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Thirty-day outcomes of the Cardioband tricuspid system for patients with symptomatic functional tricuspid regurgitation: the TriBAND study

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KEYWORDS

- femoral
- transoesophageal
- echocardiogram
- transthoracic echocardiogram
- tricuspid disease

Abstract

Background: Severe TR has limited treatment options and is associated with high morbidity and mortality.

Aims: We evaluated the safety and effectiveness of the Cardioband tricuspid valve reconstruction system (Edwards Lifesciences, Irvine, CA, USA) from the ongoing European single-arm, multicentre, prospective TriBAND post-market clinical follow-up study.

Methods: Eligible patients had chronic symptomatic functional TR despite diuretic therapy and were deemed candidates for transcatheter tricuspid repair by the local Heart Team.

Results: Sixty-one patients had ≥severe functional TR. At baseline, 85% of patients were in NYHA class III-IV, 94% had ≥severe TR (core laboratory-assessed) with 6.8% EuroSCORE II and 53% LVEF. Device success was 96.7%. At discharge, 59% ($p<0.001$) of patients achieved ≤moderate TR and 78% had at least one grade TR reduction. At 30 days, all-cause mortality and composite MAE rates were 1.6% and 19.7%, respectively; septolateral annular diameter was reduced by 20%, where 69% of patients achieved ≤moderate TR and 85% of patients had at least one grade TR reduction (all $p<0.001$). Mid-RVEDD, RA volume, and IVC diameter decreased by 10% ($p=0.005$), 21% ($p<0.001$), and 11% ($p=0.022$), respectively. 74% were in NYHA class I-II ($p<0.001$) with improvements in overall KCCQ score by 17 points ($p<0.001$).

Conclusions: In the TriBAND study, the Cardioband tricuspid system demonstrated favourable outcomes at discharge and 30 days in a challenging patient population with symptomatic ≥severe functional TR. Results showed significant reductions in annular diameter and TR severity, accompanied by early evidence of right heart remodelling and improvements in functional status and quality of life.

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Thirty-day outcomes of the Cardioband tricuspid system for patients with symptomatic functional tricuspid regurgitation: The TriBAND study

Short title: The TriBAND study 30-day outcomes

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Abstract

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Methods: Eligible patients had chronic symptomatic functional TR despite diuretic therapy and were deemed candidates for transcatheter tricuspid repair by the local heart team.

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Conclusions: In the TriBAND study, the Cardioband tricuspid system demonstrated favourable outcomes at discharge and 30 days in a challenging patient population with symptomatic ≥severe functional TR. Results showed significant reductions in annular diameter and TR severity, accompanied by early evidence of right heart remodelling and improvements in functional status and quality of life.

Classifications: Tricuspid disease, Femoral, Transthoracic echocardiogram, Transoesophageal echocardiogram

Condensed abstract:

We report the outcomes of the first 61 patients in the ongoing TriBAND post-market clinical follow-up study to evaluate the safety and effectiveness of the Cardioband tricuspid valve reconstruction system. Device success was 96.7%. At 30 days, all-cause mortality rate was 1.6%. Results in a challenging population of patients with ≥severe TR showed significant reduction in tricuspid septolateral annular diameter and tricuspid regurgitation severity accompanied with improvements in functional status and quality of life.

Abbreviations

CT = computed tomography

EQ-5D-5L = EuroQol 5-dimensions 5-level health questionnaire

EROA = effective regurgitant orifice area

KCCQ = Kansas City Cardiomyopathy Questionnaire

LVEF = left ventricular ejection fraction

MAE = major adverse event

NYHA = New York Heart Association

PISA = proximal isovelocity surface area

TEE = transoesophageal echocardiography

TR = tricuspid regurgitation

TTE = transthoracic echocardiography

Introduction

Tricuspid regurgitation (TR) is a prevalent disease and is dependent on age, sex, and concomitant left-sided heart conditions (1, 2). The prevalence of ≥moderate functional TR is as high as 23% in heart failure patients (2). Greater TR severity is associated with greater cardiovascular morbidity and mortality (2, 3). A recent epidemiological analysis and preliminary data from interventional studies suggest that TR itself may impact the clinical sequalae and outcome of patients (4). Despite some initial evidence that TR reduction may be associated with favourable outcomes, rigorous endpoint data are still lacking (5-8).

Unfortunately, treatment options for TR remain limited. Medical therapy has concentrated on preload reduction, whereas open heart surgery to treat TR is most often performed in patients undergoing left-sided heart surgery (9). Isolated TR surgery is infrequently performed given the late presentation and multiple comorbidities resulting in high perioperative morbidity and mortality rates (10, 11). Therefore, the focus is on less invasive options to treat TR.

The predominant aetiology of TR is functional, where dilatation of the tricuspid valve annulus occurs in response to either right ventricular or atrial enlargement leading to inadequate leaflet coaptation (12). Recently, transcatheter annular reduction was successfully performed with the Cardioband tricuspid valve reconstruction system (Edwards Lifesciences, Irvine, CA, USA) (5-7, 13). The single-arm, multicentre, prospective TRI-REPAIR study in patients with moderate or greater TR demonstrated favourable safety and feasibility of the Cardioband tricuspid system which significantly reduced TR, ameliorated heart failure symptoms and was accompanied with low adverse event rates (5, 6).

To extend the experience of the Cardioband tricuspid system, the TriBAND post-market clinical follow-up study was initiated, and this report summarizes the 30-day outcomes for the first 61 patients.

Methods

Trial Design

The European, single-arm, multicentre, prospective TriBAND post-market clinical follow-up study evaluates the safety and effectiveness of the Cardioband tricuspid system to treat up to 150 patients with functional TR. Herein, we report the outcomes of the first 61 patients enrolled in the ongoing study.

Key inclusion criteria were chronic symptomatic ≥moderate functional TR confirmed by echocardiographic core laboratory and heart failure symptoms with New York Heart Association (NYHA) functional class II-IV despite optimal medical therapy including diuretic therapy. Patients were deemed candidates for transcatheter tricuspid repair by the multidisciplinary local heart team. Key exclusion criteria were left ventricular ejection fraction (LVEF) <25%; pulmonary arterial systolic pressure >70 mmHg by echocardiography or right heart catheterization; tricuspid proximal isovelocity surface area (PISA) effective regurgitant orifice area (EROA) ≥2.0 cm^2; severe right ventricular dysfunction; tricuspid valve anatomy precluding proper device deployment and function; previous tricuspid valve repair or replacement; presence of trans-tricuspid valve pacemaker or defibrillator leads impinging the tricuspid valve leaflets as evaluated by echocardiography; and renal insufficiency requiring dialysis or severe kidney renal disease with eGFR ≤25 mL/min/1.73 m^2.

Study Conduct

An independent echocardiographic core laboratory assessed all echocardiograms at baseline, discharge, and 30 days, and an independent clinical events committee (CEC) adjudicated safety endpoints and all-cause mortality. The study was approved by local ethics committees and respective health authorities of the participating countries. All patients provided written informed consent and the study was conducted in conformance with the Declaration of Helsinki, Good Clinical Practice principles, and ISO 14155:2011. The study is registered at ClinicalTrials.gov (NCT03779490).

The Cardioband Tricuspid System Procedural Pre-planning

Transoesophageal echocardiography (TEE), cardiac computed tomography (CT), and fluoroscopy were used for screening patient anatomy and procedural pre-planning. All patients were qualified to have ≥moderate functional TR by site evaluation. Optimal Cardioband implant size was selected using CT measurement of the tricuspid annular circumference at the phase closest to early diastole (5-7).

The Cardioband Tricuspid System Procedure

The Cardioband implant is deployed *via* transfemoral venous access using the 26-F delivery system under TEE and fluoroscopic guidance. Intra-procedural coronary angiography is performed periodically to assess the proximity of the right coronary artery (RCA) to the implant to prevent complications. The first anchor is deployed on the atrial side of the tricuspid valve annulus at the anterior-septal commissure near the aortic root and close to the tricuspid leaflet hinge point. The Cardioband implant is advanced and positioned along the anterior and posterior regions of the tricuspid annulus by deploying a series of anchors in a stepwise manner. Upon full deployment, the implant is optimally contracted using the size adjustment tool to reduce the tricuspid annular diameter and area, thereby reducing TR (5-7).

Trial Endpoints

The primary endpoint is reduction in TR severity between baseline and discharge. Secondary endpoints include TR severity, NYHA functional class, EuroQol 5-dimensions 5-level health questionnaire (EQ-5D-5L), and overall Kansas City Cardiomyopathy Questionnaire (KCCQ) at 30 days post-implant.

The safety endpoint is a composite of major adverse events (MAEs) defined as cardiovascular mortality, myocardial infarction (MI), stroke, pericardial effusion requiring intervention, coronary artery injury requiring percutaneous or surgical intervention, arrhythmia and conduction disorders requiring permanent pacing, new need for renal replacement therapy, severe bleeding (14), non-elective tricuspid valve reintervention (percutaneous or surgical), major access site and vascular complications, and major cardiac structural complications.

Device success is calculated for patients in whom the device was attempted and is defined as device deployed and the delivery system successfully retrieved as intended at the time of the patient's exit from the cardiac catheterization laboratory (per device). Procedural success was defined as device success with 30% TR reduction in PISA EROA post-procedure relative to baseline, and without the need for intervention prior to discharge (per patient). Clinical success is defined as procedural success with no MAEs at 30 days (per patient).

Echocardiography

An independent core laboratory (Cardiovascular Research Foundation, NY) assessed all echocardiograms at baseline, discharge, and 30-day follow-up based on American Society of Echocardiography (ASE) guidelines (15). Septolateral annular dimensions were measured from the outer-to-outer borders of the device from an apical 4-chamber or RV-focused view in end-diastole. Evaluation of TR was performed using standard 2-dimensional color Doppler and

quantitative methods, while TR severity was assessed using the 5-grade scheme (16-17). Mean vena contracta was calculated as the average of vena contracta widths measured using two orthogonal planes or 4-chamber and parasternal RV inflow views. Regurgitant volume and EROA were calculated using PISA and Doppler volumetric methods, whereas LVEF was measured using Biplane Simpson's methods of discs (5-7).

Statistical Analysis

Analysis was performed on the intent-to-treat (ITT) population. Continuous variables are presented as mean ± SD using paired Student's *t*-test, whereas categorical variables are presented as a percentage using Wilcoxon signed-rank test to compare baseline and post-procedure follow-up periods. Statistical significance was set at $p<0.05$ as two-tailed tests. Delta, percent change, and p-value were calculated using paired analyses. Paired analysis for all echocardiographic and functional outcomes are provided in Supplementary Material (Supplementary Figure 1, Supplementary Figure 2, Supplementary Figure 3, Supplementary Table 1). Statistical analyses were performed using SAS Software version 9.4 (SAS Institute, Cary, NC).

Results

We report results from the first 61 patients enrolled across 13 European sites between July 2019 and December 2020.

Baseline Characteristics

Mean age was 78.6 ± 5.7 years, 75% were female, and 85% were in NYHA functional class III-IV. Mean N-terminal pro-B type natriuretic peptide (NT-pro BNP) levels were elevated to 2072 ± 1495 pg/mL. Mean EuroSCORE II (European System for Cardiac Operative Risk Evaluation) was 6.8 ± 10.1% and STS PROM (Society of Thoracic Surgeons predicted risk of mortality) mortality score was 7.1 ± 5.4% (**Table 1**).

All 61 patients had ≥severe functional TR based on their site-evaluated qualifying echocardiograms; of the 53 patients whose TR was quantified by the echocardiographic core laboratory, 94% had ≥severe TR at baseline. **(Central Illustration)**. Mean end-diastolic tricuspid septolateral diameter was 45.5 ± 4.5 mm and mean LVEF was 53.3 ± 7.6%. Comorbidities included atrial fibrillation/flutter (92%); pulmonary hypertension (46%); renal disease (43%); type II diabetes (28%); prior pacemaker or cardiac resynchronization therapy (15%); and prior MI (10%) (**Table 1**).

Of the 61 patients, 30-day follow-up was performed in 52 patients. One patient died before the visit, one patient exited from the study after an aborted procedure, and seven patients had missed or pending visits.

Procedural and Discharge Results

The device was attempted in 98.4% (n=60 of 61) ITT patients. In one patient, guidewire perforation of the RCA occurred prior to device insertion and the procedure was aborted Device success was 96.7% (n=58 of 60). Two patients did not receive the device due to partial deployment of anchors leading to inability to contract the implant (n=1) and poor TEE visibility along with RCA proximity and steep atrial wall (n=1). The procedural success was 83.9% (n=26 of 31; EROA unreadable for 30 patients). Procedure time was 202 ± 52 min and fluoroscopy time was 67 ± 27 min. The mean length of hospital stay was 6.5 ± 3.2 days; 88% of patients were discharged home; 12% were discharged to a rehabilitation facility or to a different department in the same hospital, of which one patient died prior to discharge on post-operative day (POD) 18 (**Table 2**).

Echocardiographic Results

Echocardiographic results were evaluated by the core laboratory for 54 patients at discharge and 42 patients at 30 days **(Table 3, Central Illustration)**. The end-diastolic tricuspid septolateral annular diameter was reduced by 19% ($p<0.001$) at discharge and was stable at 30 days (20%, $p<0.001$) **(Central Illustration; Panel A).** At discharge and 30 days, 59% ($p<0.001$) and 69% ($p<0.001$) of patients achieved ≤moderate TR, respectively **(Central Illustration; Panel B).** At discharge, 78% of patients achieved at least one grade TR reduction and 59% achieved at least two grade TR reduction. At 30 days, at least one grade TR reduction was achieved in 85% of patients and at least two grade TR reduction in 59% (**Central Illustration; Panel C).**

Early signs of right heart remodelling were evidenced by significant improvements in various echocardiographic indices from baseline to 30 days (**Figure 1**). Mid-right ventricular end diastolic diameter decreased by 10% ($p=0.005$), right atrial volume decreased by 21% ($p<0.001$), and inferior vena cava diameter decreased by 11% ($p=0.022$). Although RV TAPSE was significantly reduced at 30 days, there was a significant increase in left ventricular stroke volume by 12% ($p=0.007$). Similarly, estimated systolic pulmonary artery pressure (sPAP) and cardiac output increased at 30 days (**Table 2**).

Clinical Outcomes

At 30 days, all-cause mortality was 1.6% and the composite MAE rate was 19.7% (**Table 4**). Clinical success was 54.1% (n=20 of 37; could not be calculated for 24 patients). One patient developed device- and procedural-related pericardial effusion with severe bleeding requiring drainage. Intra-procedurally, the patient received 100 mL of contrast. The patient also developed uremic encephalopathy on POD 2, requiring dialysis which was declined by the patient. The

patient was transferred to the palliative care and died due to procedure-related renal failure on POD 18.

One patient experienced device- and procedural-related MI due to a transient intra-procedural occlusion of the RCA on POD 0 that resolved spontaneously. On POD 5, the patient also experienced procedure-related severe bleeding, and major access site and vascular complications due to a groin hematoma that also resolved without further treatment.

Four patients experienced coronary artery injuries requiring intervention. One patient experienced a device-related distal RCA occlusion requiring placement of three drug-eluting stents (DES). One patient experienced an RCA flow restriction following contraction of the Cardioband implant that was resolved with one DES and balloon dilatation. One patient developed ST segment elevations due to an RCA occlusion and underwent percutaneous transluminal coronary angioplasty with successful restoration of blood flow. One patient had extravasation of blood on coronary angiography due to a posterior descending artery perforation from the 13th anchor placement which was repositioned, and successfully treated by placement of a covered stent.

One patient experienced device- and procedural-related intra-procedural bradycardia due to a 3rd degree atrioventricular block, which was treated with a permanent single-chamber pacemaker.

Of the two patients who needed new renal replacement therapy, one patient died (aforementioned) and another patient had procedure-related acute kidney injury requiring dialysis.

Seven patients, all undergoing anticoagulation or antiplatelet therapy due to pre-existing atrial fibrillation/flutter, developed severe bleeding of which none were fatal and four were major

access site- and vascular complication-related. One patient developed a pericardial effusion requiring drainage (aforementioned), one patient had a partial perforation of the RCA requiring no intervention, and one patient developed a device-related access site hemorrhage from the right superficial femoral artery. Three patients had procedure-related right vascular access site hematomas. One patient had a gastrointestinal bleed not related to the device or procedure.

There were no incidents of stroke, non-elective tricuspid valve reinterventions, or major cardiac structural complications.

Functional and Quality of Life Outcomes

At baseline, 85% were in NYHA functional class III-IV. At 30 days, 74% of patients were in NYHA functional class I-II ($p<0.001$) (**Figure 2A**), overall KCCQ score improved by 17 points ($p<0.001$) (**Figure 2B**), and EQ-5D-5L health score improved by 3 points ($p=0.313$) (**Figure 2C**).

Discussion

These results from the first 61 ITT patients in the ongoing post-market TriBAND study showed reproducibility of the TRI-REPAIR study which led to the CE mark of the Cardioband tricuspid therapy. While the TriBAND study eligibility included moderate or greater TR, 94% of patients enrolled had severe or greater TR at baseline and the results were favorable.

Patients treated in this study had a mean age of 79 years and were severely compromised with multiple comorbidities. Most patients suffered from advanced heart failure, which was mostly driven by right heart disease. Although left ventricular function was preserved, right ventricular function and dimensions were severely affected. Dilatation of the right heart caused pathological septolateral annular dilatation as large as 55.0 mm with secondary malcoaptation of

the tricuspid valve leaflets, and subsequent development of functional TR. Core laboratory-adjudicated echocardiographic evaluations revealed that 94% of patients displayed ≥severe TR at baseline (40% torrential TR, 28% massive TR) - an overall challenging cohort of patients.

Device success was achieved in 97% of patients and procedural success achieved in 84%. Contraction of the device led to a 20% reduction of the septolateral annular diameter followed by significant reduction of echocardiographic parameters, such as PISA EROA and mean vena contracta at 30 days. Correspondingly, ≥severe TR was decreased from 94% at baseline to 31% of patients with 85% having at least one grade TR reduction at 30 days. Similar results were demonstrated in the TRI-REPAIR study at 30 days and were sustained to 2 years (5, 6). Continued enrollment to 150 patients and follow-up to 5 years in the TriBAND study is ongoing to evaluate long-term outcomes.

Reduction of regurgitant volume was accompanied by relief of right heart overload as demonstrated by a reduction of right atrial volume and inferior vena cava diameter within 30 days. Similar results were shown in the TRI-REPAIR and TRILUMINATE studies (5, 6, 8). Thus, reduction of regurgitant flow initiates immediate positive reductions in right heart size. The reduction in TAPSE accompanying the reduction in TR is likely a result of both the increase in afterload following reduction in TR, but also the increase in forward flow as evidence by the increase in sPAP and cardiac output. The right ventricular response to increased afterload is expected as has been shown in prior studies (18). It may be speculated that although severely diseased, TR-derived right heart disorders are in part functional in nature and can be potentially reversible, providing hope for long-term beneficial effects of the Cardioband tricuspid system.

As a functional consequence of improved right heart performance, left ventricular stroke volume significantly increased. The observed anatomical and functional improvements following

the Cardioband tricuspid system implantation led to the clinical benefits in the treated patients with improved NYHA functional class I-II from 15% at baseline to 74% at 30 days. Improvement in the overall KCCQ and EQ-5D-5L scores confirm these functional improvements. Similar to the recent studies, in the TriBAND study, even though TR severity was not reduced to ≤mild, heart failure symptoms were significantly alleviated (5-8).

There are a few constraints of the Cardioband tricuspid system that are worth mentioning. Firstly, patients with severe leaflet tethering >15.0 mm are ineligible for direct annular reduction therapy (19). Secondly, the procedure time continues to improve and warrants further development. In the TriBAND study, the device time was 146 min and total procedure time was 202 min, which is lower compared to previously reported 255 min in the TRI-REPAIR study, indicative of a shortened learning curve at the participating centres (5). Thirdly, Cardioband implantation requires anchor placement between the leaflet hinge points and the RCA and careful pre-procedural planning is necessary. Repeat angiography assists in optimal guidewire placement, while CT scan prevents anchor-RCA perforation and excludes any rare anatomies that are in proximity to the RCA or tricuspid annulus. Even with these measures, in the TriBAND study, RCA injury requiring intervention was observed in 6.6% of patients, comparable to the TRI-REPAIR study (5). Fourthly, in this high-risk heart failure population, the bleeding rates were considerable at 30 days and were mostly access site-related, highlighting the need to revisit intra-procedural and site-specific anticoagulation or anti-platelet regimen. Operator experience with the device and procedure, along with improvements in imaging quality and device technology may further reduce procedure time, while avoiding complications (5-7). Nonetheless, the promising outcomes of this study are comparable to other transcatheter repair therapies (5-8, 20).

In summary, the Cardioband tricuspid system uniquely addresses a fundamental pathology of functional TR, i.e., dilatation of the tricuspid annulus. By addressing the annulus and maintaining the native tricuspid leaflets, the Cardioband tricuspid system preserves the option for future interventions such as leaflet repair or valve replacement.

Limitations

This was a non-randomized, non-blinded study. There may be a placebo effect of the intervention, and the results should be carefully interpreted. The sample size is small, and more patients and long-term results are needed. TR severity and EROA are missing for many patients as they could not be appropriately evaluated by the echocardiographic core laboratory due to insufficient echocardiograms, warranting additional site training.

Conclusions

The Cardioband tricuspid system demonstrated favourable outcomes at 30 days in the TriBAND study in a challenging patient population with symptomatic ≥severe functional TR. The 30-day results demonstrated significant TR severity reduction through annular reduction, accompanied by early evidence of right heart remodelling and improvements in heart failure symptoms and quality of life. Study enrolment and follow-up is ongoing.

Impact on daily practice

Tricuspid regurgitation is a prevalent disease and is associated with poor clinical outcomes and limited treatment options. Many of these patients have no alternative therapy

options, even with the availability of transcatheter TR intervention. The Cardioband tricuspid system significantly reduced tricuspid regurgitation through annular reduction and consequently reduced heart failure symptoms in a challenging patient population with severe or greater TR.

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Figures

Central Illustration: Septolateral annular diameter reduction and TR severity reduction to 30 days with the Cardioband tricuspid system. (A) End-diastolic septolateral diameter at baseline, discharge, and 30 days. Values are mean, 95% confidence interval. (B) Qualifying TR severity at screening ([1]Site-reported). Core laboratory adjudicated TR severity at baseline, discharge, and 30-day follow-up. (C) Patients with at least one- and two-grade TR reduction at discharge and 30 days, respectively. [a]Paired *t*-test comparing baseline and discharge (n=50) or baseline and 30 days (n=38); [b]Paired Wilcoxon signed-rank test comparing baseline and discharge (n=51) or baseline and 30 days (n=39).

Figure 1: Early evidence of right heart remodelling from baseline to 30 days. (A) Mid-right ventricular end diastolic diameter (RVEDD), (B) Right atrial (RA) volume, and (C) Inferior vena cava (IVC) diameter at baseline and 30 days. Values are mean ± SD. Paired *t*-test comparing [a]baseline and 30 days (n=37), [b]baseline and 30 days (n=39) and [c]baseline and 30 days (n=30).

Figure 2: Improvements in functional and clinical measurements from baseline to 30 days. (A) NYHA functional class, (B) Kansas City Cardiomyopathy Questionnaire (KCCQ) score, and (C) EuroQol 5-dimensions 5-level health questionnaire (EQ-5D-5L) score at baseline and 30 days. Values are mean ± SD. Paired *t*-test or Wilcoxon signed-rank test comparing [a]baseline and 30 days (n=50), [b]baseline and 30 days (n=52) and [c]baseline and 30 days (n=53).

Tables

Table 1. Baseline characteristics

Characteristic	N=61
Age, years	78.6 ± 5.7
Female	46 (75.4%)
NYHA functional class III-IV	52 (85.2%)
EuroSCORE II (%)	6.8 ± 10.1
STS PROM score[1] (%)	7.1 ± 5.4
NT-pro BNP (pg/mL)	2072.1 ± 1495.6
Echocardiographic parameters[2]	
LVEF (%)	53.3 ± 7.6
TR grade ≥severe (n=53)	50 (94.3%)
Tricuspid annular septolateral diameter (mm)	45.5 ± 4.5
PISA EROA (cm^2)	0.76 ± 0.48
sPAP (mmHg)	33 ± 11
Comorbidities	
Pulmonary hypertension	28 (45.9%)
Hypertension	51 (85.0%)
Atrial fibrillation/flutter	56 (91.8%)
Conduction defects/heart block	7 (12.3%)
Myocardial infarction	6 (10.3%)
Stroke	8 (13.6%)
Transient ischemic attack	4 (7.1%)
Percutaneous coronary intervention/stent	14 (23.0%)
Prior pacemaker/CRT	9 (14.8%)
Coronary artery disease	7 (11.9%)
Coronary artery bypass graft	5 (8.2%)
Peripheral arterial disease	2 (3.4%)
Dyslipidemia/hyperlipidemia	20 (34.5%)
Type II diabetes	17 (27.9%)
Renal disease	26 (42.6%)
Prior valve procedure/surgery	
Aortic valve	6 (9.8%)
Mitral valve	13 (21.3%)

Data presented as n (%) or Mean ± SD. [1]Calculated based on isolated mitral valve replacement only. [2]Core laboratory adjudicated. CRT=cardiac resynchronisation therapy; ICD=implantable

cardioverter defibrillator; EF= ejection fraction; EROA=effective regurgitant orifice area; LV=left ventricle; NT-pro BNP=N-terminal pro-B type natriuretic peptide NYHA=New York Heart Association; PISA=proximal isovelocity surface area; STS PROM=Society of Thoracic Surgeons predicted risk of mortality; sPAP=systolic pulmonary artery pressure.

Table 2. Procedural and discharge characteristics

Characteristic	N=61
Device success[1]	96.7 (58/60)
Procedural success[2]	83.9 (26/31)
Clinical success[3]	54.1 (20/37)
Procedure time[4] (min)	202.2 ± 51.6 (58)
Device time[5] (min)	146.0 ± 41.4 (55)
Fluoroscopy duration (min)	67.1 ± 26.8 (61)
Implant size (mm)	
89-96	3.4 (2)
97-104	8.5 (5)
105-112	27.1 (16)
113-120	61.0 (36)
Length of hospital stay (days)	6.5 ± 3.2 (60)
Discharge location	
Home	88.3% (53/60)
Other[6]	11.7% (7/60)

Values are % (n) or % (n/N) or mean ± SD (n). [1]Device is deployed as intended and the delivery system is successfully retrieved as intended at the time of the patient's exit from the cardiac catheterization laboratory. [2]Device success with evidence of a 30% TR reduction in EROA at end of procedure relative to baseline, and without need for intervention prior to discharge; EROA unreadable for 30 patients. [3]Procedural success without MAEs at 30 days; could not be calculated for 24 patients. [4]Skin incision-to-femoral vein closure. [5]Implant delivery system insertion-to-removal. [6]Discharged to rehabilitation facility or different department in the same hospital.

Table 3. Echocardiographic variables at baseline, discharge, and 30 days by core laboratory (TTE)

Variable	Baseline	Discharge	Change[a] p-value[b]	30 days	Change[a] p-value[b]
Tricuspid annular septolateral diameter (mm)	45.5 ± 4.5 (52)	36.7 ± 5.0 (54)	-8.7 ± 3.6 **<0.001**	36.1 ± 5.0 (42)	-8.9 ± 5.1 **<0.001**
PISA EROA (cm^2)	0.76 ± 0.48 (41)	0.39 ± 0.35 (36)	-0.44 ± 0.37 **<0.001**	0.34 ± 0.27 (37)	-0.45 ± 0.36 **<0.001**
Mean vena contracta (cm)	1.50 ± 0.56 (48)	0.89 ± 0.55 (50)	-0.67 ± 0.44 **<0.001**	0.79 ± 0.52 (37)	-0.70 ± 0.43 **<0.001**
Mid-RV end diastolic diameter (4ch) (cm)	4.0 ± 0.8 (50)	3.7 ± 0.7 (51)	-0.3 ± 0.6 **0.007**	3.6 ± 0.6 (41)	-0.4 ± 0.7 **0.005**
Base RV end diastolic diameter (4ch) (cm)	5.4 ± 0.7 (52)	4.8 ± 0.6 (52)	-0.6 ± 0.4 **<0.001**	4.8 ± 0.6 (42)	-0.6 ± 0.7 **<0.001**
RA volume, single plane Simpson's (4ch) (mL)	168.8 ± 69.3 (53)	139.5 ± 63.4 (51)	-25.4 ± 42.0 **<0.001**	140.0 ± 65.8 (42)	-37.2 ± 45.4 **<0.001**
IVC diameter (cm)	2.7 ± 0.6 (46)	2.5 ± 0.7 (50)	-0.2 ± 0.4 **0.004**	2.3 ± 0.7 (39)	-0.3 ± 0.6 **0.022**
Hepatic vein flow reversal (%)			**0.031**		0.063
Yes	100 (34/34)	60.6 (20/33)		60.7 (17/28)	
No	0 (0/34)	39.4 (13/33)		39.3 (11/28)	
RV FAC (%)	37.6 ± 6.6 (46)	34.7 ± 4.9 (49)	-2.8 ± 6.5 **0.012**	36.6 ± 5.4 (41)	-0.4 ± 5.9 0.715
RV TAPSE (cm)	1.6 ± 0.3 (52)	1.4 ± 0.3 (53)	-0.2 ± 0.3 **<0.001**	1.5 ± 0.4 (42)	-0.1 ± 0.3 **0.010**
2D TV annular area (cm^2)	14.3 ± 2.7 (38)	10.0 ± 2.4 (42)	-4.6 ± 1.6 **<0.001**	9.7 ± 2.4 (36)	-4.4 ± 2.0 **<0.001**
sPAP (mmHg)	33.1 ± 11.0 (52)	41.0 ± 14.2 (54)	7.6 ± 14.0 **<0.001**	38.4 ± 9.6 (41)	3.5 ± 10.2 **0.045**
TV tenting height (cm)	0.8 ± 0.2 (46)	0.8 ± 0.2 (44)	0.01 ± 0.2 0.730	0.7 ± 0.3 (37)	-0.1 ± 0.2 **0.017**
LV stroke volume (mL)	56.2 ± 13.0 (34)	63.5 ± 15.0 (36)	6.6 ± 10.9 **0.004**	62.3 ± 13.1 (33)	6.8 ± 11.2 **0.007**

LV ejection fraction (%)	53.3 ± 7.6 (49)	54.5 ± 7.5 (48)	2.0 ± 4.7 **0.010**	54.8 ± 8.2 (41)	1.6 ± 5.9 0.123
Cardiac output (L/min)	4.2 ± 1.0 (34)	4.9 ± 1.2 (36)	0.5 ± 1.1 **0.043**	5.1 ± 1.2 (33)	0.7 ± 1.1 **0.004**

Values are mean ± SD (n) or %(n/N); [a]Change (mean ± SD) was calculated for paired observations, and [b]p-values were calculated by Student's *t-test* for paired observations. CH=chamber; FAC=fractional area change; IVC=inferior vena cava; LV=left ventricle; PISA EROA=proximal isovelocity surface area effective regurgitant orifice area; sPAP=systolic pulmonary artery pressure; TAPSE=tricuspid annular plane systolic excursion; TR=tricuspid regurgitation; RA=right atrium; RV=right ventricle; TTE=transthoracic echocardiography; TV=tricuspid valve.

Table 4. CEC adjudicated safety events at 30 days

Major adverse events	**N=61 n (%)**
Cardiovascular mortality	0
Myocardial infarction	1 (1.6)
Stroke	0
Pericardial effusion requiring intervention	1 (1.6)
Coronary artery injury requiring intervention	4 (6.6)
Arrhythmia and conduction disorders requiring permanent pacing	1 (1.6)
New need for renal replacement therapy	2 (3.3)
Severe bleeding[1]	7 (11.5)
Non-elective tricuspid valve reinterventions	0
Major access site and vascular complications	4 (6.6)
Major cardiac structural complications	0
Composite MAE rate	12 (19.7)
Other events	
All-cause mortality	1 (1.6)¶

[1]Severe bleeding is major, extensive, life-threatening or fatal bleeding, as defined by MVARC. ¶Due to procedure-related renal failure. CEC=clinical events committee; MAE=major adverse event.

Central Illustration

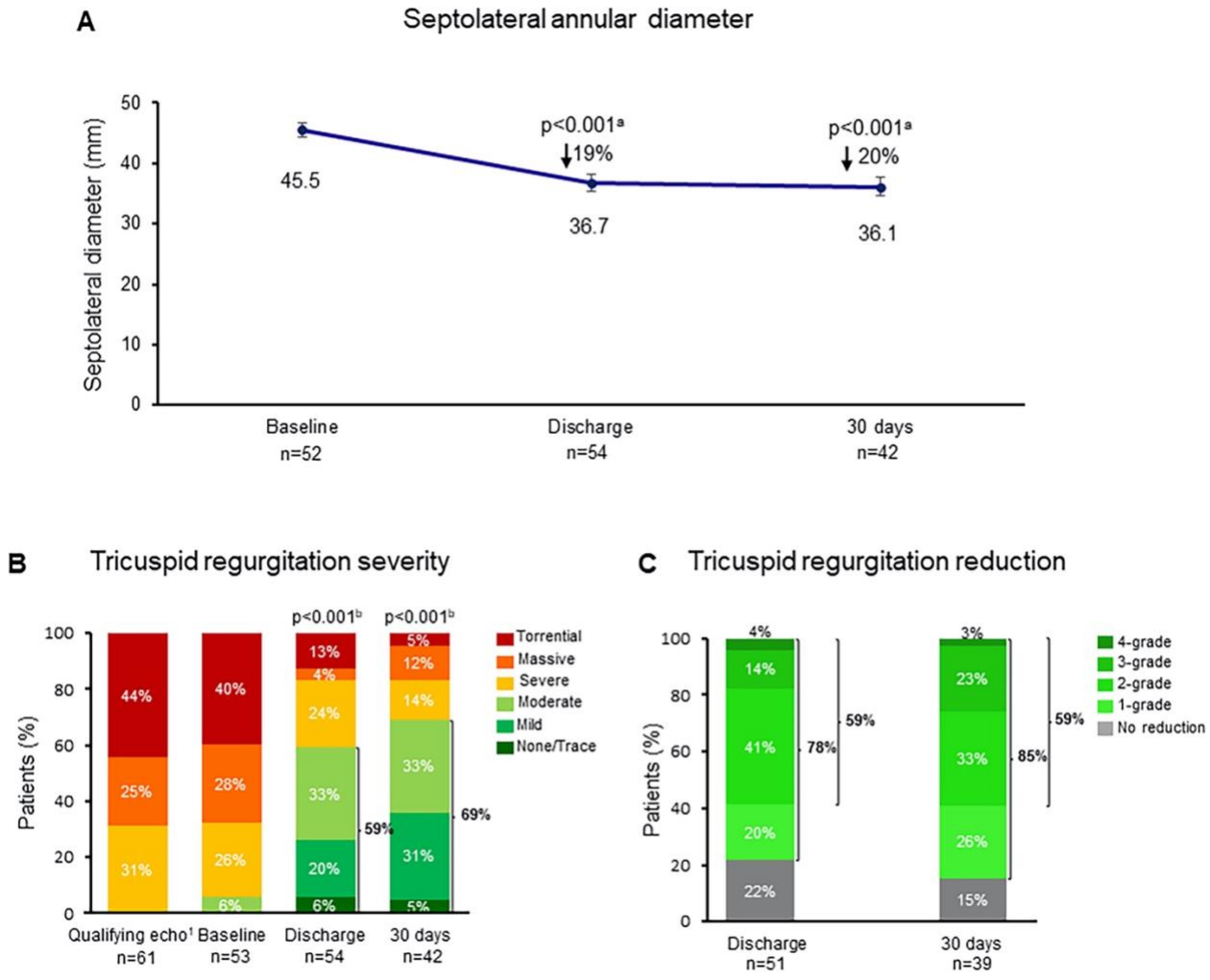


Figure 1

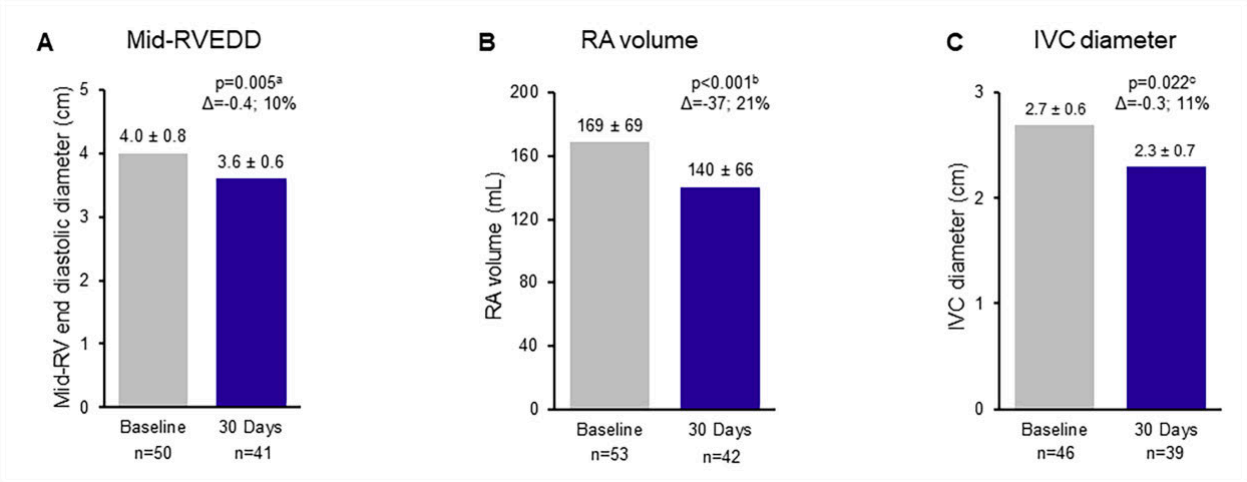
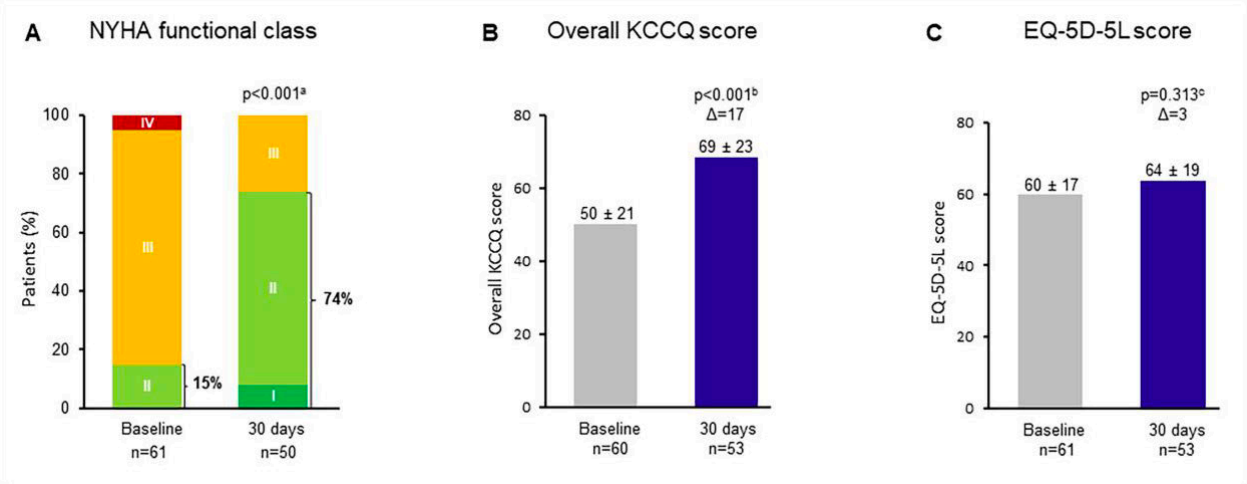


Figure 2



Supplementary Material

Supplementary Figure 1: Septolateral annular diameter reduction and TR severity reduction over 30 days with the Cardioband tricuspid System in paired analysis. (A) End-diastolic septolateral diameter at baseline, discharge, and 30 days. Values are mean, 95% confidence interval. (B) TR severity at baseline versus discharge and baseline versus 30 days. Paired *t*-test or Wilcoxon signed-rank test comparing baseline and discharge or baseline and 30 days.

Supplementary Figure 2: Early evidence of right heart remodelling from baseline to 30 days in paired analysis. (A) Mid-right ventricular end diastolic diameter (RVEDD), (B) Right atrial (RA) volume, and (C) Inferior vena cava (IVC) diameter at baseline and 30 days. Values are mean ± SD. Paired *t*-test comparing baseline and 30 days.

Supplementary Figure 3: Improvements in functional and clinical measurements from baseline to 30 days in paired analysis. (A) NYHA functional class, (B) Kansas City Cardiomyopathy Questionnaire (KCCQ) score, and (C) EQ-5D-5L score at baseline and 30 days. Values are mean ± SD. Paired *t*-test or Wilcoxon signed-rank test comparing baseline and 30 days.

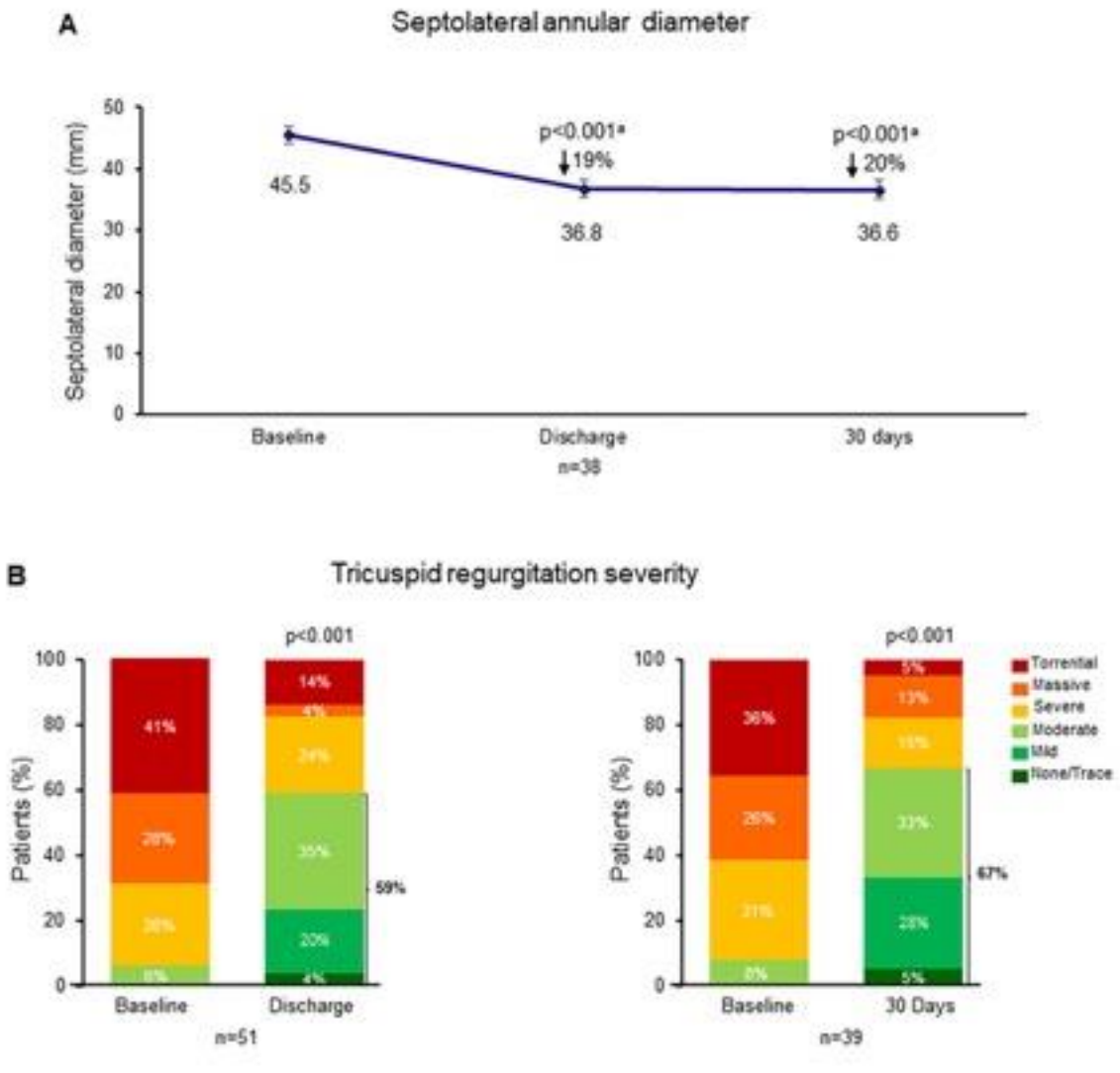
Supplementary Table 1. Paired analysis of echocardiographic variables at baseline, discharge and 30 days

TTE Variables	Baseline	Discharge	Change[a] p-value[b]	Baseline	30 days	Change[a] p-value[b]
Tricuspid annular septolateral diameter (mm)	45.6 ± 4.5	36.9 ± 5.0	-8.9 ± 3.6 (50) **<0.001**	45.5 ± 4.5	36.6 ± 4.8	-8.9 ± 5.1 (38) **<0.001**
PISA EROA (cm^2)	0.87 ± 0.52	0.42 ± 0.38	-0.44 ± 0.37 (29) **<0.001**	0.83 ± 0.54	0.38 ± 0.29	-0.45 ± 0.36 (29) **<0.001**
Mean vena contracta (cm)	1.50 ± 0.58	0.87 ± 0.55	-0.67 ± 0.44 (44) **<0.001**	1.50 ± 0.62	0.83 ± 0.54	-0.70 ± 0.43 (32) **<0.001**
Mid-RV end diastolic diameter (4ch) (cm)	4.0 ± 0.7	3.7 ± 0.7	-0.3 ± 0.6 (45) **0.007**	4.0 ± 0.8	3.6 ± 0.6	-0.4 ± 0.7 (37) **0.005**
Base RV end diastolic diameter (4ch) (cm)	5.4 ± 0.7	4.9 ± 0.6	-0.6 ± 0.4 (48) **<0.001**	5.4 ± 0.6	4.8 ± 0.6	-0.6 ± 0.7 (38) **<0.001**
RA volume, single plane Simpson's (4ch) (mL)	168.2 ± 71.7	142.8 ± 63.4	-25.4 ± 42.0 (48) **<0.001**	180.2 ± 47.1	142.9± 66.8	-37.2 ± 45.4 (39) **<0.001**
IVC diameter (cm)	2.7 ± 0.6	2.5 ± 0.7	-0.2 ± 0.4 (41) **0.004**	2.7 ± 0.6	2.4 ± 0.7	-0.3 ± 0.6 (30) **0.022**
Hepatic vein flow reversal (%)			**0.031 (23)**			0.063 (20)
Yes	100 (23/23)	73.9 (17/23)		100 (20/20)	75.0 (15/20)	
No	0 (0/23)	26.1 (6/23)		0 (0/20)	25.0 (5/20)	
RV FAC (%)	37.7 ± 7.0	34.9 ± 5.2	-2.8 ± 6.5 (39) **0.012**	36.9 ± 6.2	36.5 ± 4.9	-0.4 ± 5.9 (34) 0.715
RV TAPSE (cm)	1.6 ± 0.3	1.4 ± 0.3	-0.2 ± 0.3 (49) **<0.001**	1.6 ± 0.4	1.5 ± 0.4	-0.1 ± 0.3 (39) **0.010**
2D TV annular area (cm^2)	14.3 ± 2.1	9.7 ± 1.8	-4.6 ± 1.6 (32) **<0.001**	14.4 ± 2.4	10.0 ± 2.3	-4.4 ± 2.0 (28) **<0.001**
sPAP (mmHg)	33.4 ± 11.1	41.0 ± 14.5	7.6 ± 14.0 (50) **<0.001**	34.2 ± 11.6	37.7 ± 9.6	3.5 ± 10.2 (37) **0.045**
TV tenting height (cm)	0.8 ± 0.2	0.8 ± 0.2	-0.01 ± 0.2 (38) 0.730	0.8 ± 0.2	0.7 ± 0.2	-0.1 ± 0.2 (29) **0.017**
LV stroke volume (mL)	55.8 ± 13.5	62.4 ± 15.4	6.6 ± 10.9 (27) **0.004**	55.8 ± 14.2	62.6 ± 14.5	6.8 ± 11.2 (24) **0.007**

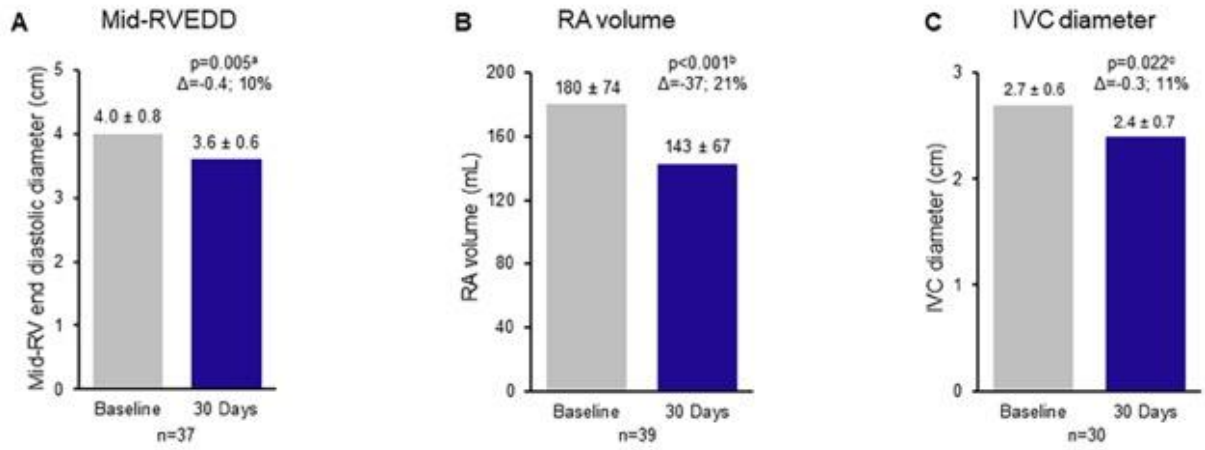
LV ejection fraction (%)	53.2 ± 7.8	55.2 ± 7.2	2.0 ± 4.7 (41) **0.010**	53.5 ± 8.0	55.1 ± 8.2	1.6 ± 5.9 (35) 0.123
Cardiac output (L/min)	4.1 ± 1.0	4.6 ± 1.2	0.5 ± 1.1 (27) **0.043**	4.2 ± 1.1	4.9 ± 1.2	0.7 ± 1.1 (24) **0.004**

Values are mean ± SD (n); [a]Change (mean ± SD [n]) was calculated for paired observations, and [b]p-values were calculated by Student's *t*-test for paired observations. CH=chamber; FAC=fractional area change; IVC=inferior vena cava; LV=left ventricle; PISA EROA=proximal isovelocity surface area effective regurgitant orifice area; sPAP=systolic pulmonary artery pressure; TAPSE=tricuspid annular plane systolic excursion; TR=tricuspid regurgitation; RA=right atrium; RV=right ventricle; TTE=transthoracic echocardiography; TV=tricuspid valve.

Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3