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Transcatheter innovations in tricuspid regurgitation: FORMA device☆

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ABSTRACT

Transcatheter tricuspid valve interventions (TTVIs) have arisen in recent years as an alternative treatment of tricuspid regurgitation (TR) in high risk patients. TTVIs can be classified as annuloplasty devices, caval valve implantation (CAVI), tricuspid valve replacement and coaptation devices. The FORMA repair system (Edwards Lifesciences, Irvine, CA, USA) aims to improve the coaptation of tricuspid leaflets by occupying the regurgitant orifice with a balloon spacer, which reduces the regurgitant orifice area. After the first-in-human reported case back in 2015, data from 18 patients treated under compassionate clinical use conditions and from 29 patients under the US early feasibility (EFS) trial have been published. The two studies included very high-risk surgical patients (Euroscore II >8 in both cohorts). Implantation success was achieved in 16 (89%) and 27 (93%) of patients, respectively. In the US EFS trial, results at 30 days showed improvements in New York Heart Association (NYHA) functional class (NYHA class ≥ III in 28% vs 84% at baseline, p =0.0002), 6-minute walking test (increase by 21 m, p = 0.012) and in the Kansas City Cardiomyopathy Questionnaire (increase by 29 points, p < 0001). In addition, the Core Lab evaluation at 30 days showed statistically significant reductions in TR severity grading in the 25 available patients. Regarding the compassionate cohort, 15 patients had available data at long-term follow-up (≥ 2 years). NYHA functional class ≥ III was reduced from 93% to 34% (p <0.001). However, two-thirds of the patients remained with significant TR at last available follow-up, and there were no significant changes in EROA (0.92 vs. 0.77 cm^2; p = 0.516). In conclusion, this first experience with the FORMA device showed the feasibility of the procedure. Despite the magnitude of TR reduction was moderate at long-term, significant improvements in heart failure symptoms and quality of life were achieved.

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Introduction

Transcatheter tricuspid valve interventions (TTVIs) have emerged in recent years as an alternative treatment of isolated tricuspid regurgitation (TR).[1] Patients with progressive TR have been traditionally managed medically, leading to progressive right ventricular dilation, dysfunction and end-stage chronic heart failure. As a result, late referral to surgical repair or replacement has been associated with the highest

Abbreviations: 6MWT, 6-Minute Walking Test; CTA, Computed tomography Angiography; EFS trial, US Early Feasibility Trial; EROA, Effective Regurgitation Orifice Area; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; RV, Right Ventricle; TEE, Transesophageal Echocardiography; TR, Tricuspid Regurgitation; TTVIs, Transcatheter Tricuspid Valve Interventions; VC, Vena Contracta.

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surgical risk among all valve procedures in contemporary practice, with operative mortality rates close to 10%.[2] The etiology of TR is functional >80% of cases[3] and often occurs in patients with already surgically-treated left-side valvular disease, implying intrinsically a higher surgical risk. In this regard, several transcatheter systems have been developed in the last decade.[1] TTVIs can be classified according to their mode of action: annuloplasty devices, caval valve implantation (CAVI), tricuspid valve replacement and coaptation devices. Among the latter, the FORMA repair system (Edwards Lifesciences, Irvine, CA, USA) aims to improve the coaptation of tricuspid leaflets by occupying the regurgitant orifice with a balloon spacer, which reduces the regurgitant orifice area. The present document focuses on the FORMA device, describing its design characteristics, main procedural steps and reported outcomes.

The FORMA repair system

Design and patient selection

The FORMA Repair System conceptual design is based on the occupation of the regurgitant orifice, reducing the amount of TR and providing a surface for native leaflets coaptation (Fig. 1). The device consists of a spacer that is advanced through a rail anchored at the septal portion of the right ventricle (RV) apex. The spacer is a foam-filled polymer balloon that passively expands via holes in the spacer shaft. The procedure is performed via the axillary or subclavian vein and a 20F or 24F sheath is required. A steerable delivery catheter is used to deliver the rail system to the ideal location in the RV apex. Two radiopaque markers help to position the spacer using fluoroscopy. With the first generation of the device, the 12-mm and 15-mm sizes were available. A later iteration included the 18-mm device, covering larger coaptation gaps. The fixation mechanism consists of 6-pronged nitinol anchors designed to minimize both the risk of penetration of the epicardial surface and the prong exposure in the RV.

Patient selection and planning includes transthoracic, transesophageal echocardiography (TEE), and computed tomography angiography (CTA). Evaluation of the axillary-subclavian venous system is mandatory to guarantee an adequate caliber to accommodate the introducer sheath and device. In addition to tricuspid annular dimensions and right ventricular geometry, the CTA scan should assess the tricuspid subvalvular apparatus and the presence of a prominent moderator band to allow successful navigation of the spacer. The presence of a permanent pacemaker or implantable cardioverter defibrillator is not a contraindication for the procedure.

Procedural steps

The FORMA system is implanted under general anesthesia with fluoroscopic and TEE guidance. Fig. 2 resumes the main steps of the procedure. Following left axillary or subclavian vein access, a large-bore sheath (20 Fr for the 12-mm device, 24-Fr for the 15-mm and 18-mm device) is advanced to the left innominate vein/superior vena cava junction. The venous access can be achieved by surgical cut-down or percutaneously with ProGlide (Abbott Vascular, Santa Clara, CA) sutures. Right ventriculography is performed (using a pigtail catheter through a secondary venous access) to locate fluoroscopically the tricuspid annular plane and RV apex. Ideally, the device should be positioned perpendicular to the tricuspid annular plane. After that, the steerable delivery catheter is positioned to advance and deploy the anchor in the RV apex. Close to the tip of the delivery system, a large balloon is inflated prior to crossing the valve, to avoid entanglement in the subvalvular apparatus. After the rail is anchored to the RV, the spacer is advanced over the rail and placed in the proper position (guided by TTE), usually 80% ventricular and 20% atrial. The device is then locked proximally, and the excess rail length is coiled and placed within a subcutaneous pocket. The entire device is fully retrievable during all stages of the procedure.

After the initial experience of the FORMA device, some iterations were added to the system.[4] In addition to the aforementioned 18-mm spacer, two enhancements in the delivery system were made: (i) a new steerable guide sheath for more coaxial alignment to the tricuspid annular plane, and (ii) a radiopaque apposition indicator which enables tissue contact visualization and allows a more predictable anchoring.

Procedural and mid-term outcomes

After the first-in-human reported case with the FORMA device,[5] data from 18 patients treated under compassionate clinical use conditions[6] and from 29 patients under the US early feasibility (EFS) trial[7] have been published. Table 1 summarizes the clinical and procedural characteristics along with mid-term follow-up from these 2 cohorts. Included patients were elderly (mean age: 76 years), with advanced New York Heart Association (NYHA) functional class and significant comorbidities (previous cardiac surgery, atrial fibrillation and chronic renal insufficiency were common in both cohorts) leading to a high surgical risk (EuroSCORE II >8 in both cohorts).

In the compassionate care cohort,[6] 2 failed procedures were reported, due to RV perforation and early device dislocation, respectively. No mortality occurred at 30-days and 1-year follow-up. A total of 14 patients with successful device implantation completed a 1- year follow-up. Among them, an improvement in NYHA functional class was observed in 86% of patients. The median increase in the 6-minutes walking

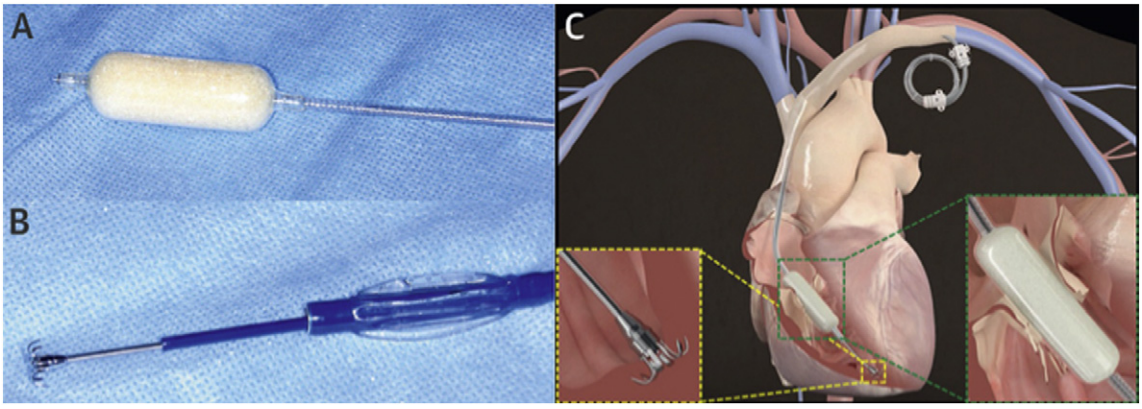

Fig. 1. The FORMA repair system. A) Spacer. B) Steerable delivery catheter and anchoring system. C) Device at the tricuspid valve annulus, anchoring system at the right ventricular apex, and excess device length coiled into a subcutaneous pocket.
Reproduced with permission from Campelo-Parada et al., J Am Coll Cardiol. 2015;66:2475–83.

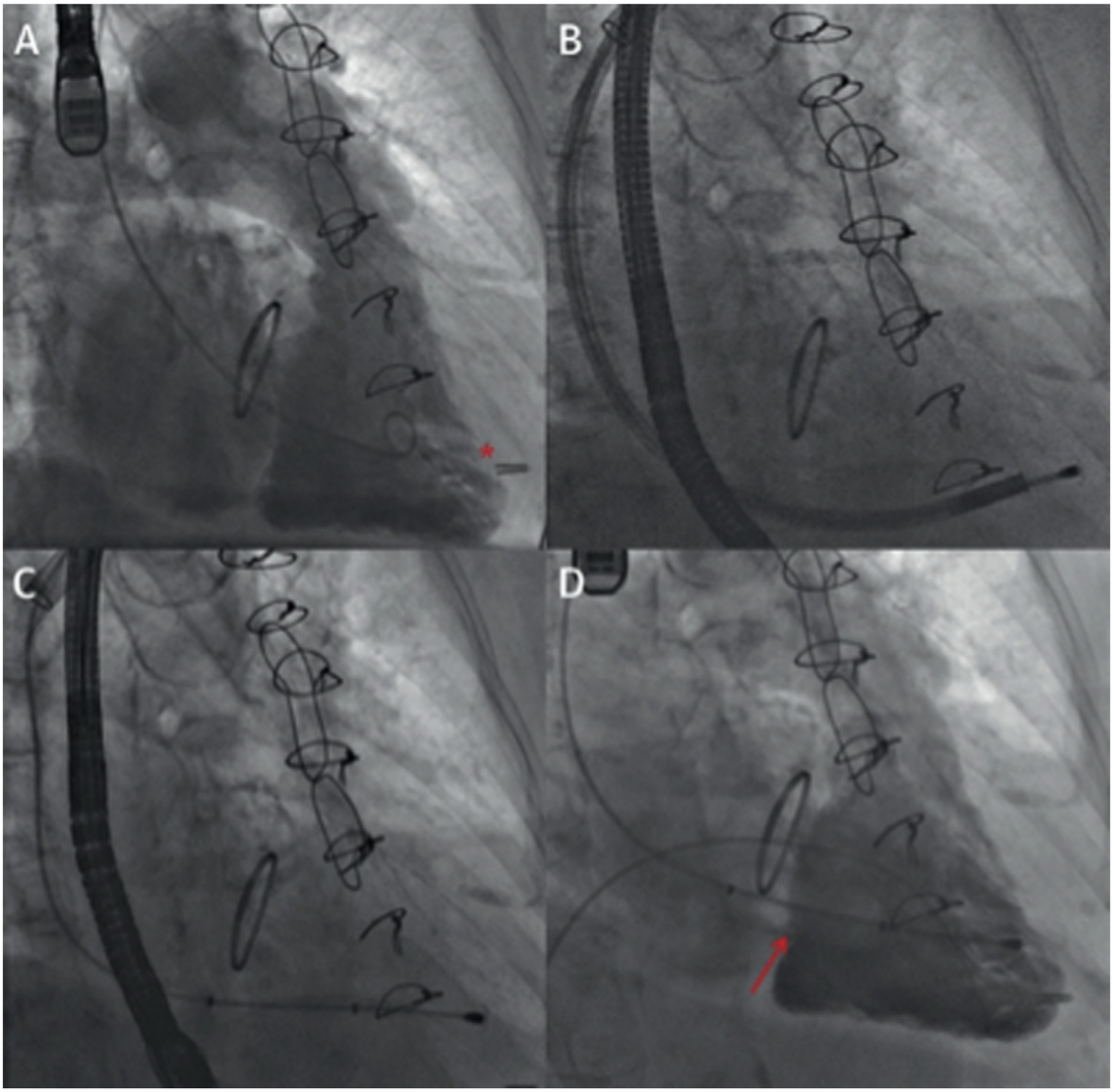

Fig. 2. Intraprocedural fluoroscopic/angiography. (A) Right ventriculography to locate the tricuspid annular plane and identify the ideal anchor location (red asterisk) on fluoroscopy. (B) Right ventricular anchoring via a steerable delivery catheter. (C) Device positioning in the tricuspid annular plane. (D) Final right ventriculography showing the device in correct position (red arrow) and reduction of tricuspid regurgitation from baseline. Reproduced with permission from Campelo-Parada et al., J Am Coll Cardiol. 2015;66:2475–83.

test (6MWT) was 84 m between baseline and 1-year follow-up ($p = 0.032$).

Regarding the data from the 29 patients in the EFS trial,[7] 2 procedural failures due to RV perforations were reported. Indeed, two devices were explanted due to the detachment of the anchor in one patient and because of endocarditis in another one. Two procedure-related deaths were reported, due to RV perforation and as a consequence of the surgical explant, respectively. Results at 30 days showed improvements in NYHA functional class (NYHA class ≥ III in 28% vs 84% at baseline, $p = 0.0002$), 6MWT (increase by 21 m, $p = 0.012$) and in the Kansas City Cardiomyopathy Questionnaire (KCCQ, increase by 29 points, $p < 0001$).

Improvements in echocardiographic parameters at 30 days were reported in both cohorts.[6,7] The Core Lab evaluation in the EFS trial showed statistically significant reductions in TR severity grading in the 25 available patients. The quantitative effective regurgitation orifice area (EROA, cm^2) was reduced by 49% (2.1 ± 1.8 cm^2 to 1.1 ± 0.9 cm^2, $p = 0.012$). Regarding the compassionate care cohort, the 30-day echocardiographic evaluation showed a reduction in the TR grade in all but one patient. At 1-year follow-up, 3/13 (23%) patients had further regression of TR to mild or moderate severity. However, EROA assessment and vena contracta (VC) width did not improve between 30 days and 1 year and 7 patients still had severe TR.[6] The latter is in contrast with the clinical improvement observed in most patients. Patients included in the compassionate cohort had often torrential TR and complete coaptation of the leaflets may not be completely achieved with the device. Despite that, the reduction in the regurgitant orifice appeared to be enough to result in a significant clinical improvement. On the other hand, the evaluation of TR after FORMA placement is challenging because the TR jet splits in multiple smaller non-circular jets. This issue made the accurate quantitative and semi-quantitative calculation of the TR severity particularly complex in FORMA recipients. Furthermore, assessment of RV reverse remodeling is suboptimal by two-dimensional transthoracic echocardiography which was used for follow-up evaluation.

Long-term outcomes

Asmarats et al have recently published the long-term outcomes from the compassionate care cohort.[8] In this first-in-human experience, clinical follow-up was available in all successfully treated patients ($n = 17$).

Table 1
Clinical, Procedural and Follow-up characteristics from the FORMA device experience.

		Compassionate care[6] (n = 18)	US EFS trial[7] (n = 29)
Baseline characteristics			
Age, years		76 ± 10	76 ± 8
Female (%)		13 (72)	19 (66)
Serum creatinine, mg/dL		1.5 ± 0.8	1.3 ± 0.4
Atrial fibrillation (%)		16 (89)	24 (83)
NYHA III–IV (%)		17 (94)	25 (86)
Prior cardiac surgery (%)		13 (72)	NA
Prior pacemaker/defibrillator (%)		3 (17)	7 (24)
EuroSCORE II		9.0 ± 5.7	8.1 ± 5.3
Procedural and 30-day outcomes			
Spacer size	12-mm	1 (5.3%)	1 (3.7%)
	15-mm	17 (89.5%)	23 (85.2%)
	18-mm	0 (0%)	3 (11.1%)
Implantation success (%)		16 (89)	27 (93)
Device embolization (%)		1 (6)	1 (3)
Device related surgery (%)		1 (6)	3 (10)
Bleeding (%)	Major	1 (6)	4 (14)
	Life threatening	1 (6)	2 (7)
30-day mortality (%)		0 (0)	2 (7)
Follow-up			
Follow-up time, months		12	1
TR severity, ≥3		12/13 (92)	NA
NYHA I-II (%)		11/14 (79)	18/25 (72)
Δ6MWT, meters		+84	+39
Mortality (%)		0 (0)	2 (7)

Values are mean SD or n/N (%). 6MWT = 6-minute walking test; EuroSCORE = European System for Cardiac Operative Risk Evaluation; NA = not available; NYHA = New York Heart Association.

At a median follow-up of 32 months, 4 (24%) patients had died (3 from terminal heart failure, 1 from sepsis) and 3 (18%) patients required re-hospitalization for heart failure. There was 1 device-related thrombosis and 1 pulmonary embolism, both in the setting of sub-therapeutic oral anticoagulation treatment. Among the 15 patients with at least 2-year follow-up, NYHA functional class ≥ III was reduced from 93% to 34% ($p < 0.001$). The 6MWT increased by an average of 54 m ($p = 0.016$) and KCCQ improved by 16 points compared with baseline ($p = 0.016$). Despite the rate of severe TR was reduced from 95% at baseline to 33% at 2- to 3-year follow-up ($p < 0.001$), two-thirds of the patients remained with a significant TR at last available follow-up (TR classified as moderate-severe). Whereas a significant reduction in VC width was observed at follow-up (from 11.8 to 8.4 mm; $p = 0.005$), there were no significant changes in EROA (0.92 cm^2 vs. 0.77 cm^2; $p = 0.516$). These findings are in line with the 1-year results[6] and suggest that despite the improvements in the 30-day echocardiographic results, a relapse in right ventricular remodeling may have occurred. The treated patients in this cohort had advanced right ventricular heart failure with severe leaflet tethering, a predictor of TR recurrence in surgical cohorts.[9,10] In this setting, a complete recovery of the chronic changes observed in right cardiac chambers would have been likely difficult with any tricuspid valve treatment (surgical or transcatheter).

Conclusions

In conclusion, the initial experience with the FORMA device in prohibitive surgical risk patients showed the feasibility of this procedure, albeit with a reasonable rate of device-related complications. The magnitude of TR reduction was moderate at long-term and significant improvements in heart failure symptoms and quality of life were achieved.

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Statement of Conflict of Interest

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