Publish Date:
September 2015
Volume 1, Issue 3

JSHD

Journal of Structural Heart Disease

OFFICIAL JOURNAL OF THE PICS FOUNDATION

PICS Foundation

PEDIATRIC AND ADULT INTERVENTIONAL CARDIAC SYMPOSIUM

Sidra Medical and Research Center

Qatar Foundation

Published by
Science International Corp.
ISSN 2325-4637

Now accepting papers at http://structuralheartdisease.org

Editorial Board

William E. Hellenbrand	Yale University (New Haven, CT)
James Hermiller	The Care Group (Indianapolis, IN)
Howard Herrmann	University of Pennsylvania (Philadelphia, PA)
David Holmes	Mayo Clinic (Rochester, MN)
Noa Holoshitz	Rush University Medical Center (Chicago, IL)
Ralf Holzer	Sidra Medical & Research Center (Doha, Qatar)
Eric Horlick	University of Toronto (Toronto, Canada)
Reda Ibrahim	Montreal Heart Institute (Montreal, Canada)
Michel Ilbawi	Rush University Medical Center (Chicago, IL)
Frank Ing	LA Children's Hospital (Los Angeles, CA)
Alexander Javois	Hope Children's Hospital (Oak Lawn, IL)
Thomas Jones	Seattle Children's Hospital (Seattle, WA)
Saibal Kar	Cedars Sinai Medical Center (Los Angeles, CA)
Clifford Kavinsky	Rush University Medical Center (Chicago, IL)
Joseph Kay	University of Colorado (Denver, CO)
Damien Kenny	Rush University Medical Center (Chicago, IL)
Morton Kern	University of California Irvine (Irvine, CA)
Michael Kim	University of Colorado (Aurora, CO)
Seong-Ho Kim	Cheju Halla General Hospital (South Korea)
Susheel Kodali	Columbia University Medical Center (New York, NY)
Jackie Kreutzer	Pittsburgh Children's Hospital (Pittsburgh, PA)
Shelby Kutty	Children's Hospital and University of Nebraska Medical Center (Omaha, NB)
Bray Patrick-Lake	PFO Research Foundation (Boulder, CO)
Michael Landzberg	Boston Children's Hospital (Boston, MA)
Geoffrey Lane	Royal Melbourne Hospital (Melbourne, Australia)
Roberto Lang	University of Chicago Medical Center (Chicago, IL)
John Lasala	Barnes Jewish Hospital, Washington University (St. Louis, MO)
Martin B. Leon	Columbia University (New York, NY)
Daniel Levi	UCLA Medical Center (Los Angeles, CA)
Scott Lim	University of Virginia Health System (Charlottesville, VA)
Michael Mack	Baylor Healthcare System (Plano, TX)
Francesco Maisano	University of Zurich (Zurich, Switzerland)
Raj Makkar	Cedars Sinai Medical Center (Los Angeles, CA)
Robert March	Rush University Medical Center (Chicago, IL)
Gwen Mayes	VP National Patient Advocate Foundation (Washington, DC)
Pat McCarthy	Northwestern Memorial Hospital (Chicago, IL)
Doff McElhinney	New York University (New York, NY)
John Messenger	University of Colorado (Denver, CO)
Friedrich Mohr	Herzzentrum Universitaet Leipzig (Leipzig, Germany)
Tarek Momenah	Prince Salman Cardiac Center (Riyadh, Saudi Arabia)
Issam Moussa	(Jacksonville, FL)
Michael Mullen	The Heart Hospital (London, England)
David Muller	St. Vincent's Hospital (Sydney, Australia)
William O'Neill	Henry Ford Hospital (Detroit, MI)
Igor Palacios	Mass General Hospital (Boston, MA)
SJ Park	University of Ulsan College of Medicine (Seoul, Korea)
Carlos Pedra	Danta Pazzanese Instituto de Cardiologia (Sao Paolo, Brazil)
Alejandro Peirone	Children's Hospital of Cordoba (Cordoba, Argentina)
Giacomo Pongiglione	Bambino Gesu Hospital (Rome, Italy)
Matthew Price	Scripps Clinic (La Jolla, CA)
Robert Quaife	University of Colorado (Denver, CO)
Shakeel Qureshi	Evelina Children's Hospital (London, UK)

Steve Ramee	Oschner Clinic (New Orleans, LA)
Mark Reisman	Swedish Medical Center (Seattle, WA)
John Rhodes	Miami Children's Hopsital (Miami, FL)
Charanjit Rihal	Mayo Clinic (Rochester, MN)
Richard Ringel	Johns Hopkins Medical Center (Baltimore, MD)
Carlos Ruiz	Lenox Hill Hospital (New York, NY)
Ernesto Salcedo	University of Colorado (Denver, CO)
Joachim Schofer	Hamburg University Cardiovascular Center (Hamburg, Germany)
Paul Sorajja	Minneapolis Heart Institute Foundation (Minneapolis, MN)
Christian Spies	Queen's Heart Physician Practice (Honolulu, HI)
Frank Silvestry	University of Pennsylvania Hospital (Philadelphia, PA)
Gregg Stone	Columbia University (New York, NY)
Corrado Tamborino	University of Catania (Catania, Italy)
Vinod Thourani	Emory University (Atlanta, GA)
Jonathan Tobis	UCLA Medical Center (Los Angeles, CA)
Murat Tuczu	Cleveland Clinic Foundation (Cleveland, OH)
Zoltan Turi	Robert Wood Johnson Medical School (Camden, NJ)
Alec Vahanian	Bichat University Hospital (Paris, France)
Joseph J. Vettukattil	Spectrum Health (Grand Rapids, MI)
Kevin Walsh	Our Lady's Hospital (Dublin, Ireland)
John Webb	St. Paul Hospital Vancouver (British Columbia, Canada)
Brian Whisenant	Intermountain Medical Center (Salt Lake City, Utah)
Matthew Williams	Mount Sinai Medical Center (New York, NY)
Neil Wilson	University of Colorado (Denver, CO)
Evan Zahn	Cedars Sinai Medical Center (Los Angeles, CA)

JSHD
Journal of Structural Heart Disease

Volume 1, Issue 3, September 2015

Original Scientific Articles

Journal of Structural Heart Disease (ISSN 2325-4637) is an online open-access journal issued bi-monthly (6 issues per year, one volume per year) by Science International Corporation.

All correspondence should be directed to: Ziyad M. Hijazi, MD, Co-Editor-in-Chief, Journal of Structural Heart Disease, PO Box 26999, Doha, Qatar. Tel.: +974-4404-2116, Fax: +974-44041779, E-Mail: jshd@scienceinternational.org

JSHD
Journal of Structural Heart Disease

Original Scientific Article

Journal of Structural Heart Disease, September 2015,
Volume 1, Issue 3: 112-126
DOI: http://dx.doi.org/10.12945/j.jshd.2015.019-14

Received: December 29, 2014
Accepted: January 05, 2015
Published online: September 2015

Update on New Devices for Transcatheter Aortic Valve Replacement

Yigal Abramowitz, MD, Tarun Chakravarty, MD, Hasan Jilaihawi, MD, Raj R. Makkar, MD*

Heart Institute, Cedars-Sinai Medical Center, Los-Angeles, California, USA

Abstract

Transcatheter aortic valve replacement (TAVR) for severe symptomatic aortic stenosis is the standard of care in inoperable patients and an alternative to surgical aortic valve replacement in high-risk operable patients. Several issues affecting outcomes with implantation of the first-generation TAVR devices remain unresolved, including neurological and vascular complications, atrioventicular conduction abnormalities, and paravalvular aortic regurgitation. New-generation TAVR devices are currently in different stages of clinical development and evaluation. Modifications in the new devices include the ability to reposition the valve before final deployment, features to reduce paravalvular leakage, lower-profile delivery systems, and cerebral protection devices. The purpose of this manuscript is to give an update on the new-generation transcatheter valvular technologies, focusing on the unique features and describing the initial clinical experience for each device.

Key Words:

New devices • Transcatheter aortic valve replacement • Transcatheter aortic valve implantation • TAVR • Transcatheter aortic valve implantation (TAVI)

Introduction

Transcatheter aortic valve replacement (TAVR) has emerged as a treatment option for inoperable or high-risk surgical patients with severe aortic stenosis (AS) [1, 2]. Since the first-in-human TAVR procedure performed by Professor Alan Cribier in 2002 [3], more than 100,000 TAVR procedures have been performed worldwide. Considerable experience has been acquired with the two first-generation TAVR devices: the balloon-expandable Edwards SAPIEN/SAPIEN XT (Edwards Lifesciences, Irvine, CA, USA) and the self-expandable Medtronic CoreValve (Medtronic, Minneapolis, MN, USA). Randomized clinical trials comparing this technology in high risk patients against surgery or medical therapy, as well as multicenter national registries have shown high success rate and increasingly predictable results [2, 4–7].

Clinical outcomes of TAVR have improved over the years, mainly as a result of appropriate patient selection, growing operator experience, and major technical refinements. Nonetheless, the rate of complications related to TAVR remains substantial. A recent meta-analysis found the risk of periprocedural stroke following TAVR to be 1.5% and a 30-day stroke/transient ischemic attack (TIA) rate of 3.3%. Paravalvular aortic regurgitation (PV-AR) after TAVR, including small or trace leaks is quite common (incidence 50–85%), with the vast majority of cases graded as mild or less [8, 9]. Increasing severity of PV-AR following TAVR have been directly associated with increased mortality [2, 7, 9, 10]. Other issues affecting short and long term outcome following TAVR include hemorrhagic and vascular complications, atrioventricular conduction abnormalities, valve malpositioning and coronary obstruction [11]. To overcome these obstacles, and in order to enable the utilization of TAVR for lower risk populations, new-generation TAVR devices

Fax +1 203 785 3346
E-Mail: jshd@scienceinternational.org
http://structuralheartdisease.org/

ISSN 2326-4004

Accessible online at:
http://structuralheartdisease.org/

*Corresponding Author:
Raj R. Makkar, MD
Cedars-Sinai Heart Institute
Cedars-Sinai Medical Center
Los Angeles, California, 90048
Tel: +1 310 423 3977, Fax: +1 310 423 0106, E-Mail: Raj.Makkar@cshs.org

Figure 1: The SAPIEN 3 (S3) valve. A balloon-expandable valve composed of a radiopaque, cobalt chromium frame and a trileaflet bovine pericardial tissue valve. The inflow of the S3 valve is covered by an internal polyethylene terephthalate skirt and an additional outer polyethylene terephthalate cuff to enhance paravalvular sealing.

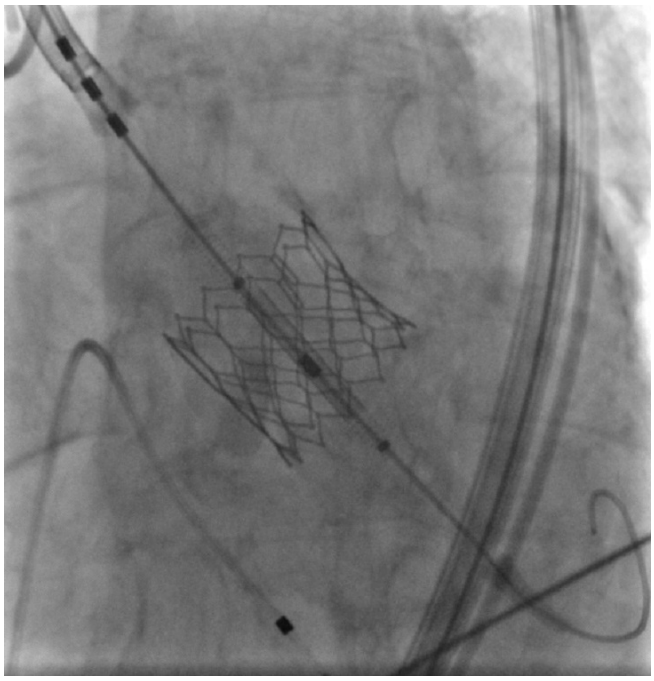
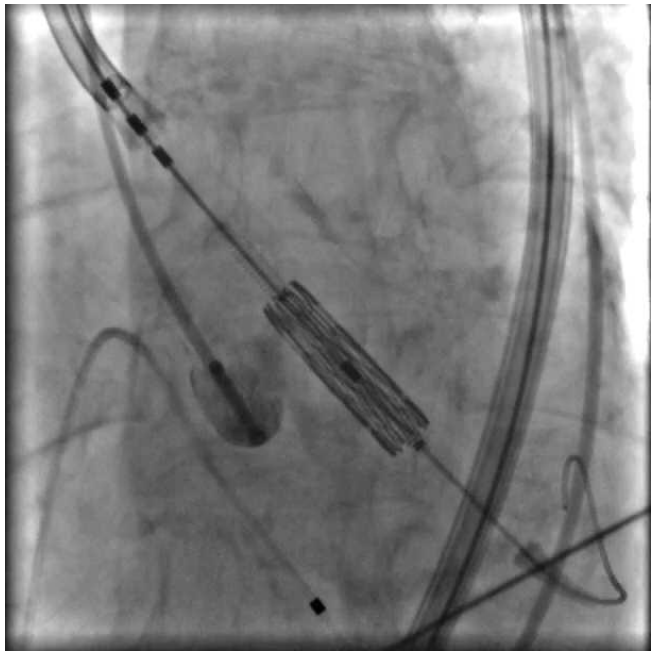


Figure 2: Angiography of SAPIEN 3 valve implantation.



Video 1: Angiography of SAPIEN 3 valve deployment.

are currently in early stages of clinical evaluation. Modifications in these new devices include the ability to reposition and recapture the valve before final deployment, features intended to minimize PV-AR, and the introduction of low- profile delivery systems. The present manuscript provides an update on the new-generation transcatheter valvular technologies, focusing on the unique features and describing the initial clinical experience for each device.

Edwards Lifesciences SAPIEN 3

The SAPIEN 3 (S3) valve (Edwards Lifesciences, Irvine, CA, USA) is a new balloon-expandable valve that can be implanted using the transfemoral, transsubclavian, transapical, or transaortic approaches. It incorporates features intended to reduce vascular complications, increase paravalvular sealing, and enhance ease of positioning [12]. This device is composed of a radiopaque, cobalt chromium frame and a trileaflet bovine pericardial tissue valve (Figures 1, 2 and Movie 1). It incorporates a stent and leaflet design that allows for crimping to a reduced profile as compared with the predicate SAPIEN and SAPIEN XT devices. The inflow of the S3 valve is covered by an internal polyethylene terephthalate skirt similar to the earlier SAPIEN XT device. However, the S3 incorporates an additional outer polyethylene terephthalate cuff to enhance paravalvular sealing thus reducing PV-AR. This sealing cuff has no filling and

functions like a parachute by bulging outward [13]. The Edwards Commander transfemoral delivery system (Edwards Lifesciences, Irvine, CA, USA) has lower profile and higher flexibility compared to the currently used NovaFlex system (Edwards Lifesciences, Irvine, CA, USA). It contains a fine adjustment wheel that permits a precise positioning of the crimped valve in the aortic annulus without unnecessary pushing or pulling. A central radiopaque marker in the balloon also assists in valve positioning. The system uses a 14-F expandable eSheath (Edwards Lifesciences, Irvine, CA, USA), that intend to reduce the potential for arterial injury during introduction but can transiently expand to accommodate passage of the compressed valve and then return to its lower profile diameter.

Recently, the 30-day outcomes of 150 patients that underwent S3 valve implantation in Europe and Canada were published [14]. A transfemoral approach was chosen in 64.0% and transapical/direct aortic in the remainder. At 30 days, PV-AR was none to mild in 96.4% and moderate in 3.5%. No patient had severe regurgitation. Transfemoral implantation was associated with low 30-day mortality (2.1%) and no disabling stroke. Alternative access was associated with higher rates of 30-day mortality (11.6%) and stroke (5.6%). This device is available in 20-, 23-, 26-, and 29-mm sizes and is expected to facilitate fully percutaneous implantation in a broader range of patients with the potential for more accurate positioning and less PV-AR. The initial 30-day outcomes of the PARTNER II S3 Trial (n=1,659) have demonstrated 30-day mortality rate of 2.2% for the overall high-risk cohort and 1.1% for the intermediate-risk cohort. Moderate or higher PV-AR at 30-days was present in 2.9% of the high-risk patients and 4.2% of the intermediate-risk patients [15]. Since June 2015, Sapien 3 has a U.S. Food and Drug Administration (FDA) approval.

Currently ongoing trials with SAPIEN 3 valve are the PARTNER II trial (Placement of aortic transcatheter valves; ClinicalTrials.gov Identifier: NCT01314313) and the safety and performance study of the Edwards SAPIEN 3 transcatheter heart valve trial (NCT01808287).

Medtronic CoreValve Evolute / Evolute R

The Evolute (Medtronic, Minneapolis, MN, USA) 23mm valve was the first next-generation CoreValve device (Figure 3). It is indicated for small (18–20 mm) aortic annuli and designed to be fully repositionable, resheathable and recapturable [16]. It has a Conformité Européenne (CE) mark for valve-in-valve implantations since 2013 and was previously described for this indication in case reports [17, 18].

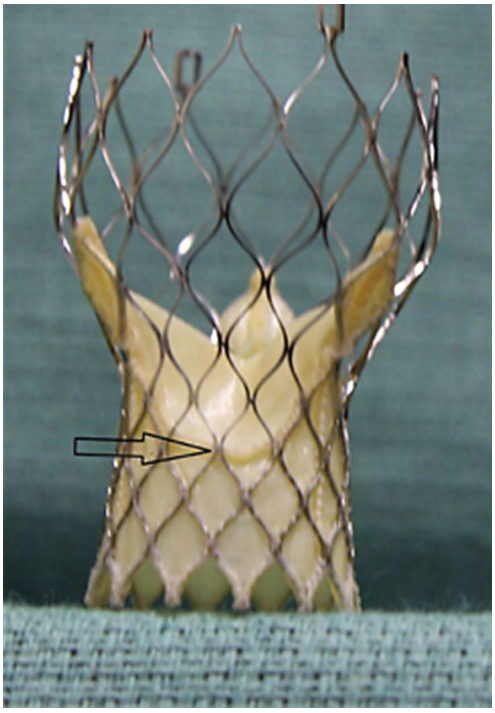


Figure 3: The Evolute valve. A self-expandable valve composed of radiopaque nitinol support frame, supra-annular trileaflet porcine pericardial leaflets, and porcine pericardium fabric skirt. The arrow corresponds to the nadir of the pericardial leaflets.

The newly designed CoreValve Evolute R (Medtronic, Minneapolis, MN, USA) is a low-profile system that retains many of the characteristics of its predecessors: radiopaque self-expanding nitinol support frame, supra-annular trileaflet porcine pericardial leaflets, and porcine pericardium fabric skirt [19]. The cell geometry and frame of this valve have been redesigned to optimize frame interaction with the native anatomy, to improve conformability to the aortic annulus and reduce PV-AR. The inflow has more consistent radial force across the sizing spectrum, and the outflow has been shortened and reshaped to provide improved alignment between valve housing and the native sinus. The valve leaflets are routinely treated with alpha-amino oleic acid to impede calcium deposition. The new EnVeo R deliv-

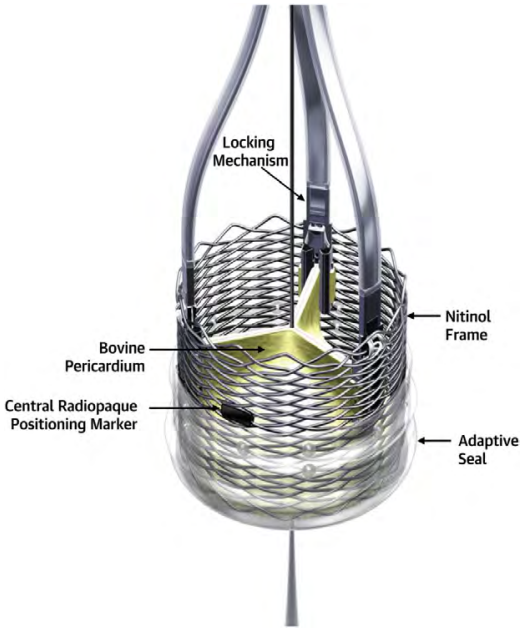


Figure 4: The Lotus Valve System . The bioprosthetic aortic valve implant comprises three bovine pericardial leaflets supported on a braided nitinol frame, and an outer adaptive seal designed to minimize PV-AR.

ery catheter (Medtronic, Minneapolis, MN, USA) features a complete redesign of the AccuTrak system (Medtronic, Minneapolis, MN, USA) that is currently employed for CoreValve implantation. The EnVeo R catheter with InLine sheath (Medtronic, Minneapolis, MN, USA) is a 14 Fr-equivalent system that can deliver the transcatheter heart valve without the requirement for a separate introducer sheath. The modified valve capsule allows the valve to be fully recaptured and repositioned during deployment. The valve is available in 23, 26 and 29 mm sizes. A report of the initial results of implantation of this device in 60 patients revealed no case of mortality at 30-days and 3.4% of moderate or higher PV-AR [20]. As of June 2015 Evolut R has a U.S. FDA approval.

Currently ongoing trials with Evolute R valve are the Medtronic CoreValve Evolute R CE mark clinical study (ClinicalTrials.gov Identifier: NCT01876420) and the Medtronic CoreValve Evolute R U.S. clinical study (NCT02207569).

Boston Scientific Lotus

The Lotus Valve System (Boston Scientific, Natick, MA, USA) comprises a bioprosthetic aortic valve implant and a catheter-based delivery system for introduction and delivery of the valve implant [21]. The bioprosthetic aortic valve implant comprises three bovine pericardial leaflets supported on a braided nitinol frame (Figure 4). An outer adaptive seal is designed to minimize PV-AR. Currently, the valve is available in 23- and 27-mm sizes; an additional valve size of 25 mm is anticipated. The transfemoral delivery system is 18 Fr compatible. The delivery handle incorporates a simple, ergonomic design that enables a controlled, predictable, and accurate deployment. If the initial deployment is suboptimal, the device can be subtly advanced or retracted as needed or even completely retracted into the delivery sheath at any time prior to the final release. The valve functions early in deployment, providing hemodynamic stability for the patient and enabling the operator to complete the delivery process in a controlled and considered fashion.

The multicenter REPRISE II study has been recently published [22]. It examined transfemoral implantation of 23- or 27-mm Lotus valve in 120 patients with severe AS. The valve was successfully implanted in all patients, with no cases of valve embolization or additional valve implantation. All repositioning (n= 26) and retrieval (n=6) attempts were successful; 34 patients (28.6%) received a permanent pacemaker. The Mean gradient improved from 46.4± 15 mm Hg to 11.5±5.2 mm Hg. At 30 days, the mortality rate was 4.2%, and the rate of disabling stroke was 1.7%; one patient had moderate PV-AR, whereas none had severe PV-AR. CE mark approval for Lotus valve system was obtained in 2013.

Four clinical trials evaluating efficacy and safety of Lotus valve implantation are currently ongoing (ClinicalTrials.gov Identifier: NCT02202434, NCT02031302, NCT01627691, NCT01383720).

Direct Flow Medical Valve

The Direct Flow Medical aortic valve (Direct Flow Medical, Santa Rosa, CA, USA) is a nonmetallic percutaneous valve with an inflatable ring cuff frame designed to encircle and capture the native valve annulus, thereby ensuring anchoring of the bioprosthesis and minimizing potential PV-AR, dislodgement or migration [23] (Figure 5). The tricuspid bovine pericardial valve is attached to a polyester

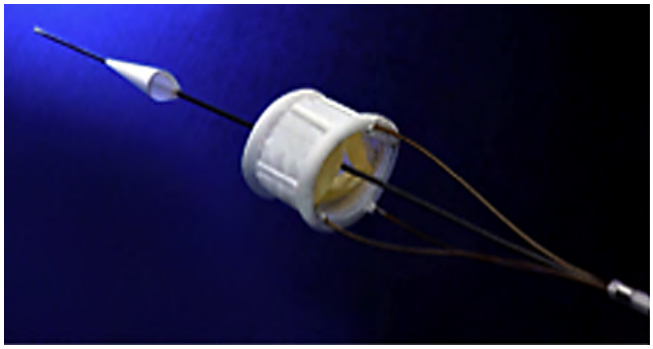


Figure 5: The Direct Flow Medical aortic valve. A tricuspid bovine pericardial valve is attached to a polyester fabric cuff which conforms to the native aortic annulus.

fabric cuff which conforms to the native aortic annulus. An upper (aortic) and lower (ventricular) ring balloon interconnected by a tubular bridging system can be inflated independently through two of the three position-fill lumens. The valve is available in 25- and 27-mm sizes. It is designed to be fully repositionable and retrievable prior to final deployment through the introducer. The 18 Fr delivery system contains three position-fill lumens which are attached to the bioprosthesis. Two of these position-fill lumens are used to inflate and deflate the ring balloons and all three are used to position the bioprosthesis.

The results of a prospective multicenter evaluation of the direct flow medical transcatheter aortic valve have been recently published [24]. One-hundred patients with severe AS underwent transfemoral implantations. Device success was 93%, all-cause mortality at 30 days was 1%, and major stroke rate was 4%. The post-implantation echocardiography results demonstrated mild or no aortic regurgitation (AR) in 99% with a mean gradient of 12.6±7.1 mm Hg and effective orifice area of 1.50±0.56 cm^2. The direct flow medical valve has received a CE mark at 2013.

Three clinical trials evaluating efficacy and safety of Direct Flow Medical aortic valve implantation are currently ongoing (NCT01845285, NCT02163850, and NCT01932099).

St. Jude Medical Portico

The trileaflet self-expanding Portico valve (St. Jude Medical, Minneapolis, MN, USA) consists of a nitinol frame, bovine pericardial leaflets processed with the

Figure 6: The Portico valve. A self-expandable valve composed of a nitinol frame, bovine pericardial trileaflets processed with the Linx anti-calcification technology and a porcine pericardial sealing cuff.

Linx anticalcification technology and a porcine pericardial sealing cuff [25, 26] (Figures 6 and 7). The outflow portion of the stent frame incorporates three retention tabs, which secure the crimped valve to the delivery system [26]. The transfemoral delivery catheter consists of a soft tapered nose cone, an 18 Fr capsule that contains the compressed valve, and a 12Fr shaft. The system is designed to deliver the valve gradually, deploying it to the point of functionality while allowing for controlled recapture, followed by

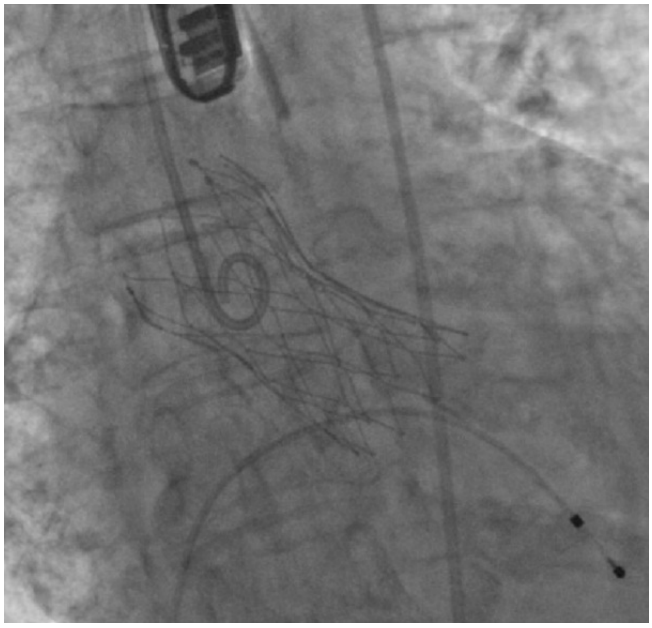


Figure 7: Angiography of a Portico valve.

Figure 8: The CENTERA valve. A self-expandable ultra-low-profile valve that consists of three bovine pericardial tissue leaflets attached to a nitinol frame with a polyethylene terephthalate skirt intended to minimize PV-AR.

either by repositioning and redeployment or by removal. Portico transaortic and subclavian delivery systems will also be available with designs similar to the transfemoral system. The 24 Fr delivery system used for transapical approach is composed of a tapered nose cone, a capsule containing the compressed valve and similarly allows repositioning of the valve if needed [27]. The Portico valve is sized according to the nominal external stent diameter at the valvular level. Currently, 23- and 25-mm devices are available for commercial use in Europe, and 27- and 29-mm devices are being evaluated in clinical trials.

First-in-human experience with Portico device included a 23-mm device implanted in 10 patients with severe AS via transfemoral approach [26]. At 30-day follow-up, echocardiographic mean transaortic gradient was reduced from 44.9±16.7 mm Hg to 10.9±3.8 mm Hg ($p < 0.001$), and aortic valve area (AVA) increased from 0.6±0.1 cm^2 to 1.3±0.2 cm^2 ($p < 0.001$). PV-AR was mild or less in 9 patients and moderate in 1 patient. There were no major strokes, major vascular complications, major bleeds, or deaths. No patient required pacemaker implantation. A case report of transapical Portico implantation has also been described [27].

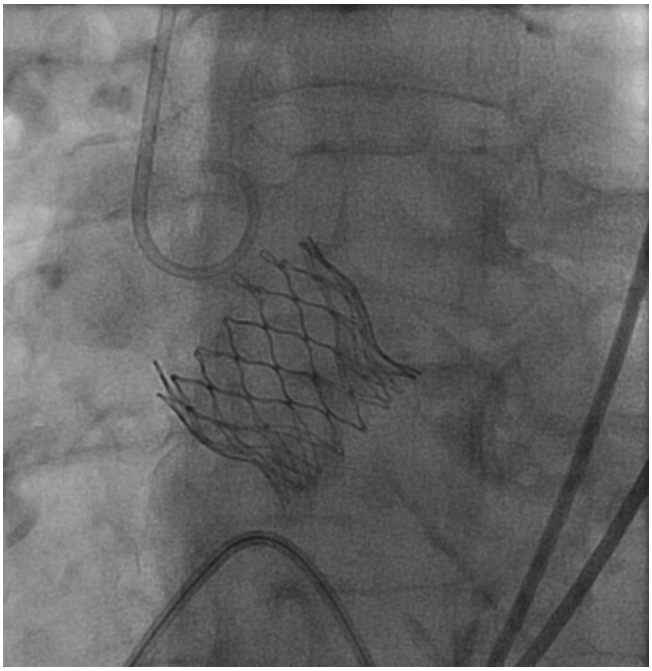


Figure 9: Angiography of a Centera valve.

Five clinical trials evaluating efficacy and safety of Portico valve implantation are currently ongoing (ClinicalTrials.gov Identifier: NCT02000115, NCT01802788, NCT01742598, NCT01493284, and NCT02088021).

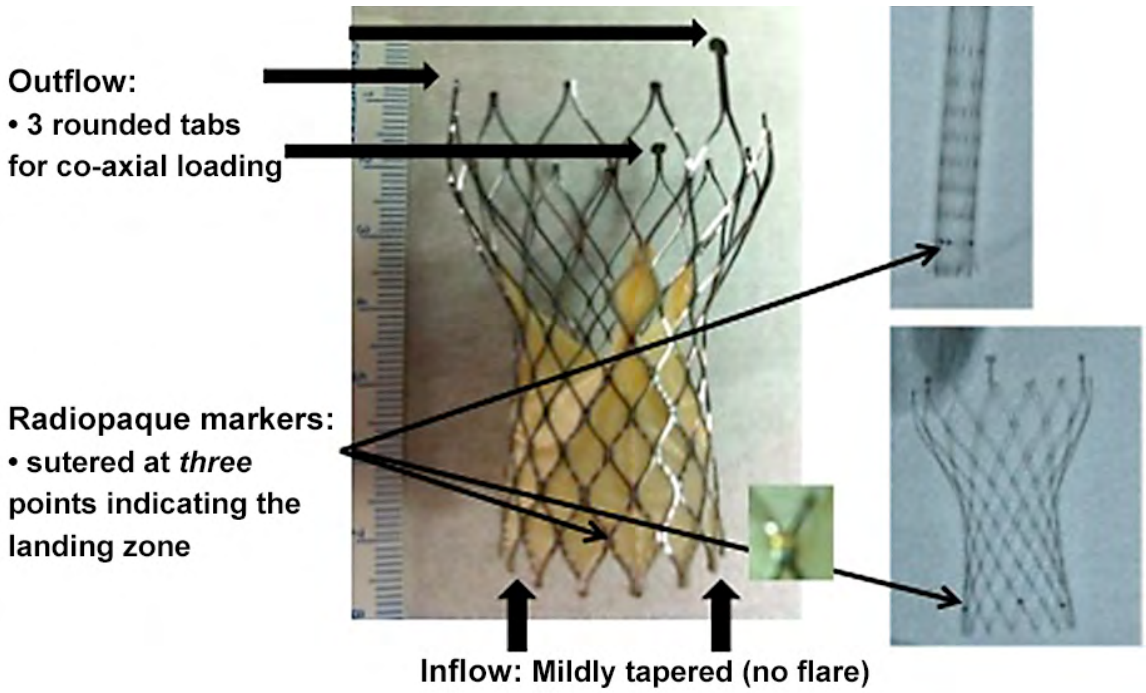


Figure 10: The Venus A valve. A self-expandable valve composed of a nitinol stent frame carrying a trileaflet bioprosthetic valve made of porcine pericardial leaflets.

Edwards Lifesciences Centera

The self-expandable CENTERA valve (Edwards Lifesciences, Irvine, CA, USA) is an ultra-low-profile valve that consists of three treated bovine pericardial tissue leaflets attached to a nitinol frame with a polyethylene terephthalate skirt intended to minimize PV-AR [28] (Figures 8 and 9). Currently, the valve is available in 23- and 26-mm sizes; an additional valve size of 29 mm is anticipated. The stent frame does not have a flared distal section that extends into the ascending aorta and therefore is shorter than that of other self-expandable valves. This facilitates self-centering and seating of the valve within the annulus, and it may also help to improve paravalvular sealing with minimal protrusion of the valve frame into the left ventricle. The delivery system consists of a delivery catheter and a detachable, battery-powered motorized handle, which can be delivered by the transfemoral or subclavian approaches. The capability to re-sheath and reposition in situ prior to complete valve deployment is an expected feature and may reduce the risk of valve malposition or embolization. The delivery system is compatible with a 14 Fr eSheath. The dynamic expansion mechanism of the eSheath allows for transient sheath expansion during valve delivery. Immediately after the valve passes through the sheath, the sheath return to a low-profile diameter thus reducing the time the access vessel is expanded, and minimizing the risk of vascular trauma.

The CENTERA valve was implanted in 15 patients with symptomatic severe AS via transfemoral (n=11) or transaxillary (n=4) approaches [29]. All 15 implantations were successful. Post-procedurally, AVA increased from 0.7±0.1 cm^2 to 1.6±0.4 cm^2 ($p < 0.01$) and mean trans-aortic gradient decreased from 36.3±14.2mmHg to 10.6±5.4mmHg ($p <0.001$). PV-AR at 30-day follow-up was none or trivial in 23%, mild in 69% and moderate in 8% of the patients. Survival was 87% at 30 days and 80% at 1 year, and four patients (27%) received a new permanent pacemaker.

The safety and performance study of the Edwards CENTERA self-expanding transcatheter heart valve trial is currently ongoing (ClinicalTrials.gov Identifier: NCT01808274).

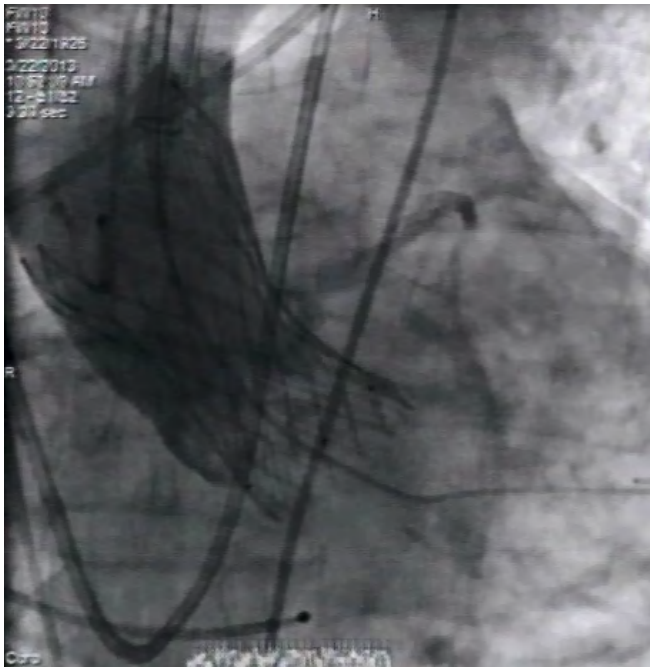


Figure 11: Aortography with contrast injection of a patient with Venus A valve following TAVR.

Figure 12: The JenaValve. A self-expandable composed of a full porcine root valve mounted on a low-profile nitinol stent. A unique clip fixation mechanism provides anchoring to the native leaflets.

Venus A Valve

The Venus A Valve (Venus Medtech, Hangzou Inc., Shanghai, China) is a self-expanding nitinol stent frame carrying a trileaflet bioprosthetic valve made of porcine pericardial leaflets (Figures 10 and 11). The delivery system is 18Fr and can be delivered sheathless by the transfemoral and transaxillary/transsubclavian approach and with a sheath for the transaortic approach [30]. The radial force of expansion for the inflow was increased early in the study, enabling a more consistent device expansion in the presence of extreme aortic valve calcification, which had been frequently observed in the treated population.

Moreover, midway in the first-in-man study, the inclusion criteria were extended to bicuspid aortic valve disease, given the frequency of cases encountered in China. Patients are treated under local anesthesia for the transfemoral and transaxillary approach and under general anesthesia for the transaortic approach. The first in-man Venus A-Valve trial is currently ongoing (ClinicalTrials.gov Identifier: NCT01683474). Recently, the initial results of Venus A valve implantation in 101 patients have been presented [30]. At 30-days, all-cause mortality was 2% and moderate-severe PV-AR rate was 6%.

JenaValve

The self-expandable JenaValve (JenaValveTechnology GmbH, Munich, Germany) consists of a full porcine root valve mounted on a low-profile nitinol stent [31] (Figure 12). In contrast to devices expanding within the aortic annulus, it relies on an active clip fixation of the native aortic valve leaflets, thereby eliminating great radial forces on cardiac and aortic structures. This allows for a short stent design that prevents coronary compromise by the native leaflets or stent struts, and that does not interfere with future coronary intervention. The unique clip fixation mechanism can provide secure anchoring to the native leaflets even in the absence of calcification and therefore may be utilized successfully for the treatment of non-calcified pure aortic regurgitation (AR) [32]. The feature of anatomically aligned positioning eliminates the need for rapid pacing during implantation. The device is delivered via transapical approach using a sheathless 32 Fr delivery catheter that is utilized for three-step deployment procedure. The valve is available in three different sizes (23mm, 25mm, and 27mm) for implantation in native aortic annuli ranging from 21- to 27-mm in diameter. A transfemoral JenaValve Plus is currently being developed with sim-

Figure 13: The ACURATE TA valve. A self-expandable valve composed of a nitinol stent frame and a biological tissue valve mounted within the stent. A polyethylene terephthalate skirt is mounted at the intra-annular part of the stent body.

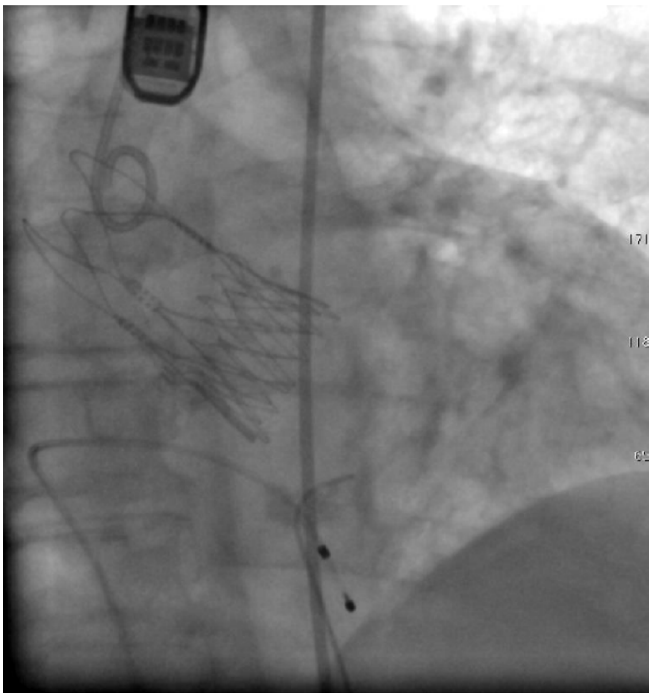


Figure 14: Angiography of an ACURATE TA valve.

ilar features and an 18 Fr delivery system that is composed of three combined coaxial catheters [33].

A pivotal study for CE mark approval included transapical JenaValve implantations in 73 patients with severe AS [34]. Mean transaortic gradient was reduced post-procedurally from 40.6±15.9 mm Hg to 10.0±7.2 mm Hg, ($p < 0.001$), and AVA increased from 0.7±0.2 cm^2 to 1.7±0.6 cm^2 ($p < 0.001$) and there was no or minimal PV-AR in 86.4% of the patients. Procedural success rate was 89.6%, perioperative stroke occurred in two cases (3%) and pacemaker implantation was necessary in six patients (9.1%). Seiffert et al. have described a case series of five patients that underwent transapical implantation of a JenaValve for moderate to severe, non-calcified AR [32]. Implantation was successful in all cases without relevant remaining AR or AS. No major device- or procedure-related adverse events occurred and all patients were alive with improved exercise tolerance at 3-month follow-up. JenaValve has a CE mark for treatment of patients with AS since 2011 and for treatment of patients with non-calcified AR since 2013.

Currently ongoing trial with JenaValve is the JUPITER registry (long-term safety and performance of the JenaValve; ClinicalTrials.gov Identifier: NCT01598844).

Symetis ACURATE TA / TF

The self-expanding ACURATE TA device (Symetis SA, Ecublens, Switzerland) has been specifically developed for the transapical approach [35]. The nitinol stent frame was designed to facilitate a simple single-operator two-step implantation technique (Figures 13 and 14). Three arches are mounted at the distal edge of the stent body to stabilize the prosthesis during final deployment. The upper crown is formed by the most distal part of the stent body and is meant to embrace the native calcified leaflets. The stent commissures are well visible under fluoroscopy with a circular radiopaque appearance which facilitates anatomical rotation of the prosthesis for commissural alignment. A biological tissue valve is

mounted within the nitinol stent. This valve has a similar leaflet thickness to conventional surgical porcine tissue valves because the design does not require excessive "crimping" of the leaflets. To minimize PV-AR, a polyethylene terephthalate skirt is mounted at the proximal (intra-annular) part of the stent body. The delivery system is based on a sheathless concept similar in size to a 28 Fr sheath system. Valve deployment is facilitated using a simple rotational knob suitable for a single-operator technique. Until final release the system allows for resheathing and repositioning. Three different sizes (labeled small, medium and large) are available allowing for treatment of patients presenting with an annulus diameter ranging from 20–27 mm. A transfemoral version of this device called ACURATE TF is very similar to the ACURATE TA device [36]. A 20 Fr delivery system has a flexible shaft facilitating easy tracking even in tortuous aortic anatomy. It allows a controlled three-step implantation of the prosthesis. There is also a newer transfemoral version called ACURATE neo that has a 15 Fr compatible delivery system.

The results of a first-in-human trial in 40 patients that underwent ACURATE TA implantation including 6 month follow-up have been published [35, 37]. Device success rate was 92.5%, mean transaortic gradient was reduced from 51.9 ±14.3 mm Hg to 11.9 ± 5.8 mm Hg. Thirty-day mortality was 12.5% and major stroke rate was 5%. At 6 months, only 3.3% of patients had more than mild PV-AR. Similar outcome have been published recently in a series of 62 patients [38]. A first-in-human trial in 20 patients treated with the ACURATE TF device has also been published [36]. The effective orifice area improved from 0.7 cm^2 to 1.8 cm^2 and only one patient had a grade 2 PV-AR. Procedural success rate was 95% with one case of stroke, and two pacemaker implantations at 30 days. ACURATE TA device has a CE mark obtained at 2011 and ACURATE neo device has a CE mark obtained at 2014.

Medtronic Engager

The Engager Aortic Valve bioprosthesis (Medtronic, Minneapolis, MN, USA) is a biological valve prosthesis composed of three leaflets cut from tissue-fixated bovine pericardium, sewn to a polyester sleeve and mounted on a compressible and self-expanding nitinol frame [39] (Figure 15). The stent assembly consists of a shaped main frame and a support frame, which are coupled together so as to form the commissural posts of the valve. Two types of sewing materials are used: polyester and expanded polytetrafluoroethylene. The valve design is intended to minimize PV-AR. The prosthesis is available in two sizes (23 mm and 26 mm) covering annulus diameters from 21 to 27 mm [40]. To achieve an anatomically correct position and to minimize the risk of coronary obstruction, the side arms fixed at the main frame of the prosthesis are designed to be placed into the sinuses of the aortic root. The valve can be repositioned before final deployment. Implantation is performed transapically with an over-the-wire delivery system comprising an introducer and a flexible delivery catheter which form one integral unit. The delivery system is composed of a 29 Fr (inner diameter) introducer and a flexible delivery catheter with a 13 Fr shaft. Engager valve has a CE mark for treatment of patients with AS since 2013.

Figure 15: The Engager Aortic valve bioprosthesis. A self-expandable valve composed of three leaflets cut from tissue-fixated bovine pericardium, sewn to a polyester sleeve and mounted on a nitinol frame.

Figure 16: The Embrella Embolic Deflector system. The device consists of an oval-shaped nitinol frame covered with a porous polyurethane membrane that is positioned at the level of the aortic arch with the purpose of deflecting embolic debris generated during TAVR procedures.

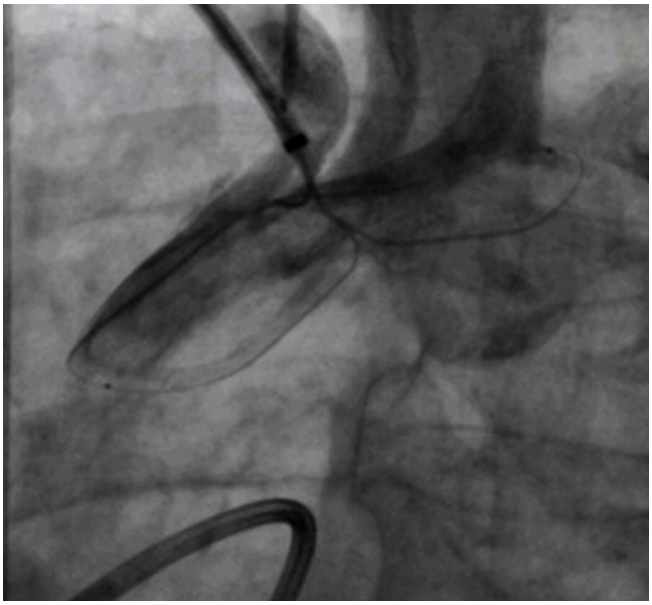


Figure 17: Angiographic image after deployment of the Embrella Embolic Deflector system at the level of the greater curvature of the aortic arch.

A feasibility study with the Engager system was conducted in 10 patients [39]. All 10 patients were implanted successfully. There were no device related complications. At 30 days, one patient died from multi-organ failure. The mean aortic gradient post-procedurally was 15.6± 4.9 mm Hg, and no more than a mild PV-AR was seen as assessed by echocardiography. The results of the first 61 patients enrolled in the European pivotal trial have showed all-cause mortality of 9.9% at 30 days, mean aortic valve gradient of 11.5±5.0 mm Hg, and no PV-AR greater than mild [41].

Two clinical trials evaluating efficacy and safety of the Medtronic Engager valve implantation are currently ongoing (ClinicalTrials.gov Identifier: NCT01348438, NCT01789567)

The Helio Transcatheter Aortic Dock

The Helio transcatheter aortic dock (Edwards Lifesciences, Irvine, CA, USA) is the first dedicated transcatheter device for the treatment of pure AR [42]. It consists of a self-expandable nitinol stent encased in polyethylene terephthalate fabric. The dock is fixed inside the aortic root and it is intended to assist in annular fixation of a standard balloon-expandable SAPIEN XT valve by incorporating and entrapping the native cusps. The currently available dock has a diameter of 25 mm, suitable for implantation with a 29 mm SAPIEN XT valve. It is intended that future devices will be compatible with a full range of balloon-expandable valves. The Helio delivery catheter is advanced through the 16 Fr eSheath over the stiff wire. The dock is then expanded within the aortic root by retracting a covering sleeve and positioned deep within the sinuses but outside the aortic valve cusps. A NovaFlex (Edwards Lifesciences, Irvine, CA, USA) delivery catheter is then advanced through the contralateral femoral sheath and a SAPIEN XT valve positioned within the dock and within the native valve. The clinical data currently available on this device is limited. In the first-in-human feasibility trial, four patients were treated successfully with a combined transfemoral-transapical approach. All of them were alive at 30 days and had no residual AR [43]. A fully percutaneous bilateral transfemoral approach is currently being evaluated.

Cerebral Protection Devices

Cerebrovascular events are among the most serious adverse events reported after TAVR and are associated with increased morbidity and mortality. The incidence of cerebrovascular events during the 30-

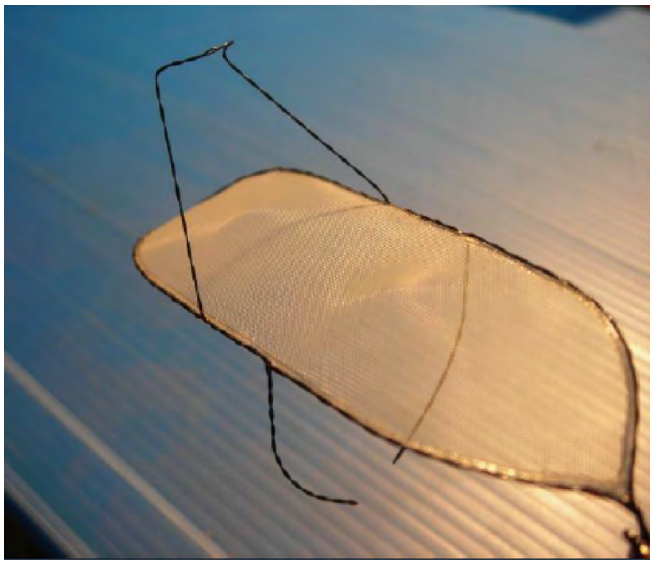


Figure 18: The TriGuard Cerebral Protection Device. The device consists of a nitinol mesh and a nitinol frame with two stabilizers that anchor the device in the brachiocephalic trunk and at the inner curvature of the aortic arch.

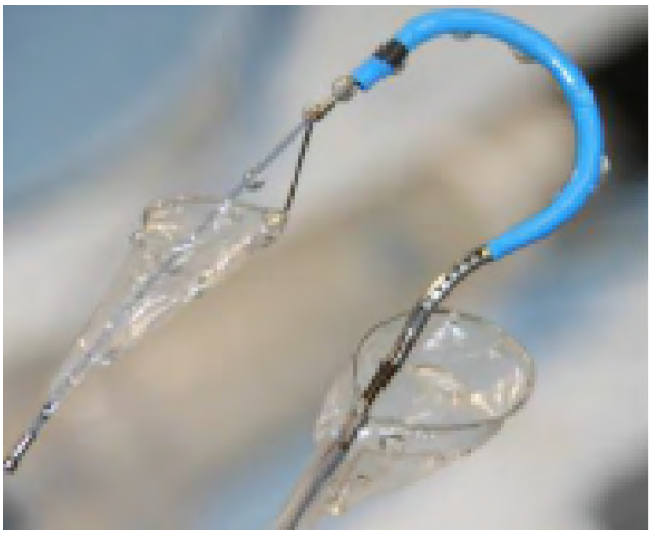


Figure 19: The Montage Dual Filter system. The conically shaped filters consist of a nitinol frame and polyurethane laser-drilled filter membrane with 140 μm-diameter pores. The filters are advanced to the brachiocephalic trunk and the left common carotid arteries before valve deployment.

day period after TAVR ranges from 3% to 7%, with the majority of patients experiencing 'major' strokes [11]. The observation that most cerebrovascular events occur within the first days after device implantation, implies that the stroke has a thromboembolic origin [44]. In order to minimize the risk of thromboembolic cerebrovascular accidents during TAVR, cerebral protection devices are currently being developed.

Embrella Embolic Deflector

The Embrella Embolic Deflector system (Edwards Lifesciences, Irvine, Ca, USA) consists of an oval-shaped nitinol frame covered with a porous polyurethane membrane that is positioned at the level of the aortic arch with the purpose of deflecting embolic debris generated during TAVR procedures [45] (Figures 16 and 17). The device is inserted via the right radial or brachial approach using a 6 Fr delivery system. The frame of the device has two opposing petals that are positioned along the greater curvature of the aorta, covering the ostia of both the brachiocephalic and the left common carotid arteries. In a pilot study recently published, the Embrella Embolic Deflector system was used in 41 patients during TAVR, compared to 11 patients that underwent TAVR without embolic protection [45]. The system was successfully deployed at the level of the aortic arch in all patients with no complications. The use of the system was associated with a lower cerebral lesion volume demonstrated with diffusion weighted magnetic resonance imaging (DW-MRI) compared with the control group (p=0.003).

TriGuard

The TriGuard Cerebral Protection Device (Keystone Heart Ltd, formerly SMT Research & Development, Caesarea, Israel) is introduced via the femoral artery. The concept is similar to that of the Embrella device with some notable differences. A 9 Fr sheath is usually used for delivery and retrieval and allows additional placement of a pigtail catheter for procedural guidance. The device itself consists of a nitinol mesh and a nitinol frame with two stabilizers that anchor the device in the brachiocephalic trunk and at the inner curvature of the aortic arch [46] (Figure 18). Initial clinical experience in 15 patients demonstrated successful placement of the embolic protection device in all of them without procedural complications [47]. No patient developed new neurological symptoms except one patient who suffered from TIA two days after the procedure. DW-MRI showed 3.2 new cerebral lesions per patient, compared to 7.2 new lesions per patient in a historical control group without the device. The

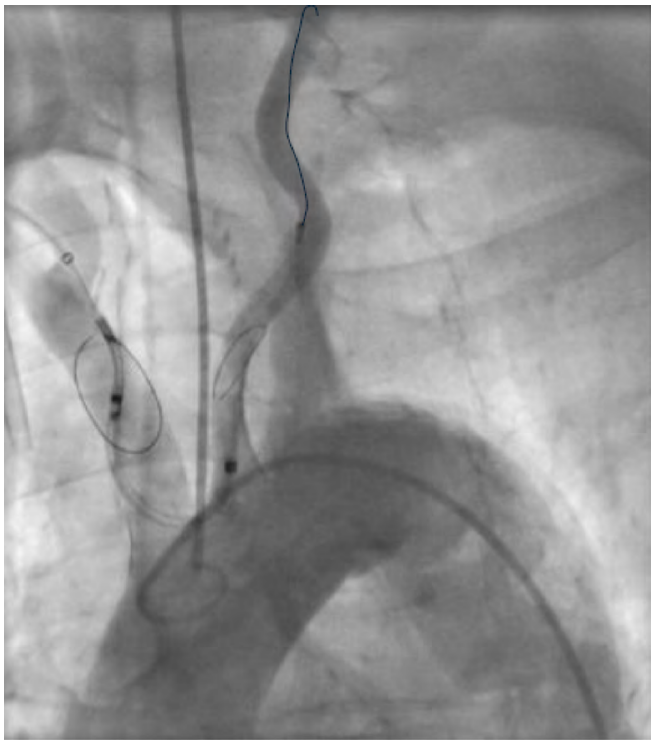


Figure 20: Angiographic image of the Montage Dual Filter System. The filters are located in the brachiocephalic trunk and the left common carotid arteries.

recently published DEFLECT III trial included 46 patients treated with TriGuard vs. 39 control patients [48]. TriGuard use was associated with greater freedom from new ischemic brain lesions (26.9 vs. 11.5%), fewer new neurologic deficits detected by the National Institutes of Health Stroke Scale (3.1 vs. 15.4%) and better performance on a delayed memory task (p=0.028).

Claret CE Pro / Montage Dual Filter System

The Montage Dual Filter System (Claret Medical Inc., Santa Rosa, CA, USA) is designed to capture embolic debris travelling to the brain in the brachiocephalic trunk and the left common carotid arteries [46]. The catheter is delivered through a 6 Fr sheath via the radial or brachial artery. The conically shaped filters consist of a nitinol frame and polyurethane laser-drilled filter membrane with 140 µm-diameter pores (Figures 19 and 20). The filter frames are radiopaque and once deployed seal against the vessel wall, allowing filtered blood to pass to the brain while trapping debris. After positioning of the first filter in the brachiocephalic trunk, the catheter is advanced further in the aortic arch under fluoroscopic guidance and the tip of the delivery system is curved towards the left common carotid artery for placement of the second filter. The safe use of the system has been demonstrated in first-in-human study, which included 40 patients [49]. Technical success rate with delivery of the proximal and distal filter was 60% for the first generation device and 87% for the second-generation device. Captured debris was documented in at least 19 of 35 implanted devices (54.3%). No procedural TIAs or strokes have occurred. Recently, the results of the CLEAN-TAVI trial were presented [50]. It is a prospective, double-blinded, randomized-controlled trial that included 100 patients. Cerebral protection device success was 96% (48/50). The number and volume of cerebral lesions as determined by DW-MRI subtraction was significantly reduced in the cerebral protection group. Two days post TAVR, neurological deficit was observed in 28% of patients in the control group compared to 13% of patients in the cerebral protection group (p=0.08).

Conclusions

TAVR has emerged as an established technique for the treatment of patients with symptomatic severe AS. Cumulative evidence has proven the short- and mid-term efficacy of this procedure, while improvements in implantation techniques and advances in TAVR technology have created high expectations for the future. The main challenges derived from the clinical experience with the first-generation TAVR devices were to reduce neurological and vascular complications and to minimize rates of PV-AR. The new-generation TAVR devices are currently in early clinical evaluation and have been specifically developed and designed to overcome these challenges. The features of these devices should allow the delivery catheter profile to be reduced, facilitate accurate positioning, repositioning and retrieval if needed, and reduce the incidence of significant PV-AR. New cerebral protection devices are expected to reduce clinical and sub-clinical embolic events. Although preliminary data with these new devices seem very promising, the clinical experience is still limited and more long-term data are required.

Nevertheless, continuous effort to develop, improve and clinically evaluate these devices and techniques will eventually enable safe alternative to aortic valve surgery for an increasing number of patients.

Conflict of Interest

Dr. Makkar is a consultant and has received grant support from Edwards Lifesciences Corporation, Medtronic Inc., and St. Jude Medical; and holds equity in Entourage Medical. Dr. Jilaihawi is a consultant for Edwards Lifesciences Corporation, St. Jude Medical, and Venus MedTech.

References

1. Makkar RR, Fontana GP, Jilaihawi H, Kapadia S, Pichard AD, Douglas PS, et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med. 2012;366:1696-1704. DOI: 10.1056/NEJMoa1202277
2. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med. 2012;366:1686-1695. DOI: 10.1056/NEJMoa1200384
3. Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: First human case description. Circulation. 2002;106:3006-3008. DOI: 10.1161/01.CIR.0000047200.36165.B8
4. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med. 2014;370:1790-1798. DOI: 10.1056/NEJMoa1400590
5. Thomas M, Schymik G, Walther T, Himbert D, Lefèvre T, Treede H, et al. Thirty-day results of the SAPIEN aortic Bioprosthesis European Outcome (SOURCE) Registry: A European registry of transcatheter aortic valve implantation using the Edwards SAPIEN valve. Circulation. 2010;122:62-69. DOI: 10.1161/CIRCULATIONAHA.109.907402
6. Gilard M, Eltchaninoff H, Iung B, Donzeau-Gouge P, Chevreul K, Fajadet J, et al. Registry of transcatheter aortic-valve implantation in high-risk patients. N Engl J Med. 2012;366:1705-1715. DOI: 10.1056/NEJMoa1114705
7. Tamburino C, Capodanno D, Ramondo A, Petronio AS, Ettori F, Santoro G, et al. Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis. Circulation. 2011;123:299-308. DOI: 10.1161/CIRCULATIONAHA.110.946533
8. Lerakis S, Hayek SS, Douglas PS. Paravalvular aortic leak after transcatheter aortic valve replacement: current knowledge. Circulation. 2013;127:397-407. DOI: 10.1161/CIRCULATIONAHA.112.142000
9. Généreux P, Head SJ, Hahn R, Daneault B, Kodali S, Williams MR, et al. Paravalvular leak after transcatheter aortic valve replacement: the new Achilles' heel? A comprehensive review of the literature. J Am Coll Cardiol. 2013;61:1125-1136. DOI: 10.1016/j.jacc.2012.08.1039
10. Moat NE, Ludman P, de Belder MA, Bridgewater B, Cunningham AD, Young CP, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. J Am Coll Cardiol. 2011;58:2130-2138. DOI: 10.1016/j.jacc.2011.08.050
11. Fassa A-A, Himbert D, Vahanian A. Mechanisms and management of TAVR-related complications. Nat Rev Cardiol. 2013;10:685-695. DOI: 10.1038/nrcardio.2013.156
12. Binder RK, Rodés-Cabau J, Wood DA, Webb JG. Edwards SAPIEN 3 valve. EuroIntervention. 2012;8(Suppl. Q):Q83-87. DOI: 10.4244/EIJV8SQA15
13. Binder RK, Rodés-Cabau J, Wood DA, Mok M, Leipsic J, De Larochellière R, et al. Transcatheter aortic valve replacement with the SAPIEN 3: a new balloon-expandable transcatheter heart valve. JACC Cardiovasc Interv. 2013;6:293-300. DOI: 10.1016/j.jcin.2012.09.019
14. Webb J, Gerosa G, Lefèvre T, Leipsic J, Spence M, Thomas M, et al. Multicenter evaluation of a next-generation balloon-expandable transcatheter aortic valve. J Am Coll Cardiol. 2014;64:2235-2243. DOI: 10.1016/j.jacc.2014.09.026
15. Kodali S. Clinical and echocardiographic outcomes at 30 days with the SAPIEN 3 TAVR system in inoperable, high-risk and intermediate-risk AS patients. Presented at ACC 2015.
16. Sinning J-M, Werner N, Nickenig G, Grube E. Medtronic CoreValve Evolut valve. EuroIntervention. 2012;8(Suppl. Q):Q94-96. DOI: 10.4244/EIJV8SQA17
17. Fairley SL, Jeganathan R, Manoharan G, Spence MS. Early experience of implantation of the new CoreValve(®) Evolut(TM) in degenerated bioprosthetic aortic valves. Catheter Cardiovasc Interv. 2014;83:485-492. DOI: 10.1002/ccd.25125
18. Zavalloni D, De Benedictis M, Pagnotta P, Scrocca I, Presbitero P. New CoreValve Evolut 23 mm technology for treatment of degenerated bioprosthesis. Heart Lung Circ. 2014;23:183-185. DOI: 10.1016/j.hlc.2013.08.002
19. Piazza N, Martucci G, Lachapelle K, de Varennes B, Bilodeau L, Buithieu J, et al. First-in-human experience with the Medtronic CoreValve Evolut R. EuroIntervention. 2014;9:1260-1263. DOI: 10.4244/EIJV9I11A215
20. Meredith IT. 6-month outcomes following transcatheter aortic valve implantation with a novel repositionable self-expanding bioprosthesis. Presented at EuroPCR 2015.
21. Meredith IT, Hood KL, Haratani N, Allocco DJ, Dawkins KD. Boston Scientific Lotus valve. EuroIntervention. 2012;8(Suppl. Q):Q70-74. DOI: 10.4244/EIJV8SQA12
22. Meredith Am IT, Walters DL, Dumonteil N, Worthley SG, Tchétché D, Manoharan G, et al. Transcatheter aortic valve replacement for severe symptomatic aortic stenosis using a repositionable valve system: 30-day primary endpoint results from the RE-

PRISE II study. J Am Coll Cardiol. 2014;64: 1339-1348. DOI: 10.1016/j.jacc.2014.05.067

23. Bijuklic K, Tübler T, Low RI, Grube E, Schofer J. Direct Flow Medical valve. EuroIntervention. 2012;8(Suppl. Q):Q75-78. DOI: 10.4244/EIJV8SQA13
24. Schofer J, Colombo A, Klugmann S, Fajadet J, DeMarco F, Tchétché D, et al. Prospective multicenter evaluation of the direct flow medical transcatheter aortic valve. J Am Coll Cardiol. 2014;63:763-768. DOI: 10.1016/j.jacc.2013.10.013
25. Manoharan G, Spence MS, Rodés-Cabau J, Webb JG. St Jude Medical Portico valve. EuroIntervention. 2012;8(Suppl. Q):Q97–101. DOI: 10.4244/EIJV8SQA18
26. Willson AB, Rodès-Cabau J, Wood DA, Leipsic J, Cheung A, Toggweiler S, et al. Transcatheter aortic valve replacement with the St. Jude Medical Portico valve: first-in-human experience. J Am Coll Cardiol. 2012;60:581-586. DOI: 10.1016/j.jacc.2012.02.045
27. Urena M, Doyle D, Rodés-Cabau J, Dumont E. Initial experience of transcatheter aortic valve replacement with the St Jude Medical Portico valve inserted through the transapical approach. J Thorac Cardiovasc Surg. 2013;146:e24-27. DOI: 10.1016/j.jtcvs.2013.06.005
28. Ribeiro HB, Urena M, Kuck K-H, Webb JG, Rodés-Cabau J. Edwards CENTERA valve. EuroIntervention. 2012;8(Suppl. Q):Q79-82. DOI: 10.4244/EIJV8SQA14
29. Binder RK, Schäfer U, Kuck K-H, Wood DA, Moss R, Leipsic J, et al. Transcatheter aortic valve replacement with a new self-expanding transcatheter heart valve and motorized delivery system. JACC Cardiovasc Interv. 2013;6:301-307. DOI: 10.1016/j.jcin.2013.01.129
30. Sievert H. The Venus A TAVR system. Presented at TVT 2015.
31. Treede H, Rastan A, Ferrari M, Ensminger S, Figulla H-R, Mohr F-W. JenaValve. EuroIntervention. 2012;8(Suppl. Q):Q88-93. DOI: 10.4244/EIJV8SQA16
32. Seiffert M, Diemert P, Koschyk D, Schirmer J, Conradi L, Schnabel R, et al. Transapical implantation of a second-generation transcatheter heart valve in patients with noncalcified aortic regurgitation. JACC Cardiovasc. Interv. 2013;6:590-597. DOI: 10.1016/j.jcin.2013.01
33. Rudolph TK, Baldus S. JenaValve–Transfemoral technology. EuroIntervention. 2013;9(Suppl.):S101-102. DOI: 10.4244/EIJV9SSA20
34. Treede H, Mohr F-W, Baldus S, Rastan A, Ensminger S, Arnold M, et al. Transapical transcatheter aortic valve implantation using the JenaValveTM system: Acute and 30-day results of the multicentre CE-mark study. Eur J Cardio-Thorac Surg. 2012;41:e131-138. DOI: 10.1093/ejcts/ezs129
35. Kempfert J, Möllmann H, Walther T. Symetis ACURATE TA valve. EuroIntervention. 2012;8(Suppl. Q):Q102-109. DOI: 10.4244/EIJV8SQA19
36. Möllmann H, Diemert P, Grube E, Baldus S, Kempfert J, Abizaid A. Symetis ACURATE TFTM aortic bioprosthesis. EuroIntervention. 2013;9(Suppl.):S107-110. DOI: 10.4244/EIJV9SSA22
37. Kempfert J, Treede H, Rastan AJ, Schönburg M, Thielmann M, Sorg S, et al. Transapical aortic valve implantation using a new self-expandable bioprosthesis (ACURATE TATM): 6-month outcomes. Eur J Cardio-Thorac Surg. 2013;43:52-56, 57. DOI: 10.1093/ejcts/ezs139
38. Seiffert M, Conradi L, Kloth B, Koschyk D, Schirmer J, Schnabel RB, et al. Single-centre experience with next-generation devices for transapical aortic valve implantation. Eur J Cardio-Thorac Surg. 2014. DOI: 10.1093/ejcts/ezu041
39. Sündermann SH, Grünenfelder J, Corti R, Rastan AJ, Linke A, Lange R, et al. Feasibility of the EngagerTM aortic transcatheter valve system using a flexible over-the-wire design. Eur. J. Cardio-Thorac. Surg. 2012;42:e48-52. DOI: 10.1093/ejcts/ezs389
40. Sündermann SH, Holzhey D, Bleiziffer S, Treede H, Falk V. Medtronic EngagerTM bioprosthesis for transapical transcatheter aortic valve implantation. EuroIntervention. 2013;9(Suppl.):S97-100. DOI: 10.4244/EIJV9SSA19
41. Holzhey D, Linke A, Treede H, Baldus S, Bleiziffer S, Wagner A, et al. Intermediate follow-up results from the multicenter engager European pivotal trial. Ann Thorac Surg. 2013;96:2095-2100. DOI: 10.1016/j.athoracsur.2013.06.089
42. Barbanti M, Ye J, Pasupati S, El-Gamel A, Webb JG. The Helio transcatheter aortic dock for patients with aortic regurgitation. EuroIntervention. 2013;9(Suppl.):S91-94. DOI: 10.4244/EIJV9SSA17
43. Pasupati S. A novel approach to aortic insufficiency: Edwards Helio System—Feasibility trial. Presented at EuroPCR 2013.
44. Stortecky S, Windecker S, Pilgrim T, Heg D, Buellesfeld L, Khattab AA, et al. Cerebrovascular accidents complicating transcatheter aortic valve implantation: frequency, timing and impact on outcomes. EuroIntervention. 2012;8:62-70. DOI: 10.4244/EIJV8I1A11
45. Rodés-Cabau J, Kahlert P, Neumann F-J, Schymik G, Webb JG, Amarenco P, et al. Feasibility and exploratory efficacy evaluation of the umbrella embolic deflector system for the prevention of cerebral emboli in patients undergoing transcatheter aortic valve replacement: The PROTAVI-C Pilot Study. JACC Cardiovasc Interv. 2014;7:1146-1155. DOI: 10.1016/j.jcin.2014.04.019
46. Praz F, Nietlispach F. Cerebral protection devices for transcatheter aortic valve implantation: is better the enemy of good? EuroIntervention. 2013;9(Suppl.):S124-128. DOI: 10.4244/EIJV9SSA26
47. Onsea K, Agostoni P, Samim M, Voskuil M, Kluin J, Budde R, et al. First-in-man experience with a new embolic deflection device in transcatheter aortic valve interventions. EuroIntervention. 2012;8:51-56. DOI: 10.4244/EIJV8I1A9
48. Lansky AJ, Schofer J, Tchetche D, Stella P, Pietras CG, Parise H, et al. A prospective randomized evaluation of the TriGuardTM HDH embolic DEFLECTion device during transcatheter aortic valve implantation: results from the DEFLECT III trial. Eur Heart J. 2015 May 19. [Epub ahead of print]. DOI:10.1093/eurheartj/ehv191
49. Naber CK, Ghanem A, Abizaid AA, Wolf A, Sinning J-M, Werner N, et al. First-in-man use of a novel embolic protection device for patients undergoing transcatheter aortic valve implantation. EuroIntervention. 2012;8:43-50. DOI: 10.4244/EIJV8I1A8
50. Linke A. CLEAN-TAVI: A prospective, randomized trial of cerebral embolic protection in high-risk patients with aortic stenosis undergoing transcatheter aortic valve replacement. Presented at TCT 2014.

Cite this article as: Abramowitz Y, Chakravarty T, Jilaihawi H. Makkar RR. Update on new devices for transcatheter aortic valve replacement. Structural Heart Disease 2015;1(3):112-126. DOI: http://dx.doi.org/10.12945/j.jshd.2015.019-14

JSHD
Journal of Structural Heart Disease

Original Scientific Article

Journal of Structural Heart Disease, August 2015,
Volume 1, Issue 3: 127-136
DOI: http://dx.doi.org/10.12945/j.jshd.2015.018-14

Received: December 24, 2014
Accepted: January 16, 2015
Published online: August 2015

An Overview of the Mitraclip Procedure

Indications, Procedural Characteristics, and Clinical Outcomes

Rahul P. Sharma, MD*, Moody Makar, MD, Saibal Kar, MD

Cedars Sinai Heart Institute, Los Angeles, California, USA

Abstract

The MitraClip procedure is a safe and effective approach to reduction of mitral regurgitation (MR) with proven durability and clinical improvement. Procedural success is dependent on patient selection, understanding of mitral valve anatomy, particularly from an echocardiographic perspective, and attention to critical elements of the implantation such as trans septal puncture.

In the United States, the FDA has approved the MitraClip device for treatment of high risk patients with primary MR. The question of long term, sustained reduction of MR and persistent clinical improvement remains to be addressed with longer duration of follow up. Based on the impeccable safety profile of the procedure and demonstrated medium term clinical durability, future studies should be aimed at the evaluation of MitraClip for treatment of patients with severe MR deemed moderate, or indeed low risk, for surgery.

Key Words

MitraClip • Mitral • Regurgitation • Valve

Anatomical Considerations

An understanding and appreciation of the complex anatomy of the mitral valve (MV) apparatus is imperative to achieving procedural success with the MitraClip (Abbott Vascular, Santa Clara, California, USA) device.

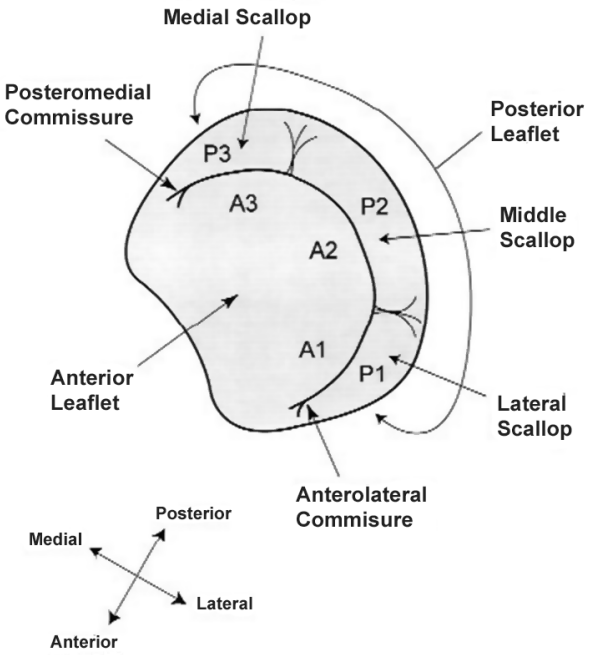


Figure 1: Mitral anatomy

The MV apparatus comprises the mitral valve, the annulus, annular attachment at the atrio-ventricular junction, tendinous chords, and the papillary muscles. The valve is made up of two leaflets, commonly referred to as the anterior and posterior leaflets (occasionally referred to as the mural and aortic leaflets, respectively). The posterior leaflet is narrow compared to the anterior leaflet and extends two-thirds around the left atrio-ventricular junction within the inlet por-

Fax +1 203 785 3346
E-Mail: jshd@scienceinternational.org
http://structuralheartdisease.org/

ISSN 2326-4004

Accessible online at:
http://structuralheartdisease.org/

* Corresponding Author:
Saibal Kar, MD
Cardiovascular Intervention Center Research
Cedars-Sinai Medical Center
Heart Institute, Los Angeles 90048, USA
Tel.: +1 310 423 3977, Fax: +1 310 423 0106, Email: Saibal.Kar2@cshs.org

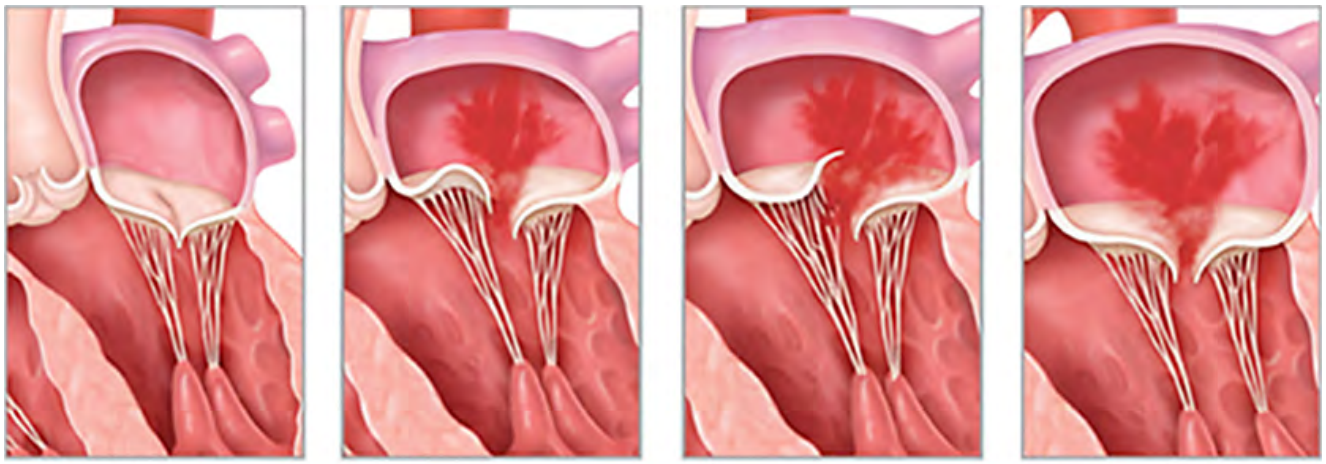


Figure 2: Primary MR vs FMR

tion of the ventricle. The leaflet has two clefts that separate the leaflet into three scallops along the free edge of the leaflet. The generally accepted nomenclature describes the most lateral scallop as P1, adjacent to the anterolateral commissure, the central scallop as P2, and the most medial as P3, which lies adjacent to the posteromedial commissure [1]. The semicircular anterior leaflet of the MV is broader than the anterior leaflet and comprises one-third of the annular circumference. The anterior leaflet shares a fibrous continuity with the left and non-coronary cusps of the aortic valve and between the aortic cusps abutting the membranous septum. The anterior leaflet is also divided into three regions, namely A1, A2, and A3 corresponding to the opposing scallops of the posterior leaflet (Figure 1). Anatomically, the most suitable pathology for MitraClip is that involving the A2/P2 leaflets. Commisural regurgitant jets pose a technical challenge, due to difficulty delivering the clip and grasping tissue at the ends of the free edge of each leaflet. Ensuring adequate insertion of both leaflets into the clip with grasp of sufficient tissue is essential to ensure division of the mitral orifice into smaller orifices with subsequent reduction in MR. Indeed, the primary purpose of the MitraClip procedure is to perform a percutaneous edge-to-edge repair and effectively create a double mitral orifice, based on the original surgical approach to MR described by Alfieri and colleagues [2].

The mitral annulus gives a point of attachment for the mitral valve and separates the left atrium from the left ventricle. The anterior aspect of the annulus is fibrous and less prone to dilatation. The remaining posterior aspect of the annulus is muscular and therefore often subject to dilatation and calcification. The annulus is a dynamic, non-rigid, oval shaped structure that alters shape throughout the cardiac cycle. This is an important consideration during the grasping process, which should be performed slowly to ensure capture of both leaflets.

The chordae tendinae are fan-shaped chords arising from the papillary muscles (PM) and inserting into the mitral leaflets. The posteromedial PM gives chords to the medial aspect of both leaflets while the anterolateral PM chords attach to the lateral aspect of the leaflets. The anterolateral and posteromedial PM arise from the mid to apical segments of the left ventricle at the anterolateral and posterior walls respectively. Awareness of the chordal structures is important when the clip passes below the valve, as entanglement may occur. This is of greater risk when more than one clip is used, as additional clips are passed through the mitral valve in a closed position and opened below the valve, in the left ventricle.

Pathophysiology

Mitral regurgitation is the passage of blood from the left ventricle back into the left atrium during ven-

tricular systole, occurring as a result of failure of the mitral leaflets to undergo complete coaptation (failure of leaflet tips to meet) or apposition (failure of the leaflets to overlap sufficiently). A simple classification system divides the etiology of mitral valve disease into either primary or functional (secondary) (Figure 2). Classification of MR has relevant implications for therapeutic intervention. In primary MR, the standard treatment is repair or replacement of the affected valve. In functional MR, therapy involves management of the underlying left ventricular dysfunction. For select patients in whom medical therapy is optimized, there may be a role for surgical correction.

The most common cause of primary MR is degenerative disease involving morphological changes to the valve due to thickening and stretching of leaflet tissue. The severity of these changes can range from involvement of a single scallop to both leaflets in their entirety. Fibroelastic deficiency describes a prolapsing segment, which is often normal in appearance. The prolapse is due to focal chordal elongation with or without rupture. Barlow's disease refers to myxomatous changes to both leaflets, more commonly affecting the posterior leaflet, associated with chordal thinning and elongation. Accordingly, segments of both leaflets prolapse into the left atrium. A more severe manifestation is a flail leaflet, characterized by complete eversion of the leaflet edge into the left atrium. A flail may be present in the event of primary chordal rupture and is often associated with severe mitral regurgitation. Other less common causes of primary mitral valve disease include infective endocarditis, congenital mitral cleft, and rheumatic mitral disease. The latter results in mitral stenosis with characteristic commissural fusion, with thickening and rigidity of the leaflets, eventually leading to regurgitation.

Functional MR occurs in the context of morphologically normal leaflets on a background of an underlying idiopathic cardiomyopathy or coronary artery disease. The regurgitation is due to geometric alterations of the left ventricle, which may or may not be associated with dilatation. Regional or generalized wall motion abnormalities of the left ventricle can alter the position of the papillary muscles during systole, resulting in chordal tension and leaflet restriction. Ventricular dilatation causes subsequent annular dilatation, resulting in failure of leaflet coaptation or inadequate apposition.

Clinical Outcomes and Procedural Indications

The clinical course of MR is usually slow and progressive, except for the rare circumstance of acute MR due to papillary muscle rupture in the setting of an acute myocardial infarction. The insidious nature of the disease is a result of the ability of the heart to compensate for increasing regurgitant volume, initially through enlargement of the left atrium. As the regurgitation becomes severe, the left ventricle is subject to overload, dilatation, dysfunction, and eventual failure. The presence of left ventricular dilatation and systolic dysfunction, particularly in the context of symptomatic functional impairment, heralds a very poor prognosis if left untreated. Annual mortality rates with medical treatment in patients aged 50 years or older are approximately 3% for moderate regurgitation and approximately 6% for severe regurgitation [3, 4]. Until recently, surgical valve repair or replacement was the only treatment proven to improve symptoms and prevent heart failure. Valve repair improves outcome compared with valve replacement and reduces mortality of patient with severe organic mitral regurgitation by about 70%. As expected, the best results are obtained in asymptomatic patients operated on in advanced repair centers with low operative mortality (<1%) and high repair rates (>80%) [5]. These results highlight the importance of early detection, assessment and management of mitral regurgitation.

Current AHA/ACC and ESC guidelines recommend surgical intervention, preferably repair, in symptomatic patients with chronic severe primary MR and in asymptomatic patients with chronic severe primary MR with evidence of systolic dysfunction or left ventricular dilatation [6, 7].

For patients with secondary MR, surgical intervention carries a higher rate of operative mortality compared to that for primary MR, largely due to the severe comorbidities of these patients. As such, the AHA and ESC guidelines suggest surgery for patients with severe secondary MR and preserved systolic function only when undergoing CABG or AVR [6, 7].

While surgery remains the gold standard of treatment, there are patients who are either at prohibi-

Table 1: Summary of MitraClip studies

Study	No. of Patients	Etiology of MR	Age	STS Score	EuroScore	MR≤2+ %	30-d Mortality %	1-yr Mortality %	MR≥3+ at 1 yr	Need for Surgery
Franzen et al.	51	DMR 31% FMR 69%	73±10	15±11	29±22	94	2	n/a	n/a	n/a
Tamburino et al.	31	DMR 42% FMR 58%	71 (62–79)	10±9	14±12	97	3.2	n/a	n/a	n/a
PERMIT-CARE	51	FMR	70±9	14±14	30±19	82	4.2	18	n/a	n/a
Rudolph et al.	104	DMR 34% FMR 66%	74±9	n/a	36 (21–54)	94	3.8	25	18	6.7
TRAMI	470	DMR 33% FMR 67%	75±5	11 (4–19)	23 (12–38)	94	2.5	n/a	n/a	n/a
EVEREST I	107	DMR 79% FMR 21%	71 (26–88)	n/a	n/a	74	0.9	4.1	n/a	29.9
EVEREST High risk registry	78	DMR 41% FMR 59%	77±10	14±8	n/a	80	7.7	24.4	20	0
ACCESS-EUROPE	567	DMR 23% FMR 77%	74±10	n/a	23±18	79	3.4	17.3	21	6.3
EVEREST II	186	DMR 73% FMR 27%	67±13	5±4	n/a	78	1	6	22	20
EVEREST II /REALISM High risk registry	351	DMR 30% FMR 70%	76±11	11.3±7.7	n/a	86	4.8	22.8	14	0.3
COAPT (enrolling)	*430*	*FMR*	-	-	-	-	-	-	-	-

tively high risk for, or do not benefit from, a surgical procedure, particularly those with functional MR. The MitraClip procedure is a novel, minimally invasive, transcatheter procedure that can be offered to such patients. To date, there have been a number of trials and registry studies examining the safety and efficacy of the MitraClip device when compared to standard medical therapy and to surgery.

The results of the relevant clinical studies are summarized in Table 1 [8-15]. In all of these studies, procedural success was achieved in the majority of patients with reduction of MR from 4+ to less than 2+. Furthermore, these results were generally achieved with an excellent safety profile without any significant rate of adverse procedural outcomes.

The EVEREST cohort is a prospective multicenter registry that analyzed the feasibility, safety and efficacy of MitraClip in patients with moderate-to-severe (3+) or severe (4+) MR with class I surgical indication. A total of 107 patients were enrolled (55 from EVEREST I and 52 in the prerandomization phase of EVEREST II), with a mean follow-up of almost 2 years. The EVEREST cohort established that the MitraClip procedure is safe, with a low periprocedural complication rate. In carefully selected patients, it has acceptable efficacy achieving significant MR reduction in more than two-thirds of patients [13].

The landmark study was Everest II, a multicenter randomized clinical trial designed to compare the efficacy and safety of percutaneous treatment with MitraClip vs. conventional repair surgery or MV replacement. Compared to surgery, at 1 year, MitraClip was less effective than surgical repair due to the increased prevalence of residual MR compared to surgery. However, the clip reduced severity of MR, improved symptoms, and led to reverse LV remodeling [16]. The improve-

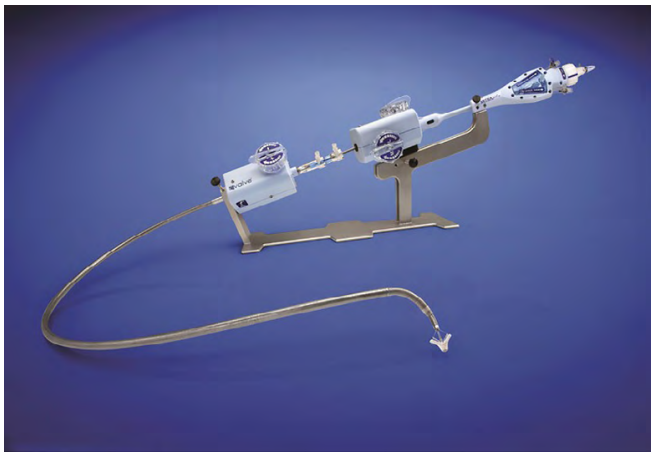


Figure 3: MitraClip device

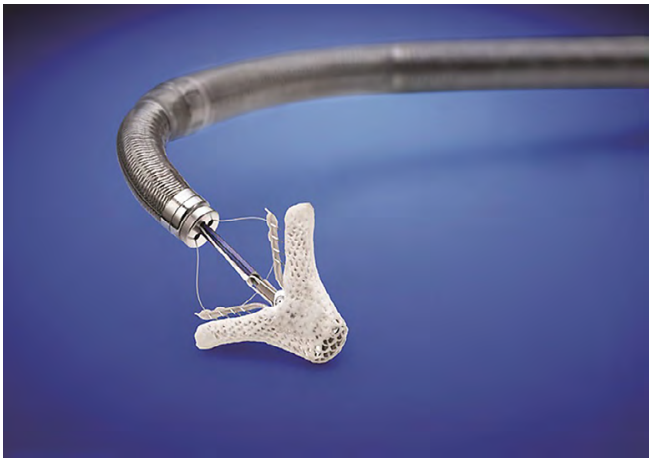


Figure 4: Clip

ment in NYHA functional class at 1 year was sustained at 4 years. The 4-year results demonstrated no mortality difference between the two groups, a low rate of MV surgery in the percutaneous repair group beyond the first 6 months of therapy, and a low rate of adverse events from 1 to 4 years in both groups [17].

The EVEREST II high-risk registry (HRR) included patients with moderate-severe or severe MR with an estimated surgical risk of 12% or greater (based on the *Society of Thoracic Surgeons* risk score or as estimated by the surgical team). Enrolment of patients has continued as part of the REALISM registry which has two arms: 1 with high-risk patients and the other with non-high risk patients, The combined REALSIM and EVEREST II High Risk Registry demonstrated an impressive 30 day mortality of less than 5% with significant improvement in symptom status, reduced rate of hospitalization and improved left ventricular remodeling at one year [15].

Based on the outcomes from Everest II the AHA/ACC guidelines state that the MitraClip should only be considered for patients with chronic primary MR who remain severely symptomatic with NYHA class III to IV HF symptoms despite optimal heart failure therapy and who are considered inoperable [6].

The ESC guidelines recommend that MitraClip may be considered in patients with symptomatic severe primary MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a 'heart team,' and have a life expectancy greater than 1 year [7].

Furthermore, based on experience the EVEREST trials and from observational studies, ESC guidelines suggest that MitraClip is feasible at low procedural risk in patients with secondary MR in the absence of severe tethering and may provide short-term improvement in functional condition and LV function [7].

While the AHA/ACC guidelines acknowledge that MitraClip provides a less invasive alternative to surgery, it is noted that the procedure is not yet approved for clinical use in the United States [6].

The COAPT trial is a currently enrolling, randomized, parallel-controlled, multicenter clinical evaluation of the MitraClip device for the treatment of clinically significant functional mitral regurgitation in symptomatic heart failure subjects who are treated per standard of care and who have been deemed ineligible for mitral valve surgery. Eligible subjects will be randomized in a 1:1 ratio to the MitraClip device or to no MitraClip device (control group). The primary outcome measures include the primary safety endpoint (composite of single leaflet device attachment, device embolizations, endocarditis requiring surgery, mitral stenosis requiring surgery, and any device related complications requiring non-elective cardiovascular surgery) and the primary effectiveness (recurrent heart failure hospitalizations). The results of this study are eagerly anticipated to prove the efficacy of MitraClip in patients with functional MR.

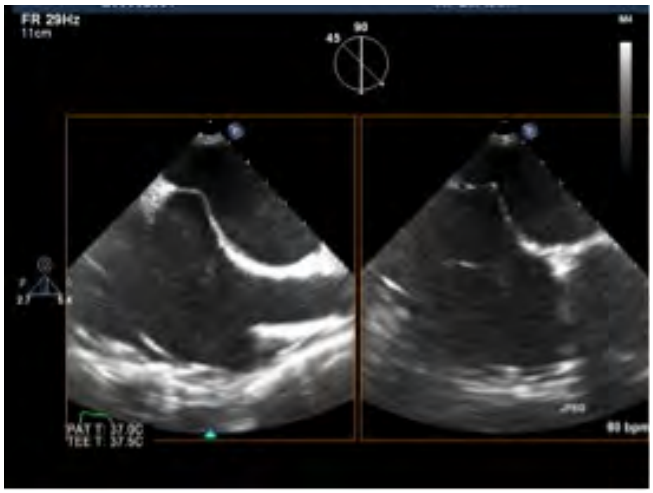


Figure 5: Trans septal puncture

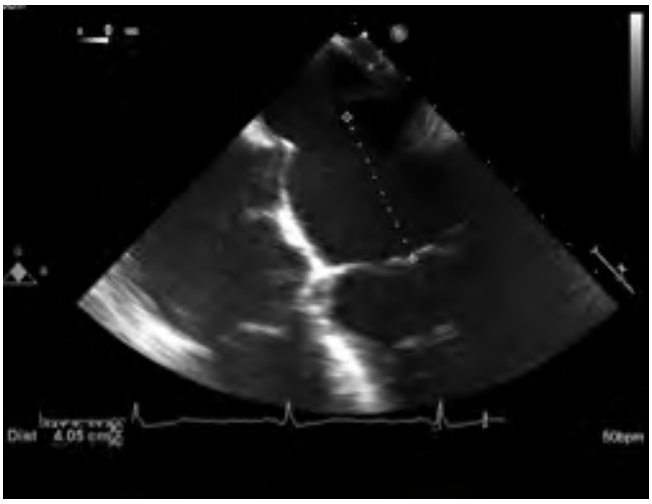


Figure 6: Device Distance

MitraClip Device

The complete device apparatus consists of a steerable Guide handle attached to the steerable sleeve and the Clip Delivery System (CDS), comprising the clip itself, the Delivery Catheter Handle (DCH), and the delivery catheter (Figure 3). The clip consists of a 4-mm wide and 8-mm long chrome-cobalt clip with two articulated arms that open from 0° (closed position) to 240° (open position), allowing grasping and drawing together of the anterior and posterior leaflets. The inner parts of the arms are grippers, lined with small frictional elements that grasp the leaflets once the device has been closed. The outer part is covered in a polyester mesh to promote tissue growth and the formation of a fibrous tissue bridge between the leaflets (Figure 4). The MitraClip device is delivered using a 24 Fr catheter guide with a mobile steerable tip to position the clip. The delivery system has two knobs that control the anterior-posterior and medial-lateral steering of the catheter tip. The DC handle comprises two levers to lock/unlock the clip and to lift/depress the gripper lines, a knob to facilitate the opening and closing of the clips and a screw to enable release of the clip from the shaft of the delivery catheter.

Procedure

The MitraClip procedure is performed under general anesthesia, primarily to enable pauses in ventilation and thereby ensure precise clip positioning.

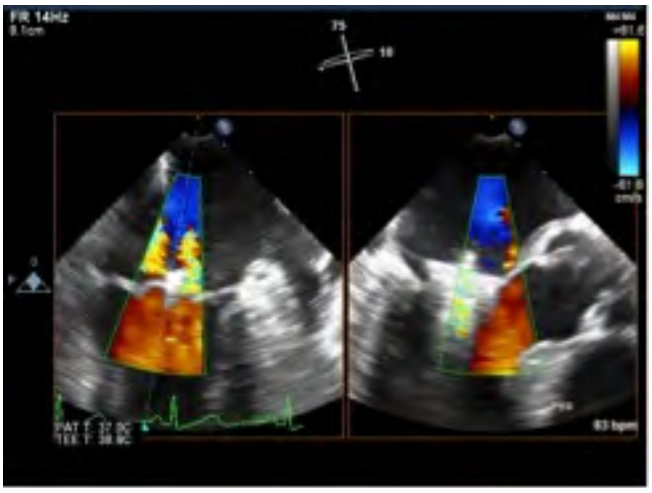


Figure 7: Bicommisural and LVOT view

The additional advantage of general anesthesia is comfort to the patient, particularly in the context of extended periods of TEE evaluation.

One of the key advantages of the MitraClip procedure is venous access. We recommend using a micropuncture needle to minimize vascular complications. The first venous access site is the jugular or femoral vein for right heart catheterization at the commencement of the procedure and immediately following release of the clip. A second venous sheath is placed in the femoral vein for eventual passage of the MitraClip apparatus. A PerClose Proglide suture can be placed in a 'pre-close' fashion to achieve hemostasis at the end of the case.

Cardiac imaging with visualization of the interatrial septum (IAS) and the mitral valve apparatus is vital to the success of the MitraClip procedure. Operators should be well versed in obtaining and interpreting echocardiographic views to guide trans-septal puncture, device positioning and clip deployment. Furthermore, operators should be aware of the parameters used to assess the success of clip deployment based on echocardiographic interrogation. At our institution, TEE is performed by a cardiac anesthesiologist experienced in MitraClip procedures, with an understanding of the expectations and requirements of the operator. Effective communication between the individual procuring the TEE images and the operator is imperative to facilitate an efficient and effective procedure.

The trans-septal puncture is arguably the most critical step of the procedure. If the puncture is inaccurate, subsequent device maneuverability and clip positioning is made difficult, often resulting in failed, or at best, unsatisfactory clip deployment position reflected by minimal or no improvement in MR. Indeed, poor clip position may in fact worsen the degree of MR or cause MS. Accordingly, we take great care to ensure precise trans-septal puncture, repeating the process if necessary to ensure an optimal starting position. The trans-septal puncture is performed under both fluoroscopic and TEE guidance using standard equipment and technique.

We recommend simultaneous viewing of a short axis image for anteroposterior positioning and a bicaval image for superoinferior positioning. The optimal puncture site is located slightly inferior and posterior on the septum (Figure 5). Once this position is located we obtain a 0 degree, 4 chamber view to measure the "device distance", defined as the distance of the septal puncture from the mitral annulus. Ideally, this distance should be 4.0–4.5 cm above the mitral annulus as measured perpendicular to the plane of mitral valve coaptation during systole (Figure 6). If difficulty is encountered puncturing the septum, such as in the case of a thickened or fibrotic septum, focal cauterization of the septum can be used to facilitate entry.

Once the needle is across the septum the entire system is advanced into the left atrium and heparin is administered for anticoagulation. The 24F Abbott

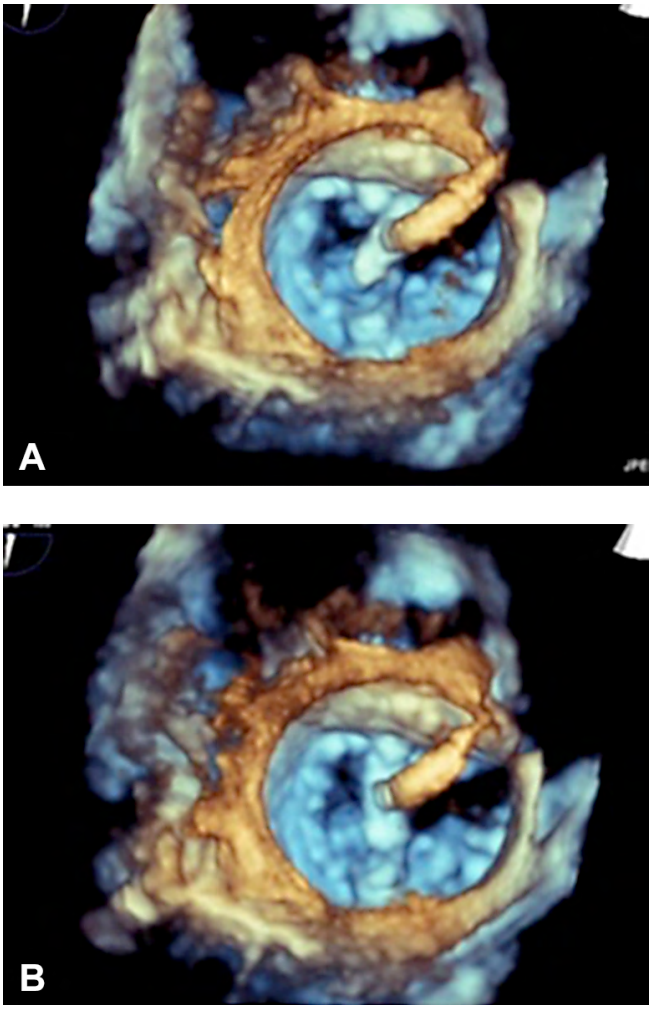


Figure 8: A. Checking orientation in 3D enface view. B. Correcting orientation in 3D enface view

MitraClip delivery steerable system is then advanced over a Superstiff wire into the left atrium. The Superstiff wire is then removed and baseline left atrial pressure is recorded. The MitraClip device is then carefully advanced into the left atrium through the device deployment sheath under fluoroscopy and TEE guidance.

From the plane of entry into the left atrium, parallel to the mitral annulus, the clip delivery system can be steered towards the valve using the mediolateral steering knob to turn the device 90 degrees and by turning the guide clockwise, aligning the clip perpendicular to the annulus. Once the device reaches just above the leaflets, an assessment is made of the position of the clip in a mediolateral and anteroposterior plane, using bicommissural and LV outflow tract

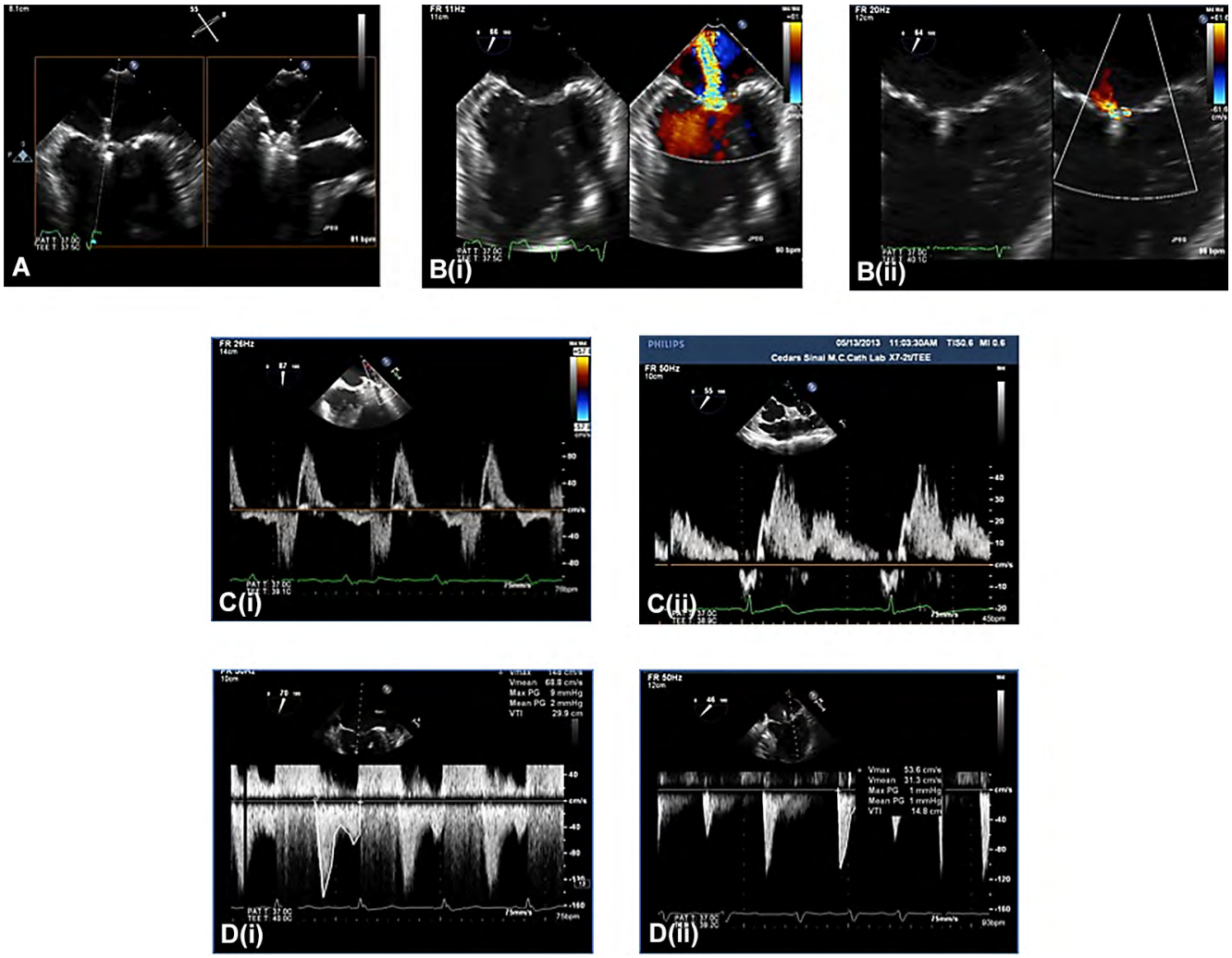


Figure 9: Pre deployment check: A. Leaflet insertion. B. Reduction in regurgitation (i) pre (ii) post. C. Pulmonary vein assessment (i) pre (ii) post. D. Mitral Stenosis (i) pre (ii) post.

echocardiographic views respectively (Figure 7). The trajectory of the clip is examined by moving the DC handle up and down while assessing the direction of the delivery shaft. Adjustments in the medial or lateral direction are made in the bi-commissural view either by moving the entire system or by adjusting the 'M' knob. Adjustments in the anterior or posterior direction are made in the LVOT view by rotating the guide handle clockwise or counter-clockwise. Once an ideal position is achieved, the clip is opened to 180 degrees and a 3-D en face surgical view of the mitral valve is obtained to assess for orientation of the clip arms relative to the leaflets (Figure 8). Any adjustments are made by rotating the DC handle in the desired direction then transmitting the torque by moving the handle up and down rapidly. Once the clip is perpendicular to the leaflets, the clip is advanced in the open position through the valve. The orientation of the clip is re-checked, the clip is closed to 120 degrees, and the DC handle retracted slowly to grasp both leaflets in the device. Once leaflet capture is confirmed the grippers are pushed down and the clip is closed. TEE interrogation is then performed in multiple views to ensure leaflet capture with adequate tissue grasp, reduction in MR (assessed by regurgitant volume, size of MR PISA and pulmonary vein Doppler), and absence of a significant gradient (Figure 9). If these procedural goals have been met,

the clip is released. The TEE evaluation is repeated once more and if there is significant residual MR and no significant gradient (>6mmHg) additional clips can be deployed. These are deployed in the previously described manner with one key difference—subsequent clips are passed through the valve in a closed position and opened below the valve in the ventricle. Placement of additional clips carries a risk of worsening MR (due to deformation of the leaflets), clip interaction and potential instability, and significant stenosis. In our experience, it is technically more challenging to place additional clips medial to the first clip. As such, when reviewing echo images prior to the procedure and expecting the need for multiple clips, or if considering an additional clip during the procedure, we aim to place the first clip in the more medial position and all subsequent clips laterally. An inherent advantage of the MitraClip procedure is the ability to remove a clip following closure and subsequent assessment. Accordingly, if the operator is dissatisfied with the result of an additional clip this can simply be opened, detached from the leaflet, brought back into the guide, and removed from the body.

The MitraClip procedure is generally safe and well tolerated. Aside from the risks associated with general anesthesia, those specific to the procedure include: femoral venous complications; trans-septal trauma resulting in an atrial septal defect (significant shunts may require closure), left atrial perforation (care must be taken to manipulate the guide catheter away from the posterior wall of the left atrium prior to removal); clip detachment and embolization (clip stability must be assessed fluoroscopically and via echocardiography prior to final release of the clip); and endocarditis. The overall rate of such adverse events in our experience is less than 1%.

Conclusion

The MitraClip procedure is a safe and effective approach to reduction of MR with proven durability and clinical improvement. The safety of the procedure is attributable to two key elements. Firstly, the percutaneous trans venous access, which limits the significance of vascular complications compared to an open surgical approach. Secondly, the trans septal approach, which is a far less invasive method of accessing the mitral valve compared to surgical access via the left atrium.

In the United States, the FDA has approved the MitraClip device for treatment of high risk patients with primary MR. The currently enrolling randomized COAPT study will help address the question regarding the benefit of MitraClip in conjunction with guideline directed medical therapy when compared to standard care in high risk patients with FMR. Furthermore, the question of long-term, sustained reduction of MR and persistent clinical improvement remains to be addressed with longer duration of follow up. Based on the impeccable safety profile of the procedure and demonstrated medium-term clinical durability, future studies should be aimed at the evaluation of MitraClip for treatment of patients with severe primary or functional MR deemed moderate, or indeed low risk, for surgery.

Conflict of Interest

Dr. Saibal Kar is a proctor for MitraClip.

Comment on this Article or Ask a Question

References

1. Carpentier A. Mitral valve annuloplasty. Ann Thorac Surg. 1990;49:508-509. PMID: 2310267
2. Alfieri O, Maisano F, De Bonis M, Stefano PL, Torracca L, Oppizzi M, et al. The double-orifice technique in mitral valve repair: A simple solution for complex problems. J Thorac Cardiovasc Surg. 2001;122:674-681. PMID: 11581597
3. Ling LH, Enriquez-Sarano M, Seward JB, Tajik AJ, Schaff HV, Bailey KR, et al. Clinical outcome of mitral regurgitation due to flail leaflet. N Engl J Med. 1996;335:1417-1423. DOI: 10.1056/NEJM199611073351902
4. Enriquez-Sarano M, Nkomo V, Mohty D, Avierinos JF, Chaliki H. Mitral regurgitation: Predictors of outcome and natural history. Adv Cardiol. 2002;39:133-143. DOI: 10.1159/000058920
5. Enriquez-Sarano M, Akins CW, Vahanian A. Mitral regurgitation. Lancet. 2009;373:1382-1394. DOI: 10.1016/S0140-6736(09)60692-9
6. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Guyton RA, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:e57-185. DOI: 10.1161/CIR.0000000000000029
7. Vahanian A, Alfieri O, Andreotti F, Antunes

MJ, Baron-Esquivias G, Baumgartner H, et al. Guidelines on the management of valvular heart disease (version 2012): The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur J Cardiothorac Surg. 2012;42:S1-44. DOI: 10.1093/ejcts/ezs455

8. Franzen O, Baldus S, Rudolph V, Meyer S, Knap M, Koschyk D, et al. Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: Emphasis on adverse valve morphology and severe left ventricular dysfunction. Eur Heart J. 2010;31:1373-1381. DOI: 10.1093/eurheartj/ehq050
9. Tamburino C, Ussia GP, Maisano F, Capodanno D, La Canna G, Scandura S, et al. Percutaneous mitral valve repair with the MitraClip system: Acute results from a real world setting. Eur Heart J. 2010;31:1382-1389. DOI: 10.1093/eurheartj/ehq051
10. Auricchio A, Schillinger W, Meyer S, Maisano F, Hoffmann R, Ussia GP, et al. Correction of mitral regurgitation in nonresponders to cardiac resynchronization therapy by MitraClip improves symptoms and promotes reverse remodeling. J Am Coll Cardiol. 2011;58:2183-2189. DOI: 10.1016/j.jacc.2011.06.061
11. Rudolph V, Lubos E, Schluter M, Lubs D, Goldmann B, Knap M, et al. Aetiology of mitral regurgitation differentially affects 2-year adverse outcomes after MitraClip therapy in high-risk patients. Eur J Heart Failure. 2013;15:796-807. DOI: 10.1093/eurjhf/hft021
12. Wiebe J, Franke J, Lubos E, Boekstegers P, Schillinger W, Ouarrak T, et al. Percutaneous mitral valve repair with the MitraClip system according to the predicted risk by the logistic EuroSCORE: Preliminary results from the German Transcatheter Mitral Valve Interventions (TRAMI) Registry. Catheter Cardiovasc Interv. 2014;84:591-598. DOI: 10.1002/ccd.25493
13. Feldman T, Kar S, Rinaldi M, Fail P, Hermiller J, Smalling R, et al. Percutaneous mitral repair with the MitraClip system: Safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) cohort. J Am Coll Cardiol. 2009;54:686-694. DOI: 10.1016/j.jacc.2009.03.077
14. Maisano F, Franzen O, Baldus S, Schafer U, Hausleiter J, Butter C, et al. Percutaneous mitral valve interventions in the real world: Early and 1-year results from the ACCESS-EU, a prospective, multicenter, nonrandomized post-approval study of the MitraClip therapy in Europe. J Am Coll Cardiol. 2013;62:1052-1061. DOI: 10.1016/j.jacc.2013.02.094
15. Glower DD, Kar S, Trento A, Lim DS, Bajwa T, Quesada R, et al. Percutaneous mitral valve repair for mitral regurgitation in high-risk patients: results of the EVEREST II study. J Am Coll Cardiol. 2014;64:172-181. DOI: 10.1016/j.jacc.2013.12.062
16. Whitlow PL, Feldman T, Pedersen WR, Lim DS, Kipperman R, Smalling R, et al. Acute and 12-month results with catheter-based mitral valve leaflet repair: the EVEREST II (Endovascular Valve Edge-to-Edge Repair) High Risk Study. J Am Coll Cardiol. 2012;59:130-139. DOI: 10.1016/j.jacc.2011.08.067
17. Mauri L, Foster E, Glower DD, Apruzzese P, Massaro JM, Herrmann HC, et al. 4-year results of a randomized controlled trial of percutaneous repair versus surgery for mitral regurgitation. J Am Coll Cardiol. 2013;62:317-328. DOI: 10.1016/j.jacc.2013.04.030

Cite this article as: Sharma R, Makar M, Kar S. An Overview of the Mitraclip Procedure. Structural Heart Disease 2015;1(3):127-136. DOI: http://dx.doi.org/10.12945/j.jshd.2015.018-14

JSHD
Journal of Structural Heart Disease

Original Scientific Article

Journal of Structural Heart Disease, August 2015,
Volume 1, Issue 3: 137-151
DOI: http://dx.doi.org/10.12945/j.jshd.2015.008.14

Received: October 19, 2014
Accepted: January 08, 2015
Published online: August 2015

Transcatheter Therapies for Tricuspid Valve Failure

Zakaria Jalal, MD[1], Rachid Zegdi, MD, PhD[2-4], Alexander Lauten, MD[5], Patel Mehul, MD[1], Younes Boudjemline, MD, PhD[1,4,6]*

Rachid Zegdi and Alexander Lauten have contributed equally to the writing of this paper.

[1] Centre de Référence Malformations Cardiaques Congénitales Complexes – M3C, Hôpital Necker-Enfants Malades, Hôpital Européen Georges Pompidou, Assistance Publique des Hôpitaux de Paris, Unité médico-chirurgicale, Paris, France

[2] Inserm U970, Faculté de Necker, Paris, France

[3] Service de Chirurgie Cardiovasculaire, Hôpital Européen Georges Pompidou, AP-HP, Paris, France

[4] Université Paris Descartes, Sorbonne Paris Cité, Paris, France

[5] Klinik für Innere Medizin 1, Kardiologie, Erlanger Allee 101, 07743 Jena, Germany

[6] EA 7328 FETUS, Faculté de Necker, Paris, France

Abstract

Tricuspid valve failure with low output state is a growing problem in the management of structural heart disease and stage D heart failure. Severe tricuspid valve disease either due to congenital or acquired etiology constitutes high risk for palliative or definitive surgical correction. Limited progress is noted so far on the evolution of durable surgical techniques on tricuspid valve disease and spiraling down refractory right heart failure continues to be the Achilles heel in the management. Over the last decade, transcatheter therapies for the management of aortic and pulmonary valves have expanded the therapeutic options for patients deemed at high risk for conventional surgery. The interventional therapies to manage tricuspid valve failure have mostly been a surrogate use of established therapies for other valves. The numerous interventional strategies used on failing tricuspid valve include percutaneous tricuspid valvuloplasty, percutaneous valve in valve, valve-in-ring implantation, and orthotopic/heterotopic valve implantation using commercially available "off-label" device or dedicated custom-made devices. This review focuses on the different percutaneous approaches and devices that have evolved for the management of tricuspid valve failure with varying anatomical substrates such as native tricuspid valves, annuloplasty rings or bioprosthesis.

Key Words:

Transcatheter • Tricuspid valve • Congenital heart diseases • Tricuspid stenosis • Tricuspid insufficiency

Introduction

A variety of congenital and acquired etiologies affect the tricuspid valve. While congenital lesions such as tricuspid valve dysplasia or Ebstein's anomaly cause organic involvement of the tricuspid valve apparatus, acquired lesions may be function with less obvious structural abnormality other than annular dilation, most commonly due to pulmonary hypertension or any other etiology causing severe right ventricular dilatation [1-3]. Once considered a dispensable valve, when tricuspid valve stenosis and/or regurgitation are severe, cardiac output decreases and patients develop spiralling down symptoms of right heart failure with congestive hepatosplenomegaly, peripheral oedema and cardiac cachexia. A wide variety of tricuspid valve surgeries such as valve repair with or without annuloplasty and even valve replacement have produced just satisfactory results mostly due to the high operative mortality of up to 22% in such patients deemed as very high-risk for perioperative events [2-4].

Fax +1 203 785 3346
E-Mail: jshd@scienceinternational.org
http://structuralheartdisease.org/

ISSN 2326-4004

Accessible online at:
http://structuralheartdisease.org/

*Corresponding Author:
Younes Boudjemline, MD, PhD
Hôpital Necker Enfants Malades
Cardiologie Pédiatrique, 75015 Paris Cedex, France
Phone: +00331 44 49 43 57; Fax: +00331 44 49 5724; Email: younes.boudjemline@nck.aphp.fr

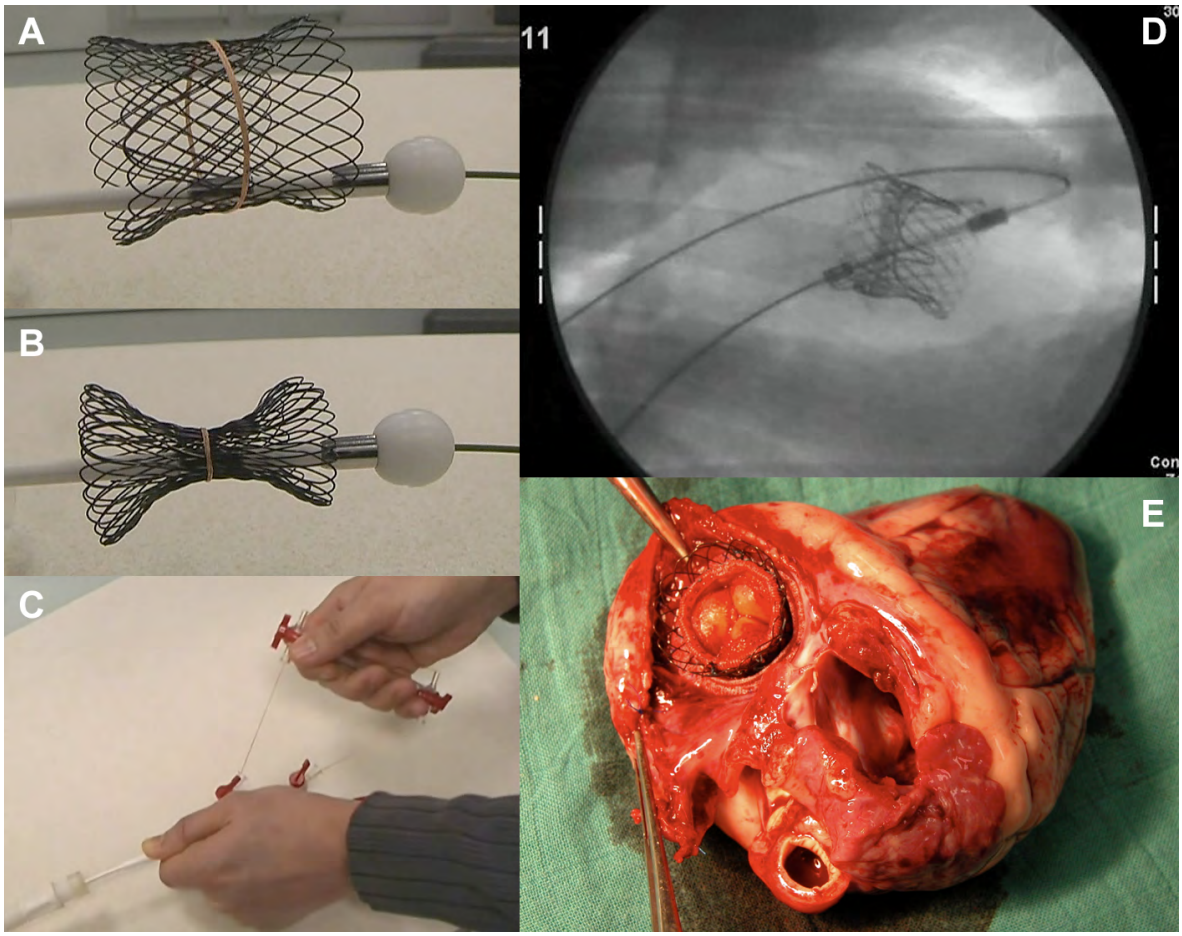


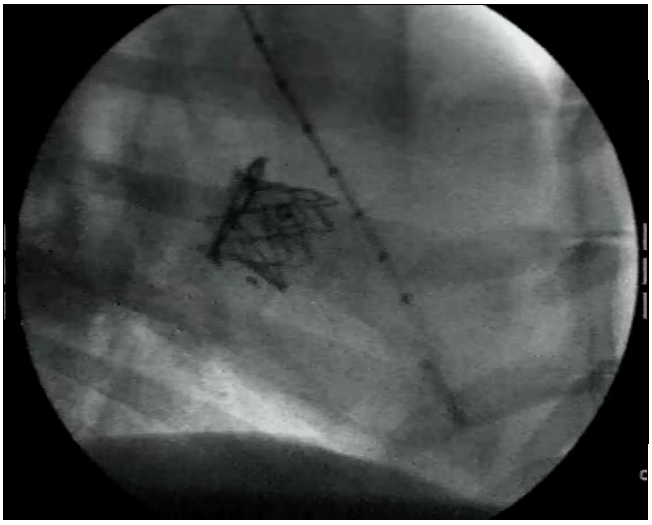
Figure 1. Repositionable valved stent (Zegdi et al. réf 11). A, B and C. Representation of the principle of compression-relaxation of the valved stent. After deployment of the nitinol self-expandable device (A), the stent can be reversibly compressed (B) by exerting traction on the encircling suture through a proximal handle (C). D. Fluoroscopy, positioning of the valved stent within a tricuspid bioprosthetic valve. E. Macroscopic posterior view of the heart showing excellent positioning of the valved stented inside the failed tricuspid bioprosthesis.

Moreover secondary tricuspid valve disease with right ventricular failure is emerging as an Achilles heel for the management of a vast population of patients with severe left sided heart failure, requiring assist devices.

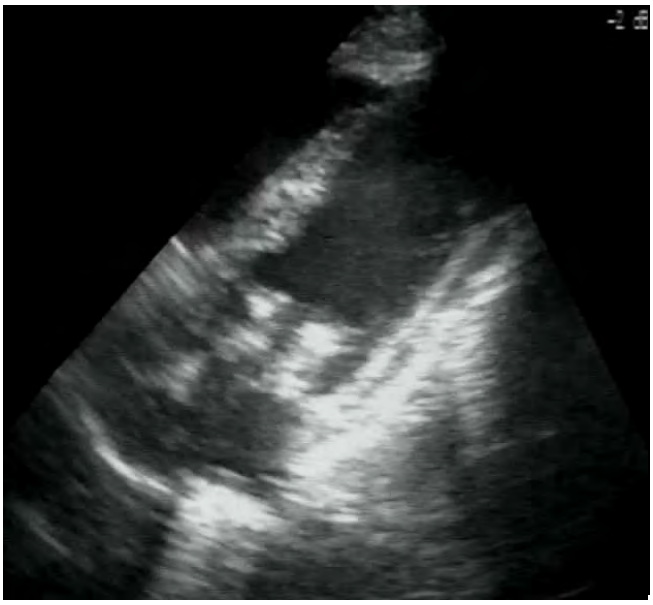
Over the last decade, transcatheter aortic and pulmonary valve implantation has revolutionized the therapeutic options for patients at high risk for conventional surgery [5-8]. There has been growing interest in the field of interventional cardiology to percutaneously treat dysfunctional tricuspid valves. Although the data is less robust compared with transcatheter pulmonary or aortic valve replacement, several experimental and clinically useful interventions to treat tricuspid valve dysfunction in various anatomical settings such as native tricuspid valves, annuloplasty rings or bioprosthesis have been described. In this review, we lay emphasis on different strategies and devices developed so far, which may serve as a useful platform for transcatheter therapy for tricuspid valve failure.

Percutaneous Treatment of Degenerated Tricuspid Bioprosthetic Valves: Valve-in-Valve Technique

Bioprosthetic cardiac valves are usually preferred in young patients due to reduced thromboembol-



Video 1. Angiogram showing the valve in valve concept in mitral position in a sheep. A bioprosthetic valve (Mosaic, Medtronic) has been surgically placed. A Melody valve has been thereafter placed inside the surgical valve used as a landing zone. (Boudjemline et al, Eur Heart J. 2005;26:2013-7)



Video 2. Echographic imaging showing the valve in valve concept in mitral position in a sheep. (Boudjemline et al, Eur Heart J. 2005;26:2013-7.)

ic risk and the need for long-term anticoagulation therapy as required with mechanical prostheses. However all bioprosthetic valves eventually fail over time with progressive age induced degeneration. Repeat sternotomy in such patients carries a high risk of morbidity and mortality. Transcatheter valve-in-valve implantation has emerged as a promising treatment option for degenerated bioprosthetic heart valves in these multi-operated high-risk patients and has been described for failing bioprosthetic valves in all four cardiac locations [9].

Evolution

In an early preclinical study, Boudjemline et al. [10] were the first to evaluate the proof of concept of mitral valve-in-valve treatment in a sheep model. A bovine jugular valve was mounted on a stent and successfully implanted off-pump through a transatrial mini-invasive approach in 6 sheep (Video 1 and Video 2). In a subsequent animal study, Zegdi et al. [11] reported the successful implantation of a repositionable valved stent (porcine aortic valve sutured on a nitinol self expandable stent) in tricuspid bioprosthetic valves. The originality of the delivery system consisted of the possibility of controlling reversibly the deployment of the valved stent as many times as needed before the final release, to allow implantation in appropriate position (Figure 1 and Videos 3 to 7).

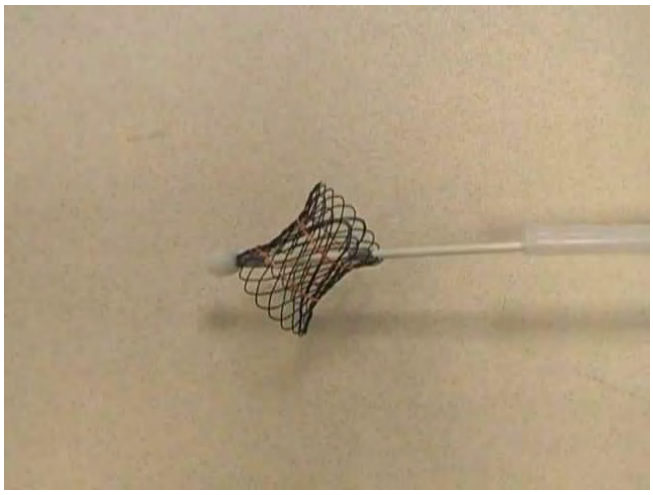
Since then successful percutaneous valve-in-valve implantations in humans have been especially reported for pulmonary and aortic valves [12, 13]. The first human case of transcatheter valve-in-valve implantation in the tricuspid position was described by Van Garsse and colleagues [14]. Since then several anecdotal case reports and small case series using two different valves: the Melody® valve (Medtronic, Minneapolis, Minnesota, USA) and the Edwards SAPIEN™ valve (Edwards Lifesciences, Irvine, California, USA) have been described [15-22]. These procedures were performed in a heterogeneous population, including children and adults with congenital heart disease, patients with prior infective endocarditis, and patients with a history of rheumatic or carcinoid heart disease.

The first multicentric series of percutaneous tricuspid VIV replacement using Melody valve in 15 patients with good results was published in 2011 (age range 8 to 64 years) [16]. The primary indication for the procedure was predominantly stenosis in 10 and regur-

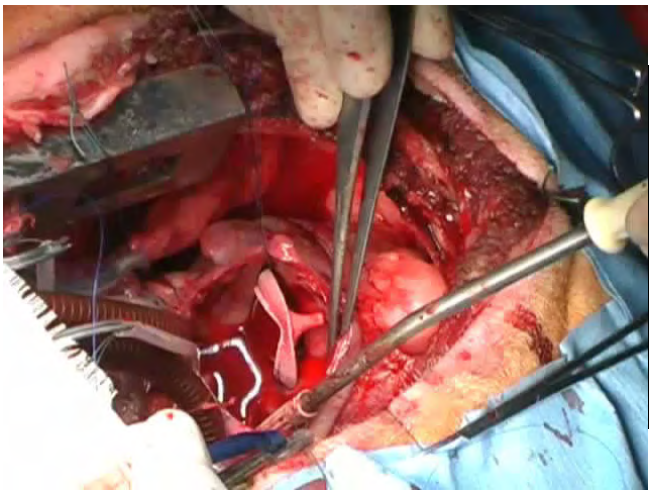
Figure 2. Implantation of a valved stent in large tricuspid annulus. Creation of a platform. The platform is created using the property of 2 different stents used simultaneously with one fitted within the second one: 1/ a bare metal stent with limited expansion (typically short EV3 LD mega) allows a restrictive region for subsequent valve insertion; 2/ a covered stent without limited expansion (typically long covered CP stent) allows anchoring to the large surgically inserted bioprosthesis. **Top left**. EV3LD mega is mounted on a long covered CP stent over a balloon. The balloon is being inflated. **Top right**. in vitro aspect after deflation and retrieval of the balloon catheter. The stent assembly has now the aspect of a Dumbbell stent creating a perfect platfrom for a valved stent. **Below/left**. front view of the stent assembly within a bioprosthetic surgical valve. The extremities of the stent assembly are holding on the frame of the bioprosthetic valve. **Below/right**. axial view of the stent assembly within a bioprosthetic surgical valve. 2 different diameters are shown. The middle part is smaller than the extremities. This middle part will hold the valved stent to be implanted.

gitation in 5. The valve was successfully placed in all patients via the femoral vein in 11 and the internal jugular vein in 4 patients. Pre-dilation or low-pressure balloon sizing was performed in four patients before valve implantation while pre-stenting was not described. Post-implantation dilation using high-pressure balloons was performed in seven patients. The median post-procedure tricuspid gradient was 2 mm Hg and no patient had more than mild regurgitation. After a median follow-up of four months, 14 of 15 patients who underwent the Melody valve implantation are alive and well. Complications included one death in a patient with pre-procedural multi-organ failure, one with third-degree heart block requiring pacemaker implantation, and one case of endocarditis requiring valve removal 2 months after implantation.

Recently, a similar case series reporting percutaneous implantation of the Melody valve within failed mitral (n=10) and tricuspid (n=9) bioprosthetic valves was published [23]. Among tricuspid patients (mean age 42 ± 24 years), mean transvalvular gradient was 10 ± 4.3 mm Hg among and seven patients had moderate or worse tricuspid valve regurgitation. Imaging was performed with intracardiac echocardiography



Video 3. In vitro Video showing a custom-made retrievable stent. (Zegdi et al, JACC. 2006;48:1365-8).



Video 4. Video showing the valve in valve concept in tricuspid position in a sheep. A regurgitant bioprosthetic valve is surgically placed (Zegdi et al, JACC. 2006;48:1365-8).

in seven patients and TEE in three patients. Balloon sizing of the prosthesis was performed in all patients, no prestenting was described. All patients underwent successful implantation of a 22-mm Melody valve with satisfactory results. No periprocedural death, stent fracture or valve embolization was observed. During follow up, two patients had vascular complications (femoral artery pseudo aneurysm and femoral vein phlebitis) and one patient was operated for a Melody valve thrombosis due to heparin-induced thrombocytopenia.

Despite the promising results of the percutaneous tricuspid valve-in-valve implantation, a case series describing early failure of Melody and Sapien valves in the tricuspid position was recently published [24]. Authors describe four procedures in three patients where implantation of percutaneous valves within bioprosthetic tricuspid valves was performed with excellent immediate post procedural results. However, in all four cases evidence of rapid valve failure within 2 weeks following intervention in three of the four cases and later in the fourth case was described. Two patients required surgical explantation and subsequent examination of the prosthesis showed degeneration with thickening and contraction of the leaflets. Routine blood tests including immunological and inflammatory markers were normal without evidence of endocarditis. Authors suggested that individual factors and/or hemodynamic conditions associated with dilated poorly contractile right atria leading to limited valve leaflet mobility may explain this rapid deterioration; however these observations remain partially unexplained. We observed similar findings in failing Fontan patients receiving a Melody in the Fontan circulation [25].

The primary indication for tricuspid valve-in-valve implantation remains a key point of this procedure. If the predominant lesion of the bioprosthetic valve is stenosis (with or without regurgitation), the procedure may be then performed using standard technique. The size of the original surgical valve is not important. The only burning question in that situation is to know if the stenosis could be opened enough to reduce the transvalvular gradient. Recently, a Spanish team reported the successful implantation of a 29-mm Edwards-SAPIEN XT prosthesis within a 31-mm stenotic tricuspid bioprosthesis through a transfemoral approach [26]. The procedure was carried out without predilatation or balloon sizing of the bioprosthesis. Prestenting is rarely performed during tricuspid valve in valve implantation. This is in contrast with percutaneous pulmonary valve implantation where pre-stenting is most of the time necessary to create a stable landing zone and to prevent stent fracture in the right ventricular outflow tract. However, as the tricuspid valve is in general far away from right ventricular muscular bands as well as from the sternum, valved stent fracture is not a major issue in the

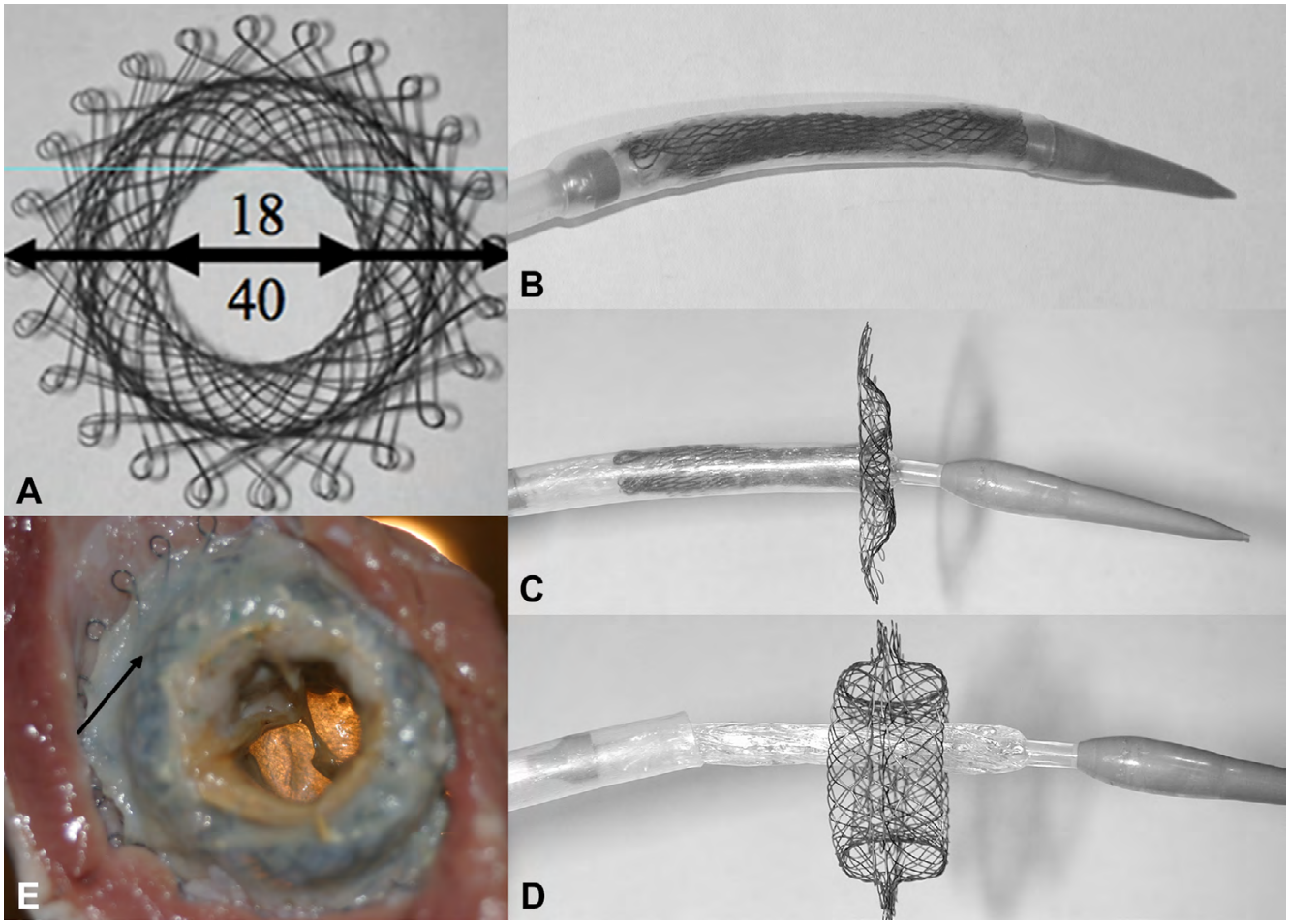
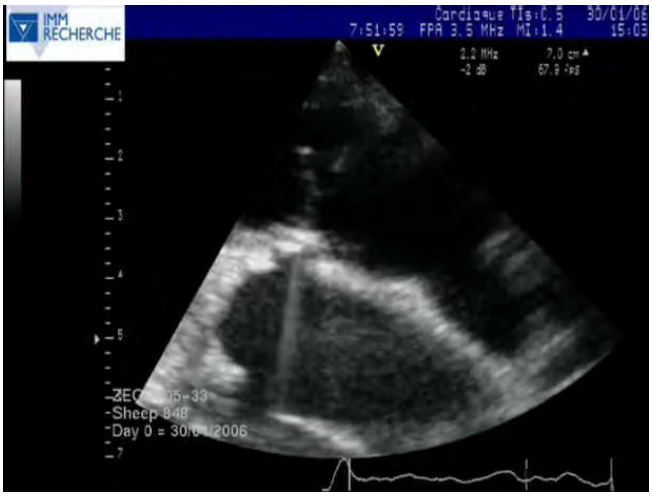


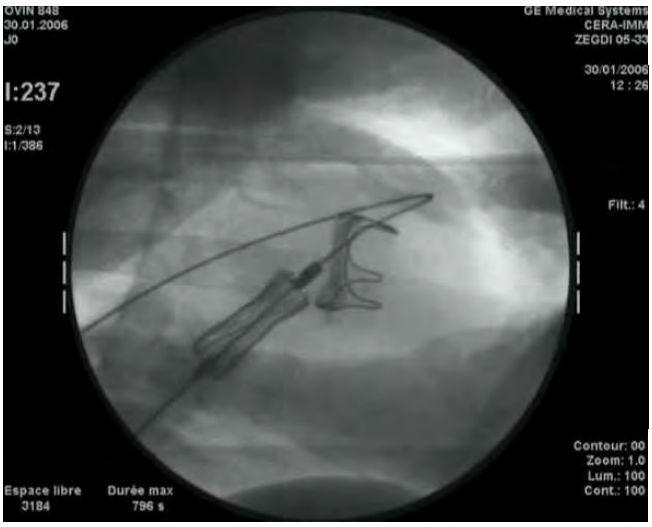
Figure 3. Self expanding valved stent for percutaneous tricuspid valve replacement (Boudjemline et al. réf 36). A. The device consists in a nitinol self-expandable stent formed of two disks (40-mm diameter) separated by a tubular part (15-mm length, 18-mm diameter) containing a bovine jugular vein valved. to guarantee the sealing of the device. B, C and D. Deployment of the device on bench testing. The device is loaded into a « homemade » delivery system (B), the right ventricular disk is deployed in the by pulling on the external sheath while maintaining the dilator in position; this disk is subsequently applied to the tricuspid annulus by pulling on the external sheath and dilator (C), then the atrial disk is delivered similarly, making the two disks sandwiching the tricuspid annulus (D). E. Macroscopic view of the valved stent from the right ventricular side. * bovine jugular vein segment sutured into the tubular part of the device; avoid paravalvular leakage, a polytetrafluoroethylene membrane is sutured outside the ventricular disk (**black arrow**).

tricuspid position. However it is important to remember that widest excursion of annular plane occurs at the tricuspid location. The structural framework present in most of the tricuspid bioprosthetic valves may offer protection from compressive and rotational forces and thus from stent fractures.

If the tricuspid valve failure leads exclusively to regurgitation, then the dimensions of the valve (especially the inner diameter) must be precisely known and evaluated by the operator during the procedure using a balloon sizing. Others and we have reported specific techniques to make these patients amenable to transcatheter valve insertion. Briefly, presenting is required in that situation. The first step is to create a restrictive landing zone to allow for a safe deployment of a Melody valve. The platform is created using the property of 2 different stents used simultaneously with one fitted within the second one: 1.) A bare metal stent with limited expansion (typically short EV3 LD mega) allows a restrictive region for subsequent valve insertion; 2.) A covered stent without limited expansion (typically long covered CP stent) allows an-



Video 5. Echographic Video showing regurgitation of the implanted bioprosthetic surgical valve (Zegdi et al, JACC. 2006;48:1365-8).



Video 6. Angiogram showing the implantation of the retrievable valve stent. The stent is slowly opened inside the bioprosthesis than closed and repositioned and finally released and left in position. (Zegdi et al, JACC. 2006;48:1365-8).

choring to the large surgically inserted bioprosthesis (Figure 2). Type and diameter of balloons used to deliver the stents largely depends on the inner diameter of the surgical valve. Following the creation of the landing zone, transcatheter valves insertion could be performed using conventional technique. Using this technique, we treated patients with regurgitant surgical valve up to 33-mm in diameter. In our experience, the creation of free tricuspid regurgitation following prestenting is well tolerated and no rush is needed to implant the valve.

Excluding the transatrial hybrid procedures with direct right atrial puncture [27], completely percutaneous tricuspid valve-in-valve implantations were performed using either a femoral or an internal jugular venous approach.

In cases where the tricuspid valve prosthesis is directed toward the superior vena cava, the transjugular approach should be preferred to obtain a better angle when positioning the valve, especially with the Edwards SAPIEN valve that is a larger and more rigid device. Nevertheless, despite these considerations, the decision about the approach has to be taken separately for each patient regarding patient's valve anatomy.

Rapid pacing is generally performed during Edwards SAPIEN implantation to allow accurate positioning of this relatively short valve. It is usually not required with the longer Melody valve. In our experience, rapid pacing is not necessary and femoral veins provide excellent access to the tricuspid. During positioning on the valved stent, the assembly can easily be aligned (horizontalized) to the tricuspid annulus by maintaining forward pressure on the stiff wire thus mimicking jugular pathway.

The Edwards SAPIEN® valve has the advantage of being available in larger sizes with relatively shorter stent lengths (the 26-mm valve measures 16-mm in length) when compared with the MELODY® Valve (the stent measures 23 mm in length when dilated to 22 mm). Moreover, its shorter stent may not protrude significantly into the adjacent cardiac chambers. On the other hand, correct positioning of this shorter valve may be more difficult, although rapid pacing may be used to allow safer implantation, and manipulation of the Melody delivery system is easier in complex anatomies with important angulation of the tricuspid annulus in relation to the superior vena cava and inferior vena cava.

Despite experience is accumulating worldwide with these two devices, there is currently lack of data to conclude that one of the devices is superior to the other in this off-label use.

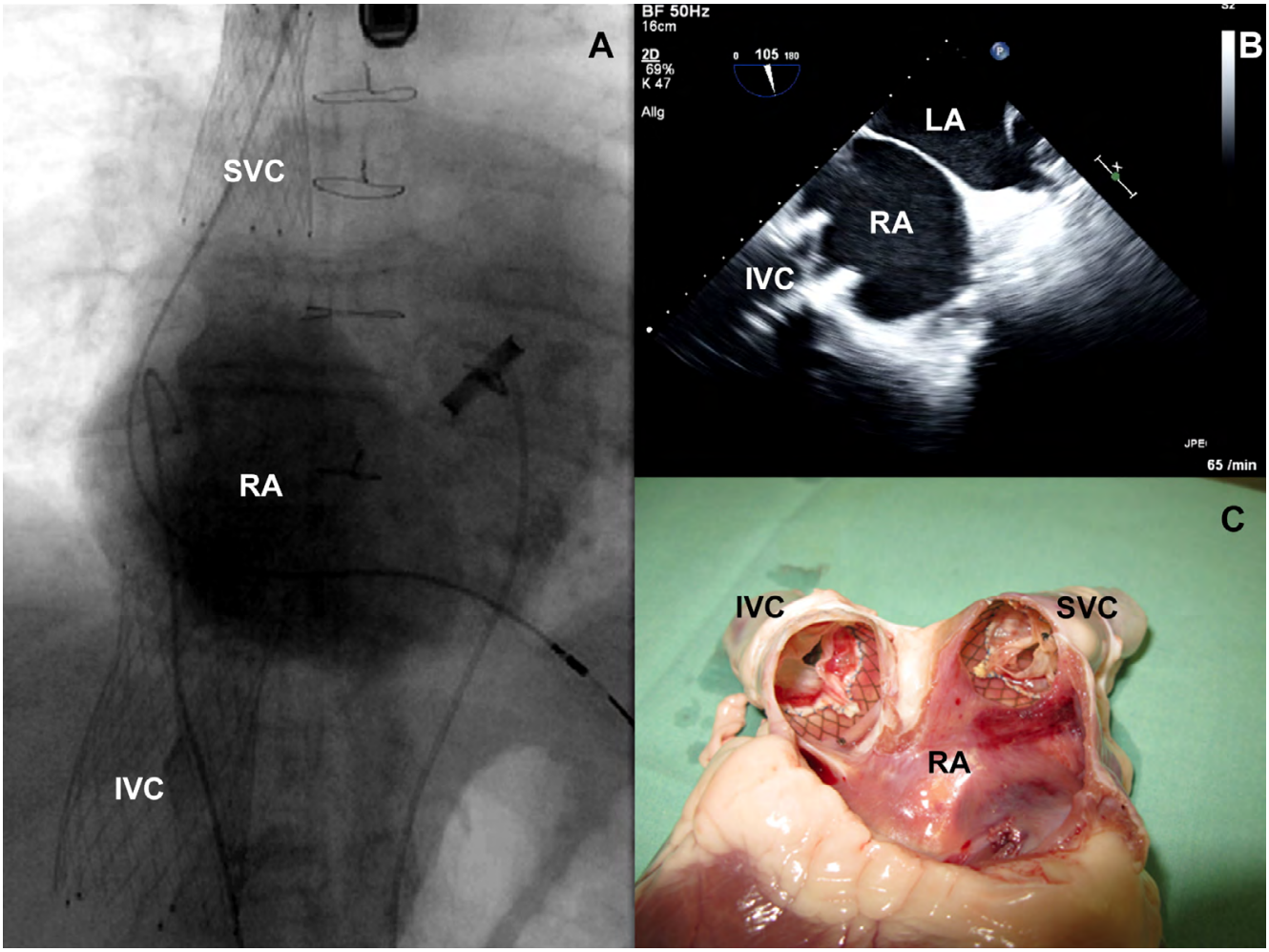


Figure 4. Transcatheter bicaval valve implantation. A. Fluoroscopy - Right atrial angiography: The inferior vena cava (IVC) valve is designed with the upper segment protruding into the right atrium (RA), the superior vena cava (SVC) device is funnel shaped to facilitate anchoring at the cavoatrial junction. Contrast is retained at the level of the valved stents. RA: right atrium; SVC: superior vena cava; IVC: inferior vena cava. B. Transoesophageal echocardiography: long-axis view of the IVC device after deployment. C. Post mortem specimen macroscopic view: the valved stents are securely anchored with the stent struts covered by fibrous tissue, fixing the devices.

Valve-in-Ring Therapy

Based on the principle of valve in valve, a completely rigid annuloplasty ring may also offer adequate anchoring support and landing zone. The first experiments were performed for the mitral valve. In an animal study, Kempfert et al. [28] showed that an off-pump transatrial transcatheter valve in ring implantation using 23-mm Edwards Sapien® valve in a 26-mm Physio® mitral ring was feasible with good heamodynamic results. One main concern was the oval shape of the Physio® ring versus the circular shape of the Sapien® valve. However, in bench testing, authors demonstrated the adaptability of the Physio® ring into a circular form at balloon insufflations. Subsequently, several papers reported mitral valve-in-ring implantation through a left ventricular trans apical approach in compassionate-use procedures for patients with high surgical risk [29, 30]. Indeed, the first in man implantation of a transcatheter valve in a mitral annuloplasty ring was performed in a 72-year-old man with ischemic heart failure (ejection fraction 35%) and severe mitral regurgitation. A 26-mm Sapien-Edwards aortic valve was successfully

implanted during rapid right ventricular pacing within the 28-mm Physio® mitral annuloplasty ring with equal proportions within the left ventricle and the left atrium, using fluoroscopy and transesophageal echocardiography guidance.

The first transcatheter tricuspid valve-in-ring implantation was described by Mazzitelli et al. [31]. They reported the case a of a combined off-pump ante grade trans-atrial implantation of a 26-mm Sapien® valve within mitral and tricuspid annuloplasty rings (Physio® 28-mm and 26-mm respectively) through an anterolateral minithoracotomy in a 61-year-old woman. The direct trans-atrial approach was considered to be ideal to treat both valves at the same time. The patient was extubated after 24 hours and discharged on the ninth postoperative day with satisfactory valvular function (minor paravalvular tricuspid regurgitation). Shuto et al. [32, 33] described the first completely percutaneous valve-in-ring implantation using the Melody® device in a mitral ring. Via standard vascular access and transseptal techniques, they successfully deployed the Melody® valve into the mitral position from the venous circulation in five sheep, without complication. Although there was a conformational change noted in the implanted Melody® valves from "round" to "oval", there was no perivalvular leakage and only trivial to mild central regurgitation was observed. These results were confirmed in another animal study using 4 distinct types of annuloplasty ring.

The complete percutaneous approach was recently used to perform a tricuspid VIR implantation in a 64-year-old female who underwent placement of a mitral valve homograft with a #34 Physio® ring (Edwards Lifesciences, Irvine CA, USA) in the tricuspid position in whom echocardiography revealed severe tricuspid stenosis with a mean gradient of 16 mm Hg with mild tricuspid regurgitation [34]. A transcatheter 26 mm Edwards SAPIEN® valve was placed in the tricuspid position through a femoral vein approach, resulting in near normalisation of tricuspid valve gradient. Prosthesis size was estimated by computed tomography, intracardiac echocardiography, and finally by balloon sizing during the procedure. Furthermore, a pre-stenting technique was used to ensure appropriate coverage of the valvular orifice and make valve positioning easier although the presence of a complete rigid Physio® ring may theoretically facilitate prosthesis apposition, and reduce the risk of device embolization or paravalvular leak. A similar case was recently reported using the same approach and the same transcatheter 26 mm Edwards SAPIEN® prosthesis [35].

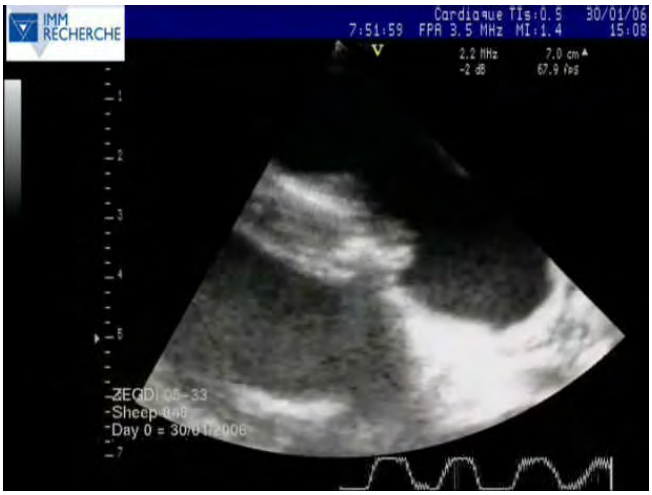
For transcatheter VIR implantations, the dimensions of the tricuspid valve annulus are better approximated by the commercially available SAPIEN® valves (up to 26 mm in diameter) than the Melody valves (maximum expandable diameter 22 mm). However, because of the conception of the Edwards valve (made of manufactured three equal pericardial leaflets), the device should be open as close as possible to its nominal diameter and as round as possible to allow enough flow and closing volume and thus avoid functional stenosis or leak. Melody valve is more versatile and can be open to various diameters and configuration without impinging the valvar function. However expansion of Melody valves to diameters larger or equal to 25-mm has been associated in with valvular incompetence and device embolization when implanted in mitral rings [33]. Nevertheless, the valve-in-ring approach for atrioventricular valves may extend the functional life of the surgical substrates in a manner analogous to Melody® and Sapien® valve treatment for dysfunctional surgical conduits in the pulmonary position.

Percutaneous Treatment of Native Tricuspid Valves

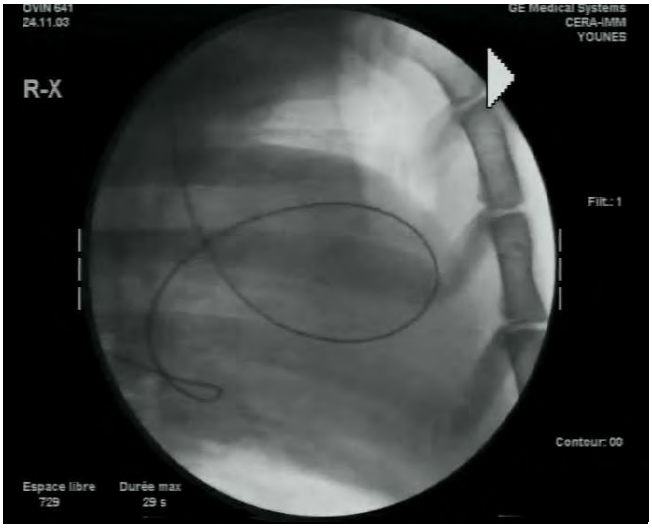
In native tricuspid valves, implanting a trancatheter prosthesis remains challenging because of the absence of a stiff region to anchor the valve, and the lack of fluoroscopic markers and the difficulties to precisely assess annulus measurements (due to the absence of tricuspid surgical markers such as ring or bioprosthesis). However, strategies have been developed to perform not only percutaneous tricuspid valve replacement whether in orthotopic or heterotopic position, but also a conservative transcatheter tricuspid valvuloplasty.

Transcatheter Orthotopic TV Replacement

In 2005, Boudjemline et al. [36] designed a new device intended to be implanted percutaneously in native tricuspid valves and published the first study



Video 7. Echographic Video after transcatheter valve implant showing correction of the regurgitation of the implanted bioprosthetic surgical valve (Zegdi et al, JACC. 2006;48:1365-8).



Video 8. Video showing the delivery of a valved stent in tricuspid native valve. The delivery system is advanced over a wire in the right ventricle. The RV disk is slowly opened in the apex of the RV and pullback in the tricuspid annulus. The device is then completely opened and delivered (Boudjemline, JACC. 2005;46:360-5).

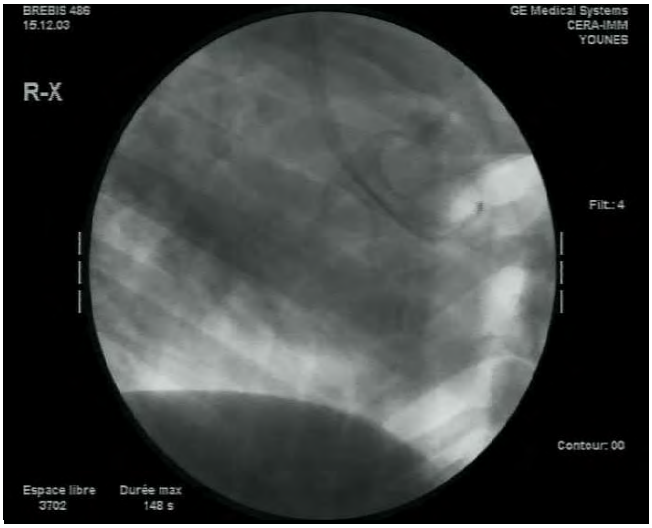
with percutaneous tricuspid valve implantation in 8 healthy ewes. This prosthesis consisted in a nitinol self-expandable stent formed of two disks (40-mm diameter) separated by a tubular part (15-mm length, 18-mm diameter) containing a bovine jugular vein valved segment. A polytetrafluoroethylene membrane was sutured outside of the ventricular disk to guarantee the sealing of the device. The diameter of the two disks was chosen to be slightly larger than the diameter of the tricuspid annulus to allow for anchoring (Figure 3 and Videos 8 to 11). Mechanical fixation was ensured by trapping the annulus between the two disks. In one animal, the device was trapped in tricuspid chordae, leading to its incomplete opening. A significant paravalvular leak was observed in one animal, due to a torn the PTFE membrane beside a weld fracture.

Other authors described a similar valved stent; a porcine pericardial valve mounted on a double-edge nitinol stent with satisfactory results in a chronic sheep model despite 2 device embolization upon 10 procedures [37].

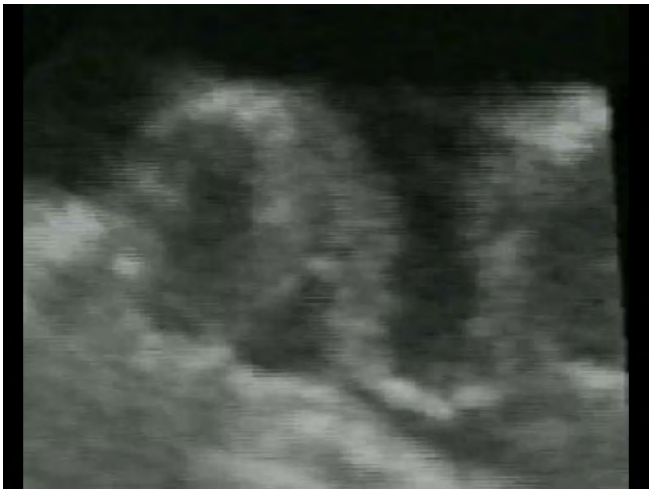
Moreover, Iino et al. describe another device, a bovine pericardial valve mounted on a self-expandable nitinol stent with a super-absorbent polymer placed beneath the right atrial element for minimizing paravalvular leak. This device was successfully implanted in pigs through a mini-thoracotomy using trans-ventricular approach with a reduction of paravalvular leakage [38].

Although these papers opened perspectives into transcatheter orthotopic native tricuspid valve replacement, no further experimental developments or human implantation were published with these devices.

Recently, Kefer et al. [39] published the first human transcatheter implantation in a "native" tricuspid valve using a 26-mm Sapien® valve after failed multiple surgical repairs in a 47–year-old female. Tricuspid annulus size was assessed by magnetic resonance imaging, three-dimensional transesophageal echocardiography and especially low-pressure balloon sizing during the procedure. Prestenting was achieved by covered stent to create a rigid landing zone and to avoid paravalvular leak. As it is the case for VIR implantations, the dimensions of the tricuspid valve annulus were better approximated by the SAPIEN® valves than the Melody valves (maximum expandable diameter 22 mm). However, after first valve implantation, severe paravalvular regurgitation was observed, related to a more apical position of the Sapien® valve.



Video 9. Angiogram after release showing the competence of the newly implanted tricuspid valve. (Boudjemline, JACC. 2005;46:360-5).



Video 10. Echographic Video in long axis view after transcatheter valve implant showing good function of the leaflets. (Boudjemline, JACC. 2005;46:360-5).

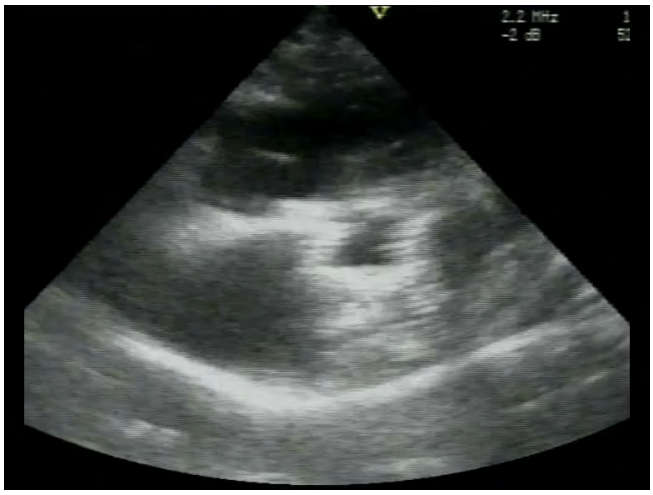
A second Sapien® valve 26 mm was then implanted just proximal to the first one solving the tricuspid leak. This is likely due to that Sapien® valve has a covered length of only 10 mm, significantly shorter than the Melody prosthesis (up to 23 mm).

These issues may be resolved in the future with the development of specific devices with larger diameters and longer covered lengths, more appropriate for transcatheter valve implantation in the tricuspid position.

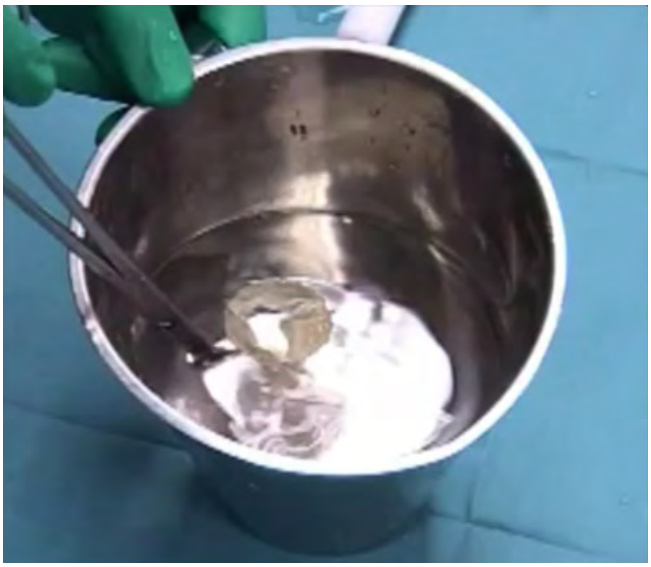
Heterotopic TV Replacement or Caval Valve Implantation (CAVI)

Lauten et al. [40, 41] evaluated in an animal study a percutaneous approach to treat native TV failure using heterotopic valve implantation in the central venous position. Using a right internal jugular vein approach authors implanted two self-expanding nitinol stents containing a porcine pulmonary valve in the superior and inferior caval veins of 13 sheep presenting severe tricuspid regurgitation. All but one valve was correctly deployed as intended (one device embolization in the right atrium) leading to a significant decrease of central venous pressure and cardiac output. This interesting concept with lack of intracardiac foreign material preventing venous flow reversals and possibly hepatic complications fails to keep the right atrial and ventricular dilatation under check and may lead to potential deleterious hemodynamic and rhythmic effects.

Subsequently, the first-in-man application of this concept was performed as a compassionate treatment in a 79-year-old female patient with severe functional tricuspid regurgitation. Through the femoral vein, a custom-made self-expanding valved stent was implanted into the inferior vena cava, anchored at the cavoatrial junction. After deployment, excellent valve function was observed without paravalvular leakage resulting in a marked reduction in caval pressure. The patient experienced improved physical capacity and a partial reduction of ascites. The patient died 3 months after the procedure from intracranial haemorrhage (Figure 4). Autopsy confirmed an unchanged position and excellent function of the valve in the IVC without evidence of degeneration, thrombus formation, or other causes of dysfunction [42, 43]. The same team published recently the case of a similar case of an 83 years-old female who underwent implantation of 2 custom-made self-expanding valved stents into the superior and inferior vena cava without complication. The procedure (CAVI) resulted in an immediate and sustained hemodynamic improvement. Moreover, the patient showed a substantial clinical



Video 11. Echographic Video in transverse axis view after transcatheter valve implant showing the position of the valve stent in regards with the original tricuspid annulus. (Boudjemline, JACC. 2005;46:360-5).



Video 12. Video showing preparation, implantation and angiogram of two self-expandable valved stents in a CAVI procedure. (Lauten, Circ Cardiovasc Interv. 2014;7:268-72).

improvement of heart failure symptoms, normalization of liver function, and improvement of physical capacity after 12 months of follow-up [44]. To avoid right heart failure by increased preload, it seems that preserved right ventricular function is mandatory for the success of this procedure. Furthermore, because these valves are implanted in the low-pressure system, lifelong anticoagulation is required.

Laule et al. [45] reported a case series of three patients who had percutaneous caval valve implantation (CAVI) for severe tricuspid regurgitation (Videos 12 and 13). Procedures were performed using Edwards Sapien XT (29 mm) valved stent following superior and inferior vena cava prestenting. No complication occurred. After 1 month, valve function remained excellent without regurgitation or leakage and all patients improved by at least 1 NYHA class. In patients with enlarged inferior vena cava, a mini-invasive surgical caval banding can be performed to allow a safe valved stent implantation in appropriate landing zone [46].

Despite encouraging first results, further studies are warranted to evaluate the benefit of the heterotopic transcatheter tricuspid valve implantation procedure during long-term follow-up in larger cohorts. Furthermore, as this concept is targeted for high-risk patients in end-stage heart disease, the costs involved for this type of procedure should be taken into account and carefully weighed against the clinical benefit.

Transcatheter Tricuspid Valvuloplasty

Percutaneous procedures may be an attractive alternative to surgery for patients who are high-risk surgical candidates. In patients with native failed tricuspid valve, some of the concepts that have been developed for the percutaneous treatment of mitral regurgitation may be adapted to percutaneous repair of the tricuspid valve (percutaneous annuloplasty, edge-to-edge repair) [47, 48]. The Millipede system (Millipede, LLC, Ann Arbor, Michigan, USA) consists in placing a new tricuspid annular ring with a unique attachment system through a minimally invasive approach - surgical or percutaneous. This repositionable and retrievable device may restore the native tricuspid annular shape and diameter and thus treat functional tricuspid regurgitation. It is currently under preclinical development. Furthermore, the use of the Mitralign Percutaneous Annuloplasty System (Mitralign Inc., Boston, Massachusetts, USA) or the QuantumCor System (QuantumCor, Inc., Bothell, Washington, USA) may in a near

future be extended to tricuspid valve as well.

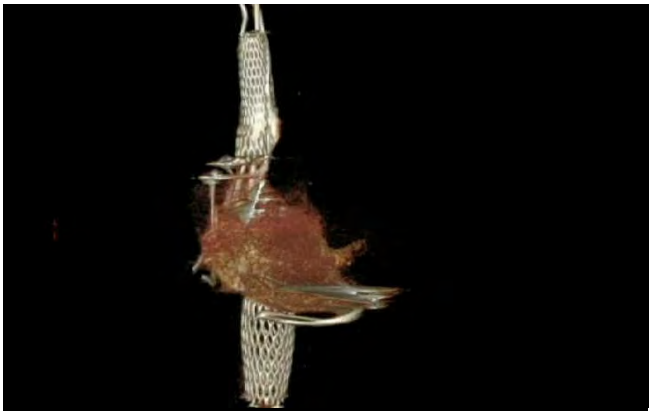
Challenges

The large diameter, dynamic and highly variable nature of tricuspid annulus with the relatively poor fibro skeletal support is an important limitation [49, 50]. With limited annular contractile property in contrast to the mitral annulus, it is important to assess load independent indices of right ventricular contractility especially of the sub-annular fibers. The minimum required RV contractility to ensure a good closing volume, the minimum required cardiac output and possibly RA contractility to ensure adequate opening of the valve without clogging and maintain long-term durability is yet to be defined. The need for a low profile self-expanding valve that may reach an outer diameter of 70 mm as known in patients with clinically significant and functional tricuspid regurgitation is another challenge. An ideal length of the covered stent is also important to prevent inadvertent encroachment of the tricuspid valve apparatus and its neighborhood including right ventricular outflow tract. Other challenges include creating a stable landing zone in native valves, preventing stent fracture and paravalvular leaks.

The exponential increase in right and left sided valvular interventions may possibly unfold the natural and unnatural history of primary and secondary tricuspid annular dilation and help our understanding for the creation of a stable, self expanding percutaneous valve with minimal paravalvar leak. Demonstrating a safe and economically viable strategy with good long-term outcomes may also be required as the devices evolve.

Conclusion

Over the past decade, there has been a paradigm shift in the interventional armamentarium for the management of valvular disease with the introduction of newer, safer and low profile percutaneous valves. While the indications for percutaneous valve implantations at the aortic and pulmonary position are expanding, there has been very limited growth on the front of percutaneous treatment of tricuspid valve diseases. In selected patients with high surgical risk, initial results of percutaneous tricuspid valve treatment is encouraging for various valvular substrates such as native valves, annuloplasty rings and bioprosthesis. Evolving strategies with newer percutaneous valves for eligible patients with tricuspid valve failure is likely to improve outcomes if done in a timely manner before the onset of irreversible right ventricular pump failure and may even reduce the need for a right ventricular assist device.



Video 13. 3D CT performed in a patient following a CAVI procedure. (Lauten, Circ Cardiovasc Interv. 2014;7:268-72).

Conflict of Interest

Younes Boudjemline is a Proctor for Medtronic Inc.

Comment on this Article or Ask a Question

References

1. Brown ML, Dearani JA, Danielson GK, Cetta F, Connolly HM, Warnes CA, et al. The outcomes of operations for 539 patients with Ebstein anomaly. J Thorac Cardiovasc Surg. 2008;135:1120–1136. DOI: 10.1016/j.jtcvs.2008.02.034
2. Carrier M, Hebert Y, Pellerin M, Bouchard D, Perrault LP, Cartier R, et al. Tricuspid valve replacement: An analysis of 25 years of experience at a single center. Ann Thorac Surg. 2003;75:47–50. PMID: 12537191
3. Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J. 2012;33:2451-2496. DOI: 10.1093/eurheartj/ehs109
4. Filsoufi F, Anyanwu AC, Salzberg SP, Frankel T, Cohn LH, Adams DH. Long-term outcomes of tricuspid valve replacement in the current era. Ann Thorac Surg. 2005;80:845–850. PMID: 16122441
5. Webb JG. Percutaneous aortic valve replacement will be a common treatment

for aortic valve disease. JACC Cardiovasc Interv. 2008;1:122–126. DOI: 10.1016/j.jcin.2007.11.010

6. Zajarias A, Cribier AG. Outcomes and safety of percutaneous aortic valve replacement. J Am Coll Cardiol. 2009;53:1829–1836. DOI: 10.1016/j.jacc.2008.11.059
7. Bonhoeffer P, Boudjemline Y, Saliba Z, Merckx J, Aggoun Y, Bonnet D, et al. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. Lancet. 2000;356:1403–1405. PMID: 11052583
8. McElhinney DB, Hellenbrand WE, Zahn EM, Jones TK, Cheatham JP, Lock JE, et al. Short- and medium-term outcomes after transcatheter pulmonary valve placement in the expanded multicenter US melody valve trial. Circulation. 2010;122:507–516. DOI: 10.1161/CIRCULATIONAHA.109.921692
9. Webb JG, Wood DA, Ye J, Gurvitch R, Gurvitch R, Masson JB, Rodés-Cabau J, et al. Transcatheter valve-in-valve implantation for failed bioprosthetic heart valves. Circulation. 2010;121:1848–1857. DOI: 10.1161/CIRCULATIONAHA.109.924613
10. Boudjemline Y, Pineau E, Borenstein N, Behr L, Bonhoeffer P. New insights in minimally invasive valve replacement: description of a cooperative approach for the off-pump replacement of mitral valves. Eur Heart J. 2005;26:2013–2017. PMID: 15872031
11. Zegdi R, Khabbaz Z, Borenstein N, Fabiani JN. A repositionable valved stent for endovascular treatment of deteriorated bioprostheses. J Am Coll Cardiol. 2006;48:1365–1368. PMID: 17010796
12. Gillespi MJ, Rome JJ, Levi DS, Williams RJ, Rhodes JF, Cheatham JP, et al. Melody valve implant within failed bioprosthetic valves in the pulmonary position a multicenter experience. Circ Cardiovasc Interv. 2012;5:862-870. DOI: 10.1161/CIRCINTERVENTIONS.112.972216
13. Walther T, Falk V, Dewey T, Kempfert J, Emrich F, Pfannmüller B, et al. Valve-in-a-valve concept for transcatheter minimally invasive repeat xenograft implantation. J Am Coll Cardiol. 2007;50:56–60. PMID: 17601546
14. Van Garsse LA, Ter Bekke RM, van Ommen VG. Percutaneous transcatheter valve-in-valve implantation in stenosed tricuspid valve bioprosthesis. Circulation. 2011;123:e219-221. DOI: 10.1161/CIRCULATIONAHA.110.972836
15. Riede FT, Dahnert I. Implantation of a Melody(R) valve in triscuspid position. Catheter Cardiovasc Interv. 2012;80:474–476. DOI: 10.1002/ccd.23404
16. Roberts PA, Boudjemline Y, Cheatham JP, Eicken A, Ewert P, McElhinney DB, et al. Percutaneous tricuspid valve replacement in congenital and acquired heart disease. J Am Coll Cardiol. 2011;58:117–122. DOI: 10.1016/j.jacc.2011.01.044
17. Gewillig M, Dubois C. Percutaneous re-revalvulation of the tricuspid valve. Catheter Cardiovasc Interv. 2011;77:692–695. DOI: 10.1002/ccd.22814
18. Eicken A, Fratz S, Hager A, Vogt M, Balling G, Hess J. Transcutaneous Melody valve implantation in "tricuspid position" after a Fontan Björk (RA–RV homograft) operation results in biventricular circulation. Int J Cardiol. 2010;142:e45–47. DOI: 10.1016/j.ijcard.2008.11.185
19. Tanous D, Nadeem SN, Mason X, Colman JM, Benson LN, Horlick EM. Creation of a functional tricuspid valve: Novel use of percutaneously implanted valve in right atrial to right ventricular conduit in a patient with tricuspid atresia. Int J Cardiol. 2010;144:e8–10. DOI: 10.1016/j.ijcard.2008.12.034
20. Roberts P, Spina R, Vallely M, Wilson M, Bailey B, Celermajer DS, et al. Percutaneous tricuspid valve replacement for a stenosed bioprosthesis. Circ Cardiovasc Interv. 2010;3:e14–15. DOI: 10.1161/CIRCINTERVENTIONS.110.957555
21. Cerillo AG, Berti S, Glauber M. Transjugular tricuspid valve-in-valve implantation: A safe and effective approach. Ann Thorac Surg. 2011;92:777–778. DOI: 10.1016/j.athoracsur.2010.12.015
22. Hon JKF, Cheung A, Ye J, Carere RG, Munt B, Josan K, et al. Transatrial transcatheter tricuspid valve-in-valve implantation of balloon expandable bioprosthesis. Ann Thorac Surg. 2010;90:1696–1697. DOI: 10.1016/j.athoracsur.2010.04.101
23. Cullen MW, Cabalka AK, Alli O, Pislaru SV, Sorajja P, Nkomo VT, et al. Transvenous, antegrade melody valve-in-valve implantation for bioprosthetic mitral and tricuspid valve dysfunction: A case series in children and adults. J Am Coll Cardiol Interv. 2013;6:598–605. DOI: 10.1016/j.jcin.2013.02.010
24. Bentham J, Qureshi S, Eicken A, Gibbs J, Ballard G, Thomson J, et al. Early percutaneous valve failure within bioprosthetic tricuspid tissue valve replacements. Cathet Cardiovasc Interv. 2013;82:428–435. DOI: 10.1002/ccd.24622
25. McElhinney DB, Cheatham JP, Jones TK, Lock JE, Vincent JA, Zahn EM. Stent fracture, valve failure, and right ventricular outflow tract reintervention after transcatheter pulmonary valve implantation: Patient-related and procedural risk factors in the US Melody valve trial. Circ Cardiovasc Interv. 2011;4(6):602–614. DOI: 10.1161/CIRCINTERVENTIONS.111.965616
26. Sanchez-Recalde A, Moreno R, Gonzalez A, Domínguez F, Leyra F, López-Sendón JL. Direct Percutaneous implantation of an Edwards-SAPIEN valve in tricuspid position in a degenerated bioprosthesis in a patient with Ebstein anomaly. Rev Esp Cardiol. 2014;67(9):769–780. DOI: 10.1016/j.rec.2014.03.013
27. Webb JG, Wood DA, Ye J, Gurvitch R, Masson JB, Rodés-Cabau J, et al. Transcatheter valve-in-valve implantation for failed bioprosthetic heart valves. Circulation. 2010;121:1848–1857. DOI: 10.1161/CIRCULATIONAHA.109.924613
28. Kempfert J, Blumenstein J, Chu MW, Pritzwald-Stegmann P, Kobilke T, Falk V, et al. Minimally invasive off-pump valve-in-a-ring implantation: The atrial transcatheter approach for re-operative mitral valve replacement after failed repair. Eur J Cardiothorac Surg. 2009;35:965–969. DOI: 10.1016/j.ejcts.2009.02.018
29. de Weger A, Ewe SH, Delgado V, Bax JJ. First-in-man implantation of a transcatheter aortic valve in a mitral annuloplasty ring: novel treatment modality for failed mitral valve repair. Eur J Cardiothorac Surg. 2011;39(6):1054-1056. DOI: 10.1016/j.ejcts.2010.09.021
30. Casselman F, Martens S, De Bruyne B, Degrieck I. Reducing operative mortality in valvular reoperations: the "valve in ring" procedure. J Thorac Cardiovasc Surg. 2011;141(5):1317-1318. DOI: 10.1016/j.jtcvs.2010.07.079
31. Mazzitelli D, Bleiziffer S, Noebauer C. Transatrial antegrade approach for double mitral and tricuspid "valve-in-ring" implantation. Ann Thorac Surg. 2013;95(1):e25-27. DOI: 10.1016/j.athoracsur.2012.09.092
32. Shuto T, Kondo N, Dori Y, Koomalsingh KJ, Glatz AC, Rome JJ, et al. Percutaneous transvenous Melody valve-in-ring procedure for mitral valve replacement. J Am Coll Cardiol. 2011;58(24):2475-2480. DOI: 10.1016/j.jacc.2011.09.021
33. Kondo N, Shuto T, McGarvey JR, Koomalsingh KJ, Takebe M, Gorman RC, et al. Melody valve-in-ring procedure for mitral valve replacement: feasibility in four annuloplasty types. Ann Thorac Surg. 2012;93(3):783-788. DOI: 10.1016/j.athoracsur.2011.12.021
34. Lilly SM, Rome J, Anwaruddin S, Shreenivas S, Desai N, Silvestry FE, et al. How should I treat prosthetic tricuspid stenosis in an extreme surgical risk patient? EuroIntervention. 2013 Jul;9(3):407-409. DOI: 10.4244/

EIJV9I3A64

35. Fassa AA, Himbert D, Brochet E, Labbé JP, Vahanian A. Transfemoral valve-in-ring implantation for a failing mitral homograft in the tricuspid position. EuroIntervention. 2014;10(2):269. DOI: 10.4244/EIJV10I2A43
36. Boudjemline Y, Agnoletti G, Bonnet D, Behr L, Borenstein N, Sidi D, et al. Steps toward the percutaneous replacement of atrioventricular valves an experimental study. J Am Coll Cardiol. 2005;46(2):360-365. PMID: 16022968
37. Bai Y, Zong GJ, Wang HR, Jiang HB, Wang H, Wu H, et al. An integrated pericardial valved stent special for percutaneous tricuspid implantation: an animal feasibility study. J Surg Res. 2010;160(2):215-221. DOI: 10.1016/j.jss.2008.10.029
38. Iino K, Lozonschi L, Metzner A, Marczynski-Bühlow M, Renner J, Cremer J, et al. Tricuspid valved stent implantation: novel stent with a self-expandable superabsorbent polymer. Eur J Cardiothorac Surg. 2011;40(2):503-507. DOI: 10.1016/j.ejcts.2010.11.051
39. Kefer J, Sluysmans T, Vanoverschelde JL. Transcatheter Sapien valve implantation in a native tricuspid valve after failed surgical repair. Catheter Cardiovasc Interv. 2014;83(5):841-845. DOI: 10.1002/ccd.25330
40. Lauten A, Figulla HR, Willich C, Laube A, Rademacher W, Schubert H, et al. Percutaneous caval stent valve implantation: investigation of an interventional approach for treatment of tricuspid regurgitation. Eur Heart J. 2010;31:1274–1281. DOI: 10.1093/eurheartj/ehp474
41. Lauten A, Figulla HR, Willich C, Jung C, Rademacher W, Schubert H, et al. Heterotopic valve replacement as an interventional approach to tricuspid regurgitation. J Am Coll Cardiol. 2010;55:499–500. DOI: 10.1016/j.jacc.2009.09.034
42. Lauten A, Ferrari M, Hekmat K, Pfeifer R, Dannberg G, Ragoschke-Schumm A, et al. Heterotopic transcatheter tricuspid valve implantation: first-in-man application of a novel approach to tricuspid regurgitation. Eur Heart J. 2011;32:1207–1213. DOI: 10.1093/eurheartj/ehr028
43. Lauten A, Hamadanchi A, Doenst T, Figulla HR. Caval valve implantation for treatment of tricuspid regurgitation: post-mortem evaluation after mid-term follow-up. Eur Heart J. 2014;35(25):1651. DOI: 10.1093/eurheartj/eht471
44. Lauten A, Doenst T, Hamadanchi A, Franz M, Figulla HR. Percutaneous bicaval valve implantation for transcatheter treatment of tricuspid regurgitation clinical observations and 12-month follow-up. Circ Cardiovasc Interv. 2014;7:268-272. DOI: 10.1161/CIRCINTERVENTIONS.113.001033
45. Laule M, Stangl V, Sanad W, Lembcke A, Baumann G, Stangl K. Percutaneous transfemoral management of severe secondary tricuspid regurgitation with Edwards Sapien XT bioprosthesis first-in-man experience. J Am Coll Cardiol. 2013;61(18):1929–1934. DOI: 10.1016/j.jacc.2013.01.070
46. Duerr GD, Endlich M, Sinning JM, Esmailzadeh B, Werner N, Mellert F, et al. Surgical banding of the inferior vena cava for the facilitation of transcatheter valve implantation in a patient with severe secondary tricuspid regurgitation. Eur Heart J. 2013;Dec 13. DOI: 10.1093/eurheartj/eht521
47. Taramasso M, Vanermen H, Maisano F, Guidotti A, La Canna G, Alfieri O. The growing clinical importance of secondary tricuspid regurgitation. J Am Coll Cardiol. 2012;59:703-710. DOI: 10.1016/j.jacc.2011.09.069
48. Agarwal S, Tuzcu EM, Rodriguez ER, Tan CD, Rodriguez LL, Kapadia SR. Interventional cardiology perspective of functional tricuspid regurgitation. Circ Cardiovasc Interv. 2009;2:565-573. DOI: 10.1161/CIRCINTERVENTIONS.109.878983
49. Cohen SR, Sell JE, McIntosh CL, Clark RE. Tricuspid regurgitation in patients with acquired, chronic, pure mitral regurgitation, II: Nonoperative management, tricuspid valve annuloplasty, and tricuspid valve replacement. J Thorac Cardiovasc Surg. 1987;94:488–497. PMID: 3657251
50. Dreyfus GD, Corbi PJ, Chan KM, Bahrami T. Secondary tricuspid re-gurgitation or dilatation: which should be the criteria for surgical repair? Ann Thorac Surg. 2005;79:127–132. DOI: 10.1016/j.athoracsur.2004.06.057

Cite this article as: Jalal Z, Zegdi R, Lauten A, Mehul P, Boudjemline Y. Transcatheter Therapies for Tricuspid Valve Failure. Structural Heart Disease 2015;1(3):137-151. DOI: http://dx.doi.org/10.12945/j.jshd.2015.008.14