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Right heart remodelling after bicaval TricValve implantation in patients with severe tricuspid regurgitation

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Severe tricuspid regurgitation (TR) is associated with significant mortality[1]; heterotopic caval valve implantation (CAVI) is an emerging transcatheter solution for patients not deemed candidates for alternative therapies, yet the structural impact upon right heart dimensions is unknown[2]. TRICUS STUDY Euro is a non-randomised, single-arm, multicentre, prospective trial that recently demonstrated a high procedural success rate and significant improvements in both quality of life and functional parameters at 6 months with the TricValve (P&F Products and Features) transcatheter bicaval valves for the superior (SVC) and inferior vena cava (IVC). However, echocardiographic analyses at 3 months demonstrated a significant increase in right ventricular (RV) and right atrial (RA) volumes, as well as a decrease in RV function[2]. The present analysis focused on the computed tomographic (CT) volumetric imaging of the right heart to provide novel mechanistic insights into right heart remodelling at 6-month follow-up along with any propensity for caval valve leaflet thrombosis or issues with stent frame integrity.

All CT images were analysed and compared at the same phase in all cases. The quality was good or acceptable in 20 cases and poor in 6 cases due to poor contrast distribution; 3D reconstruction could be performed in 25 cases (92.6%). Leaflet motion was determined through a 4D-gated scan. Virtual reconstruction was performed with Mimics (Materialise), in order to understand the anatomical interplay (right to left ventricular ratio). Furosemide administration was recorded as a furosemide equivalent dosage (40 mg oral furosemide=1 mg bumetanide=20 mg torasemide).

Of 35 patients treated with the TricValve system[2], 26 had baseline and 6-month follow-up computed tomography (CT). The mean age was 76.0±6.7 years, 84.6% were women, and the baseline tricuspid annulus plane systolic excursion was 13 mm. There was a statistically significant reduction of the RV mid-diameter at 6-month follow-up from 48.6±9.9 to 43.0±7.3 mm (p=0.001) **(Supplementary Figure 1A)** and a trend towards a decrease in tricuspid annular dimensions (mean diameter 49.2±6.0 to 47.6±5.4 mm; p=0.078) but both the SVC and IVC sizes remained similar. These findings are in agreement with the echocardiographic findings at 6-month follow-up **(Supplementary Table 1)**. The 3D reconstruction demonstrated a significant decrease in the total RV volume at follow-up (180.5±77.8 to 147.4±67.7 cm^3; p=0.037) with non-significant changes in the RA volume (289.1±123.5 vs 292.7±132.4 cm^3; p=0.789) **(Supplementary Table 1, Central illustration)**.

Regarding the safety analysis, none of the cases demonstrated SVC prosthesis thrombosis, whereas in 2 cases, stent thrombosis was detected in the IVC prosthesis. Both cases were located at the IVC-RA junction with normally functioning leaflets devoid of thrombosis **(Supplementary Figure 2)**. Contrast leakage towards

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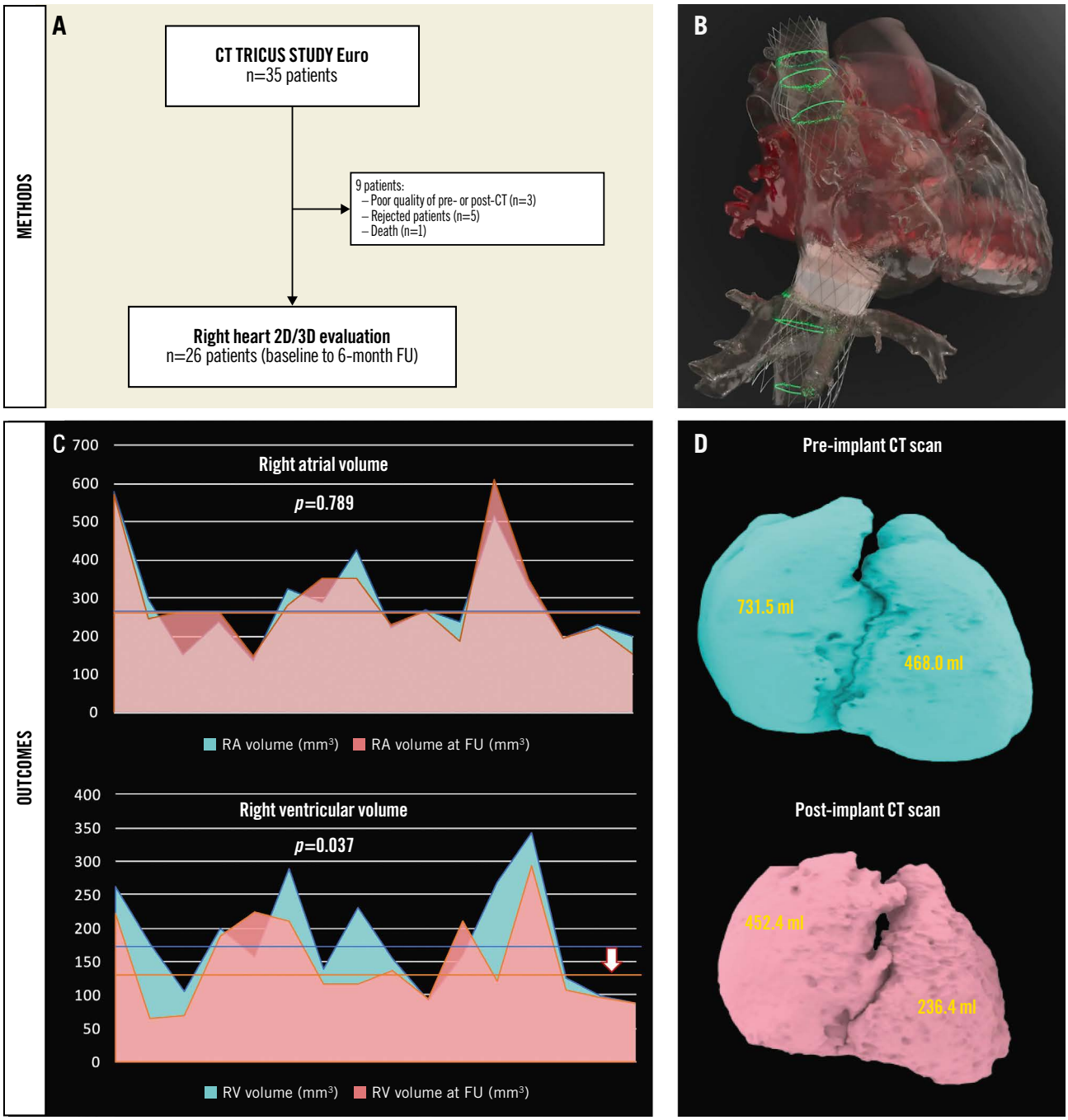
CENTRAL **ILLUSTRATION** **Right heart remodelling following TricValve implantation (CT analysis).**



Study flowchart (A). TricValve implant simulation (B) and main changes in right heart volumes, reflected as a patient-level analysis of right atrial and ventricular volumes (C) after 3D reconstruction (the arrow reflects the decrease in mean right ventricular volume). Case example of significant decrease in right chamber volume (D). 2D/3D: two-/three-dimensional; CT: computed tomography; FU: follow-up; RA: right atrial; RV: right ventricular

the IVC was detected in 5 cases; larger IVC dimensions and a marked angulation of its entrance into the RA were related to a greater risk of prosthesis leakage **(Supplementary Table 2)**. At 6-month follow-up, 3 patients had died (8.6%), none of whom had significant paravalvular leakage, and 6 patients had been readmitted because of heart failure (17.1%), one of whom had significant paravalvular leakage that was successfully percutaneously sealed. The structural integrity of the prosthesis was preserved in

all cases. Two cases of leaflet thickening were observed, one in an SVC and another in an IVC prosthesis, neither of these presenting with impaired leaflet motion.

TricValve, the first CE mark (European conformity)-approved CAVI system, demonstrated significant reverse remodelling of the RV and a strong tendency towards tricuspid annulus reverse remodelling – but not of the entire RA – despite the advanced stage of the patients enrolled in TRICUS STUDY Euro; to note, the mean furosemide equivalent dosage was reduced from 103±35 mg at baseline to 76±17 mg at 6 months, with no other relevant changes in medication. No stent fracture or leaflet thrombosis/early degeneration was detected at 6-month follow-up; however, 2 patients developed thrombi adherent to the stent frame that neither compromised leaflet/caval valve function nor were related to any clinically relevant adjudicated event. CAVI, through a reduction in RV volume overload and, less acutely, through a reduction in pulmonary arterial pressures, may induce a delayed reverse right heart remodelling. Indeed, systolic pulmonary pressure changed from 41.5±13.3 at baseline to 36.7±10.7 mmHg at 6-month follow-up, although this numerical decrease did not reach statistical significance. The detection of vena cava backflow in only 5 patients according to CT findings contrasts with the vena cava backflow reported in the 3-month echocardiographic follow-up in half of the patients[2], suggesting that the endothelialisation process and/or the right heart remodelling might help to minimise this longer term.

Further patients with longer-term follow-up are required to establish this evolving concept.

These findings may have implications for selecting the most appropriate transcatheter tricuspid therapy for each patient. Orthotopic tricuspid valve replacement in patients with RV dysfunction poses a certain risk for acute RV decompensation and the need for inotropic therapy[3]. It is plausible that CAVI offers a better-tolerated alternative by gradually promoting reverse RV remodelling, utilising the RA as a reservoir to accommodate the acute afterload mismatch faced by the RV typically seen with acute TR abolition.

Funding

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Conflict of interest statement

R. Puri serves as a consultant to P&F Products and Features and V-Dyne. I.J. Amat-Santos, I. Cruz-Gonzalez, A. Sánchez-Recalde, and O. Abdul-Jawad Altisent have served as consultants to P&F Products and Features. A. Iñiguez-Romo and R. Estevez-Loureiro received an institutional grant as principal investigators of the TRICUS STUDY Euro. J.L. Zamorano received an institutional grant for echocardiography corelab analysis. R. Estevez-Loureiro is proctor for Abbott Vascular. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Table 1. Comparison of computed tomography and echocardiographic findings before and 6 months after a successful TricValve procedure.

Supplementary Table 2. Baseline factors associated with leakage of contrast into the inferior vena cava at 6-month follow-up post-TricValve implantation.

Supplementary Figure 1. One- to 6-month changes in right ventricular dimensions according to computed tomography.

Supplementary Figure 2. Presence of thrombus adhered to the inferior vena cava stent frame of the prosthesis in two patients.

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Supplementary data

Supplementary Table 1. Comparison of computed tomography and echocardiographic findings before and 6 months after a successful TricValve procedure.

Parameter	Screening	6-month follow-up	p-value
CT PARAMETERS (N=26)			
RA volume (cm3)	289.1±123.5	292.7±132.4	0.789
RV volume (cm3)	180.5±77.8	147.4±67.7	**0.037**
Right Heart Volume (cm3)	481.9±184.8	453.5±153.5	0.181
RV/LV Ratio *	1.29±0.24	1.22±0.28	0.357
RV basal cavity diameter (mm)	57.3±8.8	55.3±9.3	0.071
RV mid-cavity diameter (mm)	48.6±9.9	43.0±7.3	**0.001**
RV longitudinal length (mm)	76.7±9.4	74.6±9.1	0.265
Tricuspid annulus maximal diameter (mm)	53.5±7.7	51.9±6.2	0.363
Tricuspid annulus minimal diameter (mm)	44.9±5.3	43.3±6.2	0.054
Tricuspid annulus mean diameter (mm)	49.2±6	47.6±5.4	0.078
Tricuspid Perimeter (mm)	159.3±20.7	155.9±19.9	0.297
SVC maximal diameter (mm)	27.2±3.1	28.9±3.8	0.711
SVC minimal diameter (mm)	21.9±1.7	25.7±4.4	0.136
SVC area (mm^2)	470.6±55.5	578.8±177.1	0.504
IVC maximal diameter (mm)	40.8±3.1	41.2±4.9	0.881
IVC minimal diameter (mm)	33.3±4.1	37.7±5.2	0.315
IVC area (mm^2)	998.1±163.0	1214.4±229.9	0.201
ECHOCARDIOGRAPHIC PARAMETERS (N=26)			
RA larger diameter (mm)	69.3±13.2	71.5±11.6	0.102
RA smaller diameter (mm)	55.9±11.7	59±11.2	0.143
RA area (mm2)	3564±1205	3650±1259	0.413
RV basal cavity diameter (mm)	49.1±7.4	46.9±6.8	0.222
RV mid-cavity diameter (mm)	41.4±8.9	37.1±8.1	**0.025**
RV longitudinal length (mm)	70.9±9.9	64.3±8.2	**0.001**
Tricuspid annulus diameter (mm)	44.8±7	43.9±3.5	0.586
SPPA (mmHg)	41.5±13.3	36.7±10.7	0.100
RV longitudinal strain (%)	-16.8±5.1	-12.7±10.5	0.196
TAPSE (mm)	19.3±3.6	17.8±4.6	0.141
LVEF (%)	60.9±9.7	61.3±8.2	0.872
TR EROA (mm2)	0.58 (0.37-0.88)	0.98 (0.64-1.5)	0.055
TR regurgitant volumen (mL)	46.2±15.2	58.8±22.6	0.208

CT: Computed tomography; EROA: Effective regurgitant orifice area; IVC: Inferior vena cava; RA: Right atrium; RV: Right ventricle; SPPA: Systolic pressure of pulmonary artery; SVC: Superior vena cava; TR: Tricuspid regurgitation.

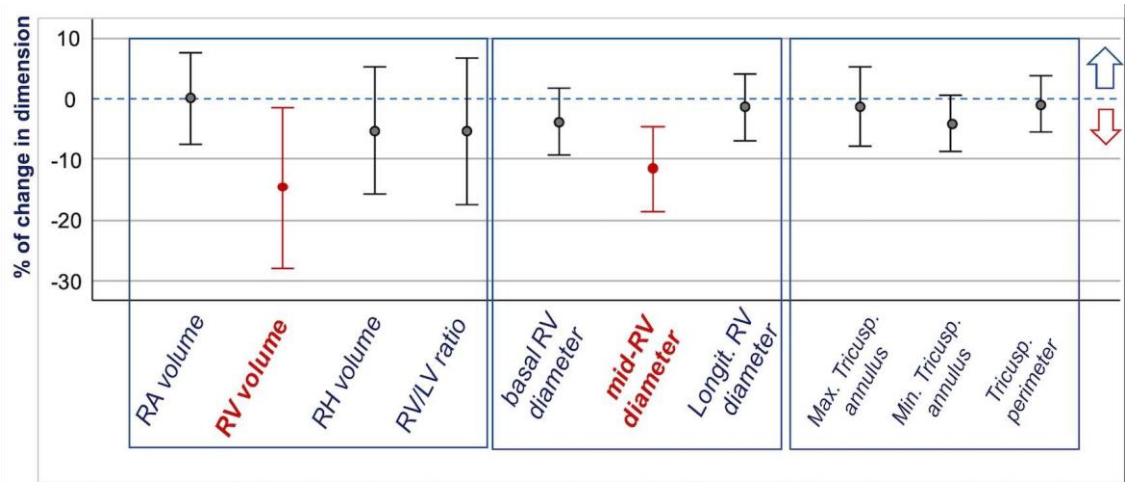
*Four chambers view.

Supplementary Table 2. Baseline factors associated with leakage of contrast into the inferior vena cava at 6-month follow-up post-TricValve implantation.

Parameter	No contrast in IVC (n=21)	Contrast leakage in IVC of any degree (n=5)	p-value
COMPUTED TOMOGRAPHY			
SVC maximal diameter (mm)	28.7±4.8	24.7±0.8	0.192
SVC minimal diameter (mm)	23.9±4.5	23.6±1.7	0.905
SVC area (mm^2)	541.6±188.6	435.1±37.5	0.366
Angle of IVC (º)*	15.6±4.1	25.6±8.8	**0.041**
IVC maximal diameter (mm)	37.3±5.8	44.6±2.5	0.054
IVC minimal diameter (mm)	28.6±4.1	37.4±4.5	**0.014**
IVC area (mm^2)	835.3±216.7	1276.5±240.3	**0.017**
BIOCHEMICAL PARAMETERS			
Baseline GFR (mL/min)	52.1 ± 16.1	51.9 ± 16.4	0.893
6-month FU GFR (mL/min)	56.2 ± 15.3	54.3 ± 14.9	0.210
Baseline AST (U/L)	29.8 ± 11.0	30.7 ± 11.3	0.905
6-month FU AST (U/L)	30.1 ± 15.2	31.2 ± 14.9	0.703
Baseline ALT (U/L)	17.9 ± 7.9	18.4 ± 8.2	0.304
6-month FU ALT (U/L)	21.2 ± 8.7	22 ± 8.9	0.415
Baseline NTproBNP (pg/mL)	2631 ± 2834	2661 ± 2900	0.832
6-month FU NTproBNP (pg/mL)	3001 ± 2432	3058 ± 2602	0.801

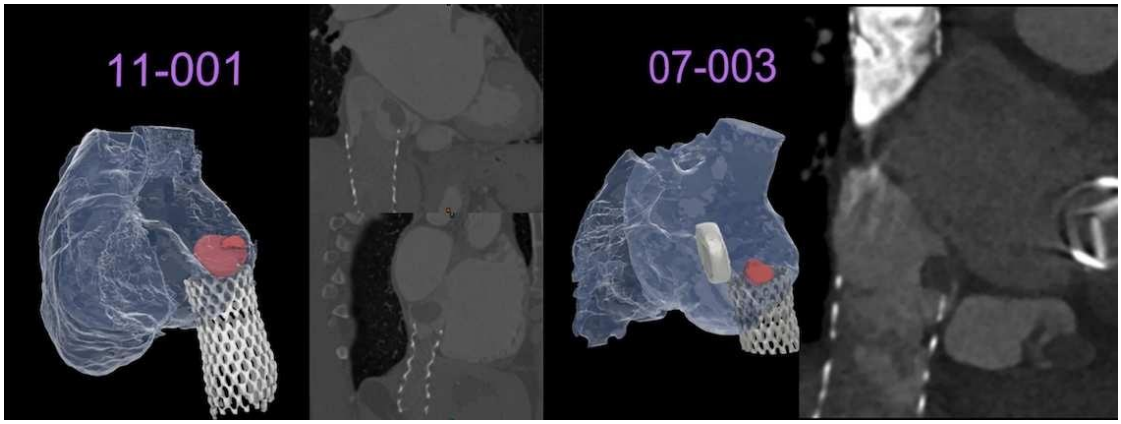
ALT: alanine amino-transferase; AST: aspartate amino-transferase; FU: follow up; GFR: glomerular filtration rate; IVC: Inferior vena cava; SVC: Superior vena cava.

*Measured as explained in Reference 3.



Supplementary Figure 1. One- to 6-month changes in right ventricular dimensions according to computed tomography.

diff: Difference in; LV: Left ventricle; min: Minimal; RV: Right ventricle.



Supplementary Figure 2. Presence of thrombus adhered to the inferior vena cava stent frame of the prosthesis in two patients.