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Transcatheter innovations in tricuspid regurgitation: Navigate☆

Haytham Elgharably [a], Serge C. Harb [b], Samir Kapadia [c], Lars G. Svensson [a], Jose L. Navia [a,*]

[a] Department of Thoracic & Cardiovascular Surgery, Cleveland Clinic – Heart & Vascular Institute, Cleveland, OH, USA
[b] Department of Cardiovascular Imaging, Cleveland Clinic – Heart & Vascular Institute, Cleveland, OH, USA
[c] Department of Cardiovascular Intervention, Cleveland Clinic – Heart & Vascular Institute, Cleveland, OH, USA

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ABSTRACT

Patients with isolated functional or recurrent tricuspid regurgitation are often considered high risk and denied surgery. There has been growing experience for transcatheter tricuspid valve implantation through valve-in-valve or valve-in-ring, and recently, but to a lesser extent, in native annulus. The NaviGate is a novel self-expanding valved-stent designed with unique features to treat tricuspid regurgitation, particularly, in the settings of severely dilated tricuspid annulus. Herein, we present the innovation facets and clinical application of the NaviGate system.

Contents

Introduction

An increasing number of patients presents in the current era with isolated functional or recurrent tricuspid regurgitation (TR) after being ignored or inadequately treated at the time of the previous cardiac procedure. Only ≈8000 tricuspid valve surgeries are performed annually in the face of ≈1.6 million patients suffer from more than moderate TR.[1] Part of the magnitude of the problem is related to the high rate of TR recurrence after valve repair which reaches 60% of recurrent more than moderate TR.[2] These patients typically receive medical treatment for prolonged periods in a trial to manage their volume status and delay the progress of right heart failure (HF). As a consequence, these patients are referred for surgical evaluation after failure of medical therapy and development of right HF manifestations. Surgical intervention in the former settings is known to be associated with high mortality.[3–5] With marked development in the trans-catheter valve therapy, there has been an increased interest in application of this technology to treat tricuspid valve disease. Several groups have reported successful transcatheter tricuspid valve implantation (TTVI) using valve-in-ring or valve-in-valve approaches, but not in a native tricuspid annulus.[5–7] This could be attributed to anatomical features of the native tricuspid valve annulus that pose challenges to transcatheter valve implantation (e.g. large and less defined annulus or absence of well-defined fluoroscopic landmarks).[7] The NaviGate stented-valve (NaviGate Cardiac Structures Inc., Irvine, CA, US) is designed in particular to address these technical challenges with proper preclinical testing and satisfactory early clinical results.[8,9] Herein, we present the unique features of the NaviGate system and the growing experience of the device clinical application.

Abbreviations: CT, computed tomography; HF, heart failure; RV, right ventricle or ventricular; TR, tricuspid regurgitation; TTVI, transcatheter tricuspid valve implantation.

☆ Statement of conflict of interest: see page 495.

* Address reprint requests to: Jose L. Navia, MD, Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, 2950 Cleveland Clinic Blvd, Weston, FL 33331.
E-mail address: naviaj@ccf.org (J.L. Navia).

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The NaviGate system

The NaviGate stented-valve is a trileaflet valve fabricated from equine pericardium and mounted on a self-expanding tapered nitinol stent (Fig 1). The valved stent has three unique design features: First, it has a cone stent configuration that produces a diffuser effect to optimize the transvalvular gradient with a low height profile of 21 mm that reduce the possibility of RV outflow tract obstruction and protrusion of the valve into the right side heart cavities. Second, the anchoring mechanisms of the stent to the tricuspid annulus involves: (1) radially arranged winglets on the atrial component of the stent that engage the tricuspid annulus which are supported with a lining of woven microfiber polyester fabric; (2) radially arranged graspers on the ventricular component of the stent that engage the tricuspid leaflets and the subvalvular apparatus within the right ventricle (RV). This design secures the stent to the tricuspid annulus, prevents dislodgement to the right atrium during systole, minimizes para-valvular leakage, avoids right coronary artery compression, and third, it is manufactured in different sizes, 36 mm, 40 mm, 44 mm, 48 mm, and 52 mm to fit the significant variability of TV annulus sizes. This is particularly necessary in patients with severe TR and severe remodeling process of the RV. The current valved-stent is not recapturable after the ventricular winglets are released of the delivery system.

Currently, a new delivery system is being developed with the feature of recapturing the device after delivery. During deployment of the valved-stent, the ventricular winglets are exposed first in a controlled fashion, which enables the operator to readjust the depth and the angle of the device in relation to the tricuspid annulus guided by imaging modality. The preclinical testing of the NaviGate valved-stent demonstrated safe and feasible implantation through trans-atrial and transjugular approaches.[8] Successful implantation in a preclinical model resulted in a secure and stable engagement of the native annulus, with excellent hemodynamic and valve performance.

Preoperative assessment for TTVI

Potential candidates for TTVI are evaluated by the Heart Team at our institution. Inclusion criteria for the TTVI procedures are: severe symptomatic TR, prohibitive risk for conventional surgery (significant comorbidities, hazardous redo-sterntomy, severe RV dysfunction), pulmonary artery pressure ≤90 mmHg (by echocardiography and right heart catheterization), and favorable anatomy. Pre-operative assessment included a cardiac-gated 4D computed tomography (CT) for anatomical characterization of the tricuspid valve, navigation pathway through cardiac structures, and vascular access. Additionally, based on the 4D CT study, we developed a 3D printing model of the right heart structures for preoperative simulation of the navigation and implantation steps of the NaviGate device.[10]

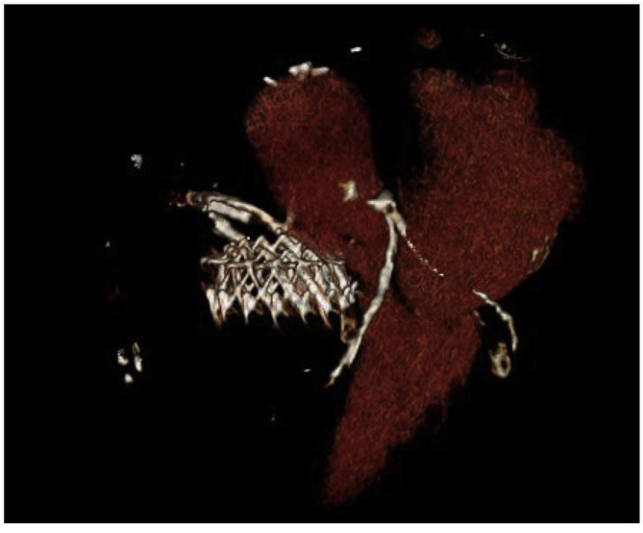

Fig 1. Postoperative focused 4-dimensional computed tomography showing the NaviGate valved-stent well seated in the tricuspid annulus.

Premier NaviGate implantation

First-in-human implantation of the NaviGate valved-stent was performed successfully at our institution.[9] Thereafter, our group has performed three successful implantation procedures (Table 1). All patients were evaluated by our Heart Team and the multidisciplinary recommendation was made for TTVI over conventional surgery. Notably, the commercially available surgical valved-stents do not include sizes that matched a severely dilated tricuspid annulus. Moreover, results of valve-in-ring using these prostheses have not been optimal.[11] Therefore, patients were considered for compassionate use of investigational, catheter-delivered NaviGate prosthesis that received both Food & Drug Administration and Institutional Review Board approvals.

All four planned implantation procedures were performed successfully on a beating heart with no need for cardiopulmonary bypass or ventricular pacing. Three implantations were performed through trans-atrial approach (small right anteriolateral thoracotomy) and one implantation through trans-jugular approach (percutaneous). Our preference is to oversize the device by 5% to the annulus or the prior ring size to achieve better sealing. There were no conduction abnormalities, coronary artery complications, or stent dislodgement after implantation. Additionally, the NaviGate valve is mounted on a self-expanding nitinol stent that could potentially increase sealing surface over time. We also recognized a technical challenge in achieving perfect perpendicular positioning of stented-valve across the tricuspid annulus using the original delivery system. Modifications have been applied and tested to shorten the distal angulation part of the delivery system, which lead to excellent results in patients 3 and 4. In regard to the approach, we use CT scan to examine the vascular anatomy before surgery and we do not use venous access with diameter <15 mm. There was no hospital mortality, re-exploration for bleeding, or major cardiac-related events. The degrees of TR and hemodynamics have markedly improved compared to pre-procedure. There was one death during follow-up due to ischemic colitis and sepsis. The other three patients continue to experience clinical improvement with stable TR and RV function (Table 1).

Clinical experience of NaviGate implantation

Since the first implantation of the NaviGate valved-stent at our institution, there has been a growing experience reported by other groups.[12–14] Hahn et al. reported their experience of NaviGate valved-stent in 5 patients with severe TR.[14] All patients underwent successful NaviGate valved-stent implantation through trans-atrial approach. They reported one hospital death with complicated post-operative event for prolonged mechanical ventilation and renal failure requiring dialysis. One patient required temporary pacing for bradycardia, but not permanent pacing. Three patients had significant bleeding and one patient required re-exploration. Four of the five patients were discharged on anti-coagulation except one patient for esophageal bleeding post-procedure. The former patient was readmitted for pleural effusion was found to have a thrombus on the valved-stent, which was treated and resolved by anti-coagulation. Follow-up at 3–6 months showed improvement in symptoms, echocardiographic evidence of RV remodeling, and increase in forward cardiac output. One patient developed a small fistula between the non-coronary aortic sinus of Valsalva and the RV but did not require intervention.[14]

Table 1
Patient characteristics.

	Patient 1	Patient 2	Patient 3	Patient 4
Baseline characteristics				
Age (years)	64	78	77	79
Sex	Female	Male	Female	Female
Non-cardiac comorbidity	CKD, COPD	CKD, DM, COPD	HTN	HTN
Cardiac comorbidity	PAP 75 mmHg, AF Chest radiation CAD (prior CABG)	PAP 90 mmHg, AF Prior cardiac surgery ×3 CAD (prior CABG)	PAP 50 mmHg Atrial flutter CAD (prior CABG)	PAP 45 mmHg AF Prior cardiac surgery ×1 PPM
Tricuspid annulus diameter (mm)	50	34 (tricuspid annuloplasty ring)	46	51
Procedure				
Implantation	Successful	Successful	Successful	Successful
Approach	Trans-atrial	Trans-jugular	Trans-atrial	Trans-atrial
NaviGate size (mm)	48	38	48	52
Gradient (peak/mean mmHg)	4.5/3 30/12	7/4 28/6	6/2 30/10	4/1.5 35/12
CVP (pre/post mmHg) implantation time (min)	10	12	15	7
Early outcomes				
30-day mortality	None	None	None	None
Pre-discharge TR	Mild to moderate para-valvular	Mild para-valvular TR	Trivial TR	Trivial TR
Hospital stay (days)	29	7	7	15
Follow-up				
Last follow-up (months)	6	18	6	6
Clinical status	"Re-admitted for ischemic colitis, sepsis, subsequently died"	Functional improvement	Functional improvement	Functional improvement
TR	Moderate paravalvular TR	Moderate paravalvular TR	Mild central TR	Trivial central TR
RV dysfunction	Severe	Moderate	Mild	Mild

AF: atrial fibrillation; PPM: permanent pacemaker; CABG: coronary artery bypass grafting; CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; HTN: hypertension; TR: tricuspid regurgitation; RV: right ventricle.

Comment

Indeed, there is a great need for advancement of the current TTVI technology to treat the increasing numbers of patients presenting with recurrent TR and decompensated right heart failure, as reoperation for recurrent TR has been associated with high mortality favoring a less invasive approach.[3–5] However, anatomical features of the tricuspid valve render trans-catheter valve therapy challenging such as being a larger non-circular less defined annulus, absence of rigid landing structure or fluoroscopic marks, and proximity of important structures to the tricuspid annulus such as the atrio-ventricular node, bundle of His, the coronary sinus, and the right coronary artery.[7,13] Hence, the current trials of TTVI have been focused on valve-in-valve (bioprosthesis) and valve-in-ring.[5–7] The NaviGate valved-stent design provides unique features that facilitates implantation in dilated native tricuspid annulus. The early results of NaviGate implantation have demonstrated safety and feasibility through trans-atrial or trans-jugular approaches on a beating heart with no ventricular pacing. Interval reduction of significant TR resulted in clinical and functional improvement. There is no doubt that the learning curve of TTVI is evolving which was evident in our group and Hahn's group early results. This current technology represent a promising alternative to treat a complex group of patients with severely dilated tricuspid annulus, severe TR, and refractory right HF for whom traditional surgery carries high risk.

Statement of conflict of interest

J. Navia is the inventor on patents related to this device, and is a consultant to NaviGate Cardiac Structures, Inc. (NCSI).

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