were performed under general anaesthesia, with fluoroscopic and transoesophageal echocardiographic guidance, using a percutaneous approach by the right common femoral vein **(Figure 1, Moving image 3-Moving image 9)**. All subjects experienced acute procedural and clinical success, with residual moderate TR and a mean gradient of ≤2 mmHg. The oral anticoagulation therapy, administered for permanent atrial fibrillation (AFib), was maintained after the procedure. The median implantation time (from skin incision to delivery system removal) and in-hospital stay were 140 min (range 80-190) and 9 days (range 4-25), respectively. One patient experienced ProGlide (Abbott) failure, treated with vascular surgery, and postprocedural transient renal failure that was induced by computed tomography (CT) contrast, requiring 10 days of ultrafiltration. The median follow-up time was 10 months (range 6-12). Four weeks after the intervention, the first patient needed an uneventful single-chamber ventricular permanent pacemaker (PM) implantation due to slow-rate AFib. At 10 months of follow-up, he developed PM pocket infection and systemic sepsis. Prosthetic endocarditis was excluded by multiple transoesophageal echocardiograms. Nevertheless, he died at 360 days. No other adverse events were recorded during follow-up. The TR grade remained moderate in all patients. No device thrombosis was observed. Reductions in right atrial volume, TV annulus and inferior vena cava diameters were noted at follow-up, along with improvement of the RV dimension and function and health status **(Supplementary Figure 1)**.

Transcatheter TV therapy with TRiFlO has shown to be feasible and safe in patients with torrential symptomatic TR and impaired RV function, offering promising benefits in a selected population **(Figure 1)**. Its unique design provides several advantages that suggest that the TRiFlO device could have a significant role in the expanding therapeutic options for TR. The device is adaptable to variable TV geometries and can be securely placed in the commissural scallops, maintaining excellent anatomical compliance. Its small footprint and anchoring mechanism ensure that RV contractility is preserved while the integrity of the native leaflets is maintained, allowing for effective coaptation with the implant leaflets during systole. The device avoids creating an atrioventricular gradient, and the polymeric implant leaflets have demonstrated excellent antithrombotic properties. Following implantation, we observed significant echocardiographic and functional improvements for up to 12 months **(Supplementary Figure 2)**. Further clinical validations of our findings are necessary.

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Conflict of interest statement

G.P. Ussia is co-founder and scientific advisor for TriFlo Cardiovascular. V. Cammalleri has received speaker honoraria from Abbott. A. Mangieri serves as proctor for P+F Products + Features GmbH, and AliveCor; has received an institutional grant from Boston Scientific; and has received speaker honoraria from Boston Scientific, Concept Medical, Edwards Lifesciences, and Abbott. The other authors have no conflicts of interest relevant to the contents of this paper to declare.

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Supplementary data

Supplementary Figure 1. Echocardiographic results of transcatheter tricuspid valve therapy with the TRiFlO device.

Supplementary Figure 2. Improvement in transthoracic echocardiographic and clinical parameters in the first three patients treated with TRiFlO under compassionate use.

Moving image 1. Echocardiographic assessment of the tricuspid valve morphology and aetiology of tricuspid regurgitation in patients treated with TRiFlO.

Moving image 2. TRiFlO animation.

Moving image 3. Positioning of the steerable catheter in the right atrium.

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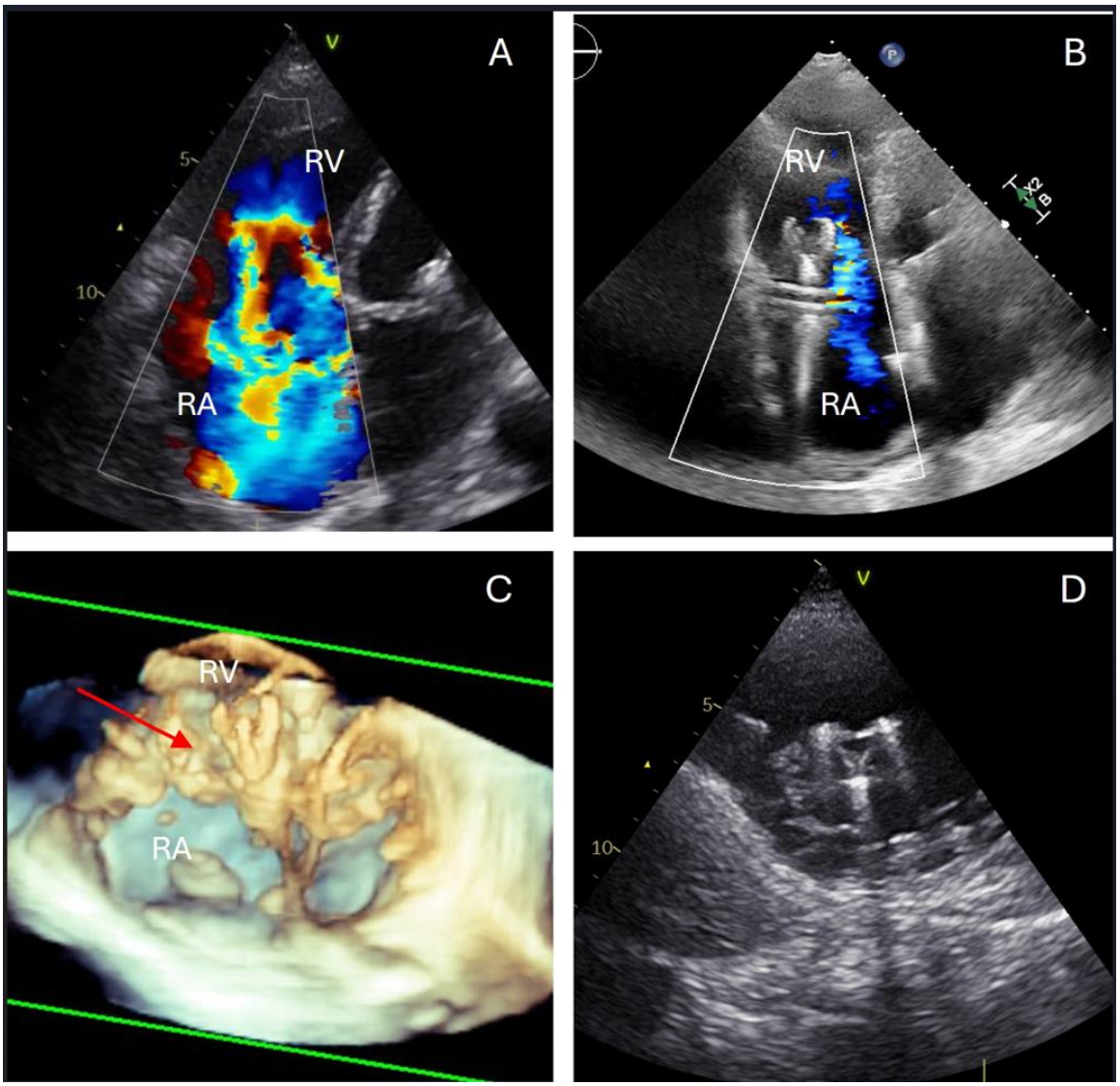
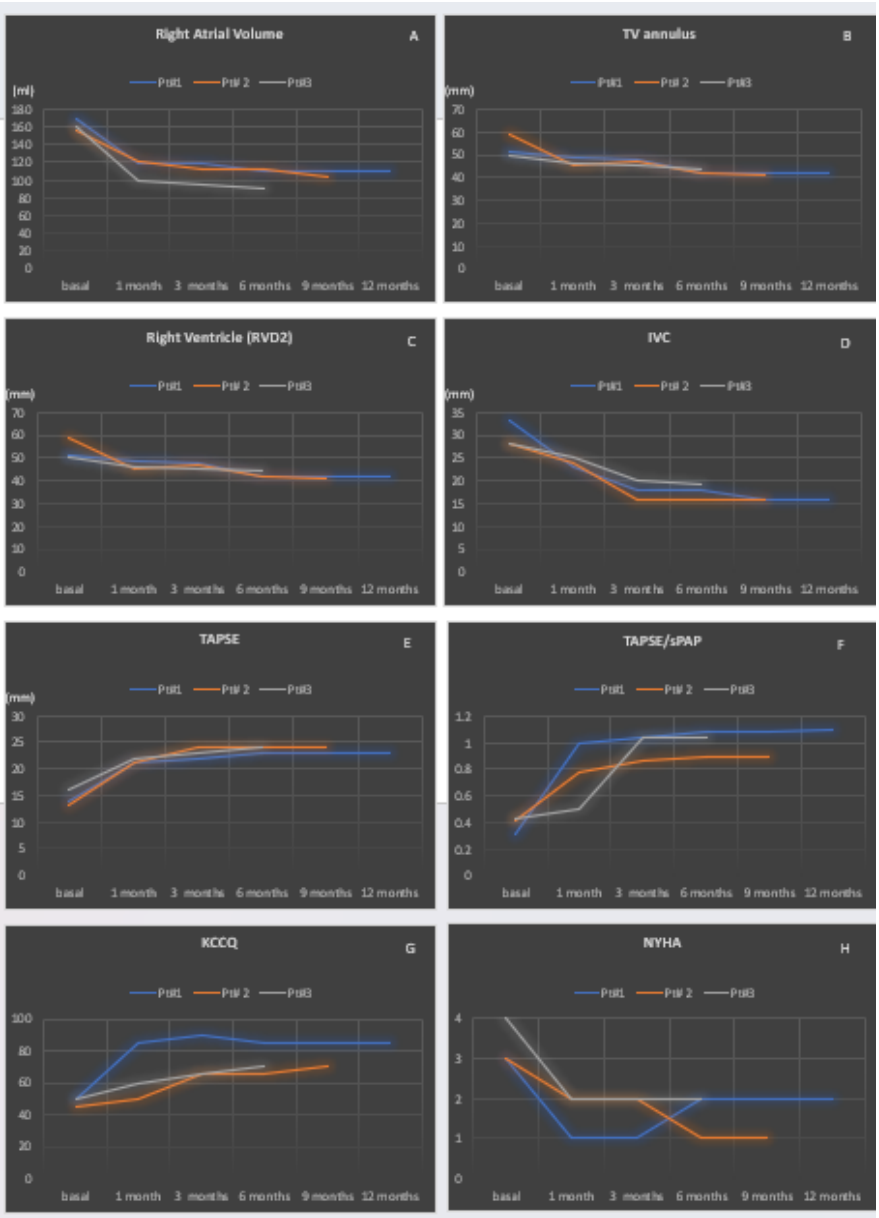
Supplementary data



Supplementary Figure 1. Echocardiographic results of transcatheter tricuspid valve therapy with the TRiFlO device.

Transthoracic echocardiogram of the third patient showing massive tricuspid regurgitation (TR) at baseline (A), which significantly reduced to moderate at the 6-month follow-up (B), with a stable device position and function (C, red arrow), and no echocardiographic signs of device thrombosis (D).
RA: right atrium; RV: right ventricle.



Supplementary Figure 2. Improvement in transthoracic echocardiographic and clinical parameters in the first three patients treated with TRiFlO under compassionate use.

By optimising the regurgitant flow through the tricuspid valve (TV), the TRiFlO device aims to induce remodelling of the right cardiac chambers, by reducing the dimensions of the right atrium (A), septal-lateral dimension of the TV annulus (B), diameter of the right ventricle (RV) (C) and inferior vena cava (D), along with improving of RV function (E) and ventricular-arterial coupling (F). A significant improvement in health status was also observed, as reflected in the Kansas City Cardiomyopathy Questionnaire (G) and NYHA class (H) variation.
IVC: inferior vena cava; RVD2: right ventricle diameter 2 (mid); KCCQ: Kansas City Cardiomyopathy Questionnaire; NYHA: New York Heart Association; Pt: patient; TAPSE: tricuspid annular plane systolic excursion; TAPSE/sPAP: tricuspid annular plane systolic excursion/systolic pulmonary artery pressure; TV: tricuspid valve.

Moving image legends

Moving image 1. Echocardiographic assessment of the tricuspid valve morphology and aetiology of tricuspid regurgitation in patients treated with TRiFlO.

Pt #1 (a) had previous De Vega annuloplasty, with residual annular dilatation (SL diameter 57 mm) and posterior leaflet flail; multiple leaflets indentations (Type IV morphology) were observed. Pt #2 (b) had huge right atrium and severe dilatation of the right ventricle and tricuspid annulus (SL diameter 56 mm), leaflets were fibrotic with systo-diastolic restricted motion and a type IIIB morphology was identified. Pt #3 (c) had prevalently secondary atrial tricuspid regurgitation (SL diameter 57 mm), with associated right ventricle dilatation and dysfunction, Type IV morphology with deep indentations in the anterior and posterior leaflets.

Moving image 2. TRiFlO animation.

The steerable catheter (SC) is positioned over a stiff wire in the right atrium, the delivery catheter is inserted, and the TRiFlO is exposed with the three arms closed. Under fluoroscopy and transesophageal echocardiography (TEE) monitoring it is oriented coaxial and coplanar to the tricuspid valve annulus using the three directions of steerability of the SC. The arms are partially released and orientation toward the three commissures is checked using customized TEE views. Then the arms are released one by one. After checking the correct position, the TFO is adjusted in height and rotation tilting for obtaining the optimal coaptation with the native leaflets. Then, the device is detached and released.

Moving image 3. Positioning of the steerable catheter in the right atrium.

The steerable catheter (SC) is positioned under fluoroscopy and transoesophageal echocardiography (TOE) in the right atrium. The delivery catheter and TRiFlO device are inserted inside the SC and slowly advanced in the right atrium. A TOE bicaval view is helpful in this step.

Moving image 4. Deflection of the steerable catheter and right ventriculogram.

The steerable catheter is deflected to achieve the optimal coaxial and coplanar position of the collapsed TRiFlO device relative to the tricuspid valve annulus. A right ventriculogram is

performed using a 6F pig tail catheter, in order to obtain a fluoroscopic reference of the tricuspid valve annulus.

Moving image 5. Alignment of the TRiFlO device.

The device is positioned coaxial and coplanar to the tricuspid valve. This alignment is carefully monitored using transesophageal echocardiography. The mid(deep) esophageal view with biplane is needed in this step.

In the fluoroscopic image, it can be appreciated the previously implanted MitraClip (Abbott Vascular, Santa Clara, CA, USA) for severe mitral valve regurgitation and a multi-fenestrated occluder device used to close the iatrogenic interatrial communication following the MitraClip procedure in the third patient.

Moving image 6. Arm orientation.

The device is now coaxial and coplanar to the tricuspid valve and the arms are oriented towards the relative commissures. The first arm, identifiable by three small holes, has already been released in the antero-posterior commissure. The second arm, identifiable by two holes, is going to be released in the antero-septal commissure. The correct engagement of the commissures is checked with customized transesophageal
echo views.

Moving image 7. TFO position optimisation under TOE.

Once the three arms are released in the commissures, the TFO position is optimised under TOE monitoring to achieve the best possible coaptation with the native leaflets.

The fluoroscopy shows the advancement of the TFO within the tricuspid valve annulus. At this stage, the transgastric short-axis view with biplane imaging can be useful.

Moving image 8. Rotation control following TFO height optimisation.

Cine-fluoroscopy demonstrates the stable anchoring of the three arms on the relative commissural scallops, along with the adjustment (rotation) of the TFO on the regurgitant orifice. The transgastric short-axis without and with color Doppler allows to appreciate the coaptation between the native leaflet and TFO.

Moving image 9. Detachment and release of the TRiFlO.

The fluoroscopy and the transesophageal echocardiogram post-TRiFlO deployment confirm stable device implantation and synchronized movement of the arms with the systolic-diastolic longitudinal excursion of the tricuspid valve plane. This finding suggests that this novel concept of device implantation does not interfere with right ventricular function at the annulus level.