Committed to Advancing Transcatheter Heart Valve Therapy

Edwards SAPIEN XT Transcatheter Heart Valve

Approved for Pulmonic Procedures

The SAPIEN XT valve is approved for pulmonic procedures in pediatric and adult patients with a dysfunctional, non-compliant right ventricular outflow tract (RVOT) conduit.

SAPIEN XT Valve Sizing—Pulmonic

<table>
<thead>
<tr>
<th>Diameter of intended location within the conduit</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 mm</td>
</tr>
<tr>
<td>20-23 mm</td>
</tr>
</tbody>
</table>

Edwards Lifesciences is driving the innovation, collaboration, and education needed to bring transcatheter technology to more patients worldwide.

» Visit Edwards.com/pulmonic for more information

See adjacent page for Important Safety Information.

CAUTION: Federal (United States) law restricts this device to sale by or on the order of a physician.

Edwards, Edwards Lifesciences, the stylized E logo, Edwards SAPIEN, Edwards SAPIEN XT, SAPIEN, and SAPIEN XT are trademarks of Edwards Lifesciences Corporation. All other trademarks are the property of their respective owners.

© 2017 Edwards Lifesciences Corporation. All rights reserved. PP–US–1832 v1.0

Edwards Lifesciences • One Edwards Way, Irvine CA 92614 USA • edwards.com
EDWARDS APIEN XT TRANSCATHETER HEART VALVE WITH THE NOVAFLEX+ DELIVERY SYSTEM – PULMONIC

Indications: The Edwards SAPIEN XT transcatheter heart valve (THV) systems are indicated for use in pediatric and adult patients with a dysfunctional, non-compliant right ventricular outflow tract (RVOT) conduit with a clinical indication for intervention and: pulmonary regurgitation ≥ moderate and/or mean RVOT gradient ≥ 35 mmHg.

Contraindications: The THV and delivery systems are contraindicated in patients with inability to tolerate an anticoagulant/antiplatelet regimen or who have active bacterial endocarditis.

Warnings: The devices are designed, intended, and distributed for single use only. Do not resterilize or reuse the devices. There are no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing. Assessment for coronary compression risk prior to valve implantation is essential to prevent the risk of severe patient harm. Incorrect sizing of the THV may lead to paravalvular leak, migration, embolization and/or RVOT rupture. Accelerated deterioration of the THV may occur in patients with an altered calcium metabolism. Prior to delivery, the THV must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. THV leaflets mishandled or damaged during any part of the procedure will require replacement of the THV. Do not use the THV if the tamper evident seal is broken, the storage solution does not completely cover the THV, the temperature indicator has been activated, the THV is damaged, or the expiration date has elapsed. Do not mishandle the Novaflex+ delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g., kinked or stretched), or the expiration date has elapsed. Use of excessive contrast media may lead to renal failure. Measure the patient’s creatinine level prior to the procedure. Contrast media usage should be monitored. Patient injury could occur if the delivery system is not un-flexed prior to removal. Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials. The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting. THV recipients should be maintained on anticoagulant/antiplatelet therapy as determined by their physician. This device has not been tested for use without anticoagulation. Do not add or apply antibiotics to the storage solution, rinse solutions, or to the THV.

Precautions: Safety, effectiveness, and durability of the THV have not been established for implantation within a previously placed surgical or transcatheter pulmonic valve. Long-term durability has not been established for the THV. Regular medical follow-up is advised to evaluate THV performance. Glutaraldehyde may cause irritation of the skin, eyes, nose and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, immediately flush the affected area with water and seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Material Safety Data Sheet available from Edwards Lifesciences. Patient anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device. To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon. Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis. Safety and effectiveness have not been established for patients with the following characteristics/comorbidities: Echocardiographic evidence of intracardiac mass, thrombus, or vegetation; a known hypersensitivity or contraindication to aspirin, heparin or sensitivity to contrast media, which cannot be adequately pretreated; pregnancy; and patients under the age of 10 years.

Potential Adverse Events: Potential risks associated with the overall procedure including potential access complications associated with standard cardiac catheterization, balloon valvuloplasty, the potential risks of conscious sedation and/or general anesthesia, and the use of angiography: death; respiratory insufficiency or respiratory failure; hemorrhage requiring transfusion or intervention; cardiovascular injury including perforation or dissection of vessels, ventricle, myocardium or valvular structures that may require intervention; pericardial effusion or cardiac tamponade; embolization including air, calcific valve material or thrombus; infection including septicemia and endocarditis; heart failure; myocardial infarction; renal insufficiency or renal failure; conduction system defect arrhythmia; arteriovenous fistula; reoperation or reintervention; ischemia or nerve injury; pulmonary edema; pleural effusion, bleeding; anemia; abnormal laboratory test results (including electrolyte imbalance); hypertension or hypotension; allergic reaction to anesthesia, contrast media, or device materials; hematoma or ecchymosis; syncope; pain or changes at the access site; exercise intolerance or weakness; inflammation; angina; fever. Additional potential risks associated with the use of the THV, delivery system, and/or accessories include: cardiac arrest; cardiogenic shock; emergency cardiac surgery; coronary flow obstruction/transvalvular flow disturbance; device thrombosis requiring intervention; valve thrombosis; device embolization; device malposition requiring intervention; valve deployment in unintended location; structural valve deterioration (wear, fracture, calcification, leaflet tear/tearing from the stent posts, leaflet retraction, suture line disruption of components of a prosthetic valve, thickening, stenosis); paravalvular or transvalvular leak; valve regurgitation; hemolysis; device explants; nonstructural dysfunction; and mechanical failure of delivery system, and/or accessories.

Edwards Crimpler

Indications: The Edwards crimper is indicated for use in preparing the Edwards SAPIEN XT transcatheter heart valve for implantation.

Contraindications: No known contraindications.

Warnings: The device is designed, intended, and distributed for single use only. Do not resterilize or reuse the device. There are no data to support the sterility, nonpyrogenicity, and functionality of the device after reprocessing. Do not mishandle the device. Do not use the device if the packaging or any components are not sterile, have been opened or are damaged, or the expiration date has elapsed.

Precautions: For special considerations associated with the use of this device prior to THV implantation, refer to the SAPIEN XT transcatheter heart valve Instructions for Use.

Potential Adverse Events: No known potential adverse events.

CAUTION: Federal (United States) law restricts this device to sale by or on the order of a physician.

Edwards, Edwards Lifesciences, the stylized E logo, Edwards SAPIEN, Edwards SAPIEN XT, Novaflex, Novaflex+, SAPIEN, and SAPIEN XT are trademarks or service marks of the Edwards Lifesciences Corporation. All other trademarks are the property of their respective owners.

© 2017 Edwards Lifesciences Corporation. All rights reserved. PP-US-1832 v1.0
Edwards Lifesciences • One Edwards Way, Irvine CA 92614 USA • edwards.com
Melody™
Transcatheter Pulmonary Valve (TPV) System

Designed Specifically for Pulmonary Valve Replacement

The Melody valve is the longest studied transcatheter pulmonary valve at seven years post-implant.

Proven Valve Competence
98.1%
of subjects with ≤ mild PR*

Proven to Delay Conduit Replacement
88.8%
freedom from reoperation*

*US IDE Study
Melody™ Transcatheter Pulmonary Valve, Ensemble™ II Transcatheter Valve Delivery System

Important Labeling Information for the United States

Indications: The Melody TPV is indicated for use in the management of pediatric and adult patients who have a clinical indication for intervention on a dysfunctional right ventricular outflow tract (RVOT) conduit or surgical bioprosthesis pulmonary valve that has ≤ moderate regurgitation, and/or a mean RVOT gradient ≥35 mm Hg.

Contraindications: None known.

Warnings/Precautions/Side Effects:
- DO NOT implant in the aortic or mitral position. Pre-clinical bench testing of the Melody valve suggests that valve function and durability will be extremely limited when used in these locations.
- DO NOT use if patient’s anatomy precludes introduction of the valve, if the venous anatomy cannot accommodate a 22 Fr size introducer, or if there is significant obstruction of the central veins.
- DO NOT use if there are clinical or biological signs of infection including active endocarditis. Standard medical and surgical care should be strongly considered in these circumstances.
- Assessment of the coronary artery anatomy for the risk of coronary artery compression should be performed in all patients prior to deployment of the TPV.
- To minimize the risk of conduit rupture, do not use a balloon with a diameter greater than 110% of the nominal diameter (original implant size) of the conduit for pre-dilation of the intended site of deployment, or for deployment of the TPV.
- The potential for stent fracture should be considered in all patients who undergo TPV placement. Radiographic assessment of the stent with chest radiography or fluoroscopy should be included in the routine postoperative evaluation of patients who receive a TPV.
- If a stent fracture is detected, continued monitoring of the stent should be performed in conjunction with clinically appropriate hemodynamic assessment. In patients with stent fracture and significant associated RVOT obstruction or regurgitation, reintervention should be considered in accordance with usual clinical practice.

Potential procedural complications that may result from implantation of the Melody device include the following: rupture of the RVOT conduit, compression of a coronary artery, perforation of a major blood vessel, embolization or migration of the device, perforation of a heart chamber, arrhythmias, allergic reaction to contrast media, cerebrovascular events (TIA, CVA), infection/sepsis, fever, hematoma, radiation-induced erythema, pain, swelling or bruising at the catheterization site.

Potential device-related adverse events that may occur following device implantation include the following: stent fracture, stent fracture resulting in recurrent obstruction, endocarditis, embolization or migration of the device, valvular dysfunction (stenosis or regurgitation), paravalvular leak, valvular thrombosis, pulmonary thromboembolism, hemolysis.

The term “stent fracture” refers to the fracturing of the Melody TPV. However, in subjects with multiple stents in the RVOT it is difficult to definitively attribute stent fractures to the Melody frame versus another stent.

For additional information, please refer to the Instructions for Use provided with the product or available on http://manuals.medtronic.com.

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.
Together, we make it possible.

Made for Partnerships. Made for Patients. Made for You.

At Canon Medical Systems we partner with our customers to truly understand their needs in imaging and beyond. We develop a full range of imaging solutions, including CT, X-Ray, Ultrasound and MR that address time pressures, workflow constraints, patient comfort and imaging precision to deliver true efficiency coupled with best in class tools for diagnosis. Together, we work on an education plan and develop service solutions that meet your every need.

Our goal is to work hand in hand with our partners to deliver optimum health opportunities for patients through uncompromised performance, comfort and imaging accuracy. Together, we make it possible.
Occlutech Paravalvular Leak Device

Paravalvular leak closure

The Occlutech PLD is an ideal device for closing paravalvular leaks as it offers a range of outstanding features:

- User-friendly and easy to use.
- Optimal positioning by two gold markers.
- Repositionable and fully retrievable.
- Optimized concave shape facilitates placement around the implanted valve.
- Available with wide range of sizes for closing from small leaks to large leaks.
- Available with different design options for different PVL morphologies: Rectangular and Square.

The Occlutech PLD is available with two types of connections between the discs, Waist or Twist. Example shown on a Occlutech PLD Square.
# Editorial Board

## Editor-in-Chief

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziyad M. Hijazi</td>
<td>Sidra Medical &amp; Research Center (Doha-Qatar)</td>
</tr>
</tbody>
</table>

## Co-Editor-in-Chief

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oscar Mendiz</td>
<td>Fundacion Favaloro (Buenos Aires, Argentina)</td>
</tr>
</tbody>
</table>

## Assistant Editors

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Damien Kenny</td>
<td>Rush University Medical Center (Chicago, IL)</td>
</tr>
</tbody>
</table>

## Editorial Board

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teiji Akagi</td>
<td>Okayama University (Okayama, Japan)</td>
</tr>
<tr>
<td>Bagrat Alekyan</td>
<td>Bakoulev Scientific Center for Cardiovascular Surgery (Moscow, Russia)</td>
</tr>
<tr>
<td>Zahid Amin</td>
<td>Children's Hospital of Georgia (Augusta, GA)</td>
</tr>
<tr>
<td>Steven Bailey</td>
<td>University of Texas, San Antonio (San Antonio, TX)</td>
</tr>
<tr>
<td>Lee Benson</td>
<td>Hospital for Sick Kids (Toronto, Canada)</td>
</tr>
<tr>
<td>Lisa Bergerse</td>
<td>Boston Children's Hospital (Boston, MA)</td>
</tr>
<tr>
<td>Younes Boudjemline</td>
<td>Hospital Necker (Paris, France)</td>
</tr>
<tr>
<td>Elchanan Bruckheimer</td>
<td>Schneider's Children's Medical Center (Petach Tikva, Israel)</td>
</tr>
<tr>
<td>Maurice Buckbinder</td>
<td>Stanford University (Palo Alto, CA)</td>
</tr>
<tr>
<td>Massimo Caputo</td>
<td>Rush University Medical Center (Chicago, IL)</td>
</tr>
<tr>
<td>Mario Carminati</td>
<td>San Donato Milanese (Milan, Italy)</td>
</tr>
<tr>
<td>John Carroll</td>
<td>University of Colorado Denver (Aurora, CO)</td>
</tr>
<tr>
<td>John P. Cheatham</td>
<td>Ohio State University (Columbus, OH)</td>
</tr>
<tr>
<td>Jae Young Choi</td>
<td>Severance Cardiovascular Hospital (Seoul, Korea)</td>
</tr>
<tr>
<td>Antonio Colombo</td>
<td>St. Raffaele Hospital (Milan, Italy)</td>
</tr>
<tr>
<td>Costantino Costantini</td>
<td>Hospital Cardiologico Costantini (Curitiba, Brazil)</td>
</tr>
<tr>
<td>Alain Cribier</td>
<td>Charles Nicolle Hospital (Rouen, France)</td>
</tr>
<tr>
<td>Roberto Cubeddu</td>
<td>Aventura Hospital (Miami, FL)</td>
</tr>
<tr>
<td>Bharat Dalvi</td>
<td>Glenmark Cardiac Centre (Mumbai, India)</td>
</tr>
</tbody>
</table>

## Associate Editors

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clifford J. Kavinsky</td>
<td>Rush University Medical Center (Chicago, IL)</td>
</tr>
<tr>
<td>Bray Patrick Lake</td>
<td>PFO Research Foundation (Boulder, CO)</td>
</tr>
<tr>
<td>John Messenger</td>
<td>University of Colorado (Aurora, CO)</td>
</tr>
</tbody>
</table>

## Managing Editor

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hussam Suradi</td>
<td>Rush University Medical Center (Chicago, IL)</td>
</tr>
</tbody>
</table>

## Associate Editors

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jo De Giovanni</td>
<td>Birmingham Children's Hospital (Birmingham, United Kingdom)</td>
</tr>
<tr>
<td>Helene Eltchannino</td>
<td>University Hospital (Rouen, France)</td>
</tr>
<tr>
<td>Maay El Syed</td>
<td>Ain Shams University (Cairo, Egypt)</td>
</tr>
<tr>
<td>Thomas Fagan</td>
<td>University of Colorado (Denver, CO)</td>
</tr>
<tr>
<td>Ted Feldman</td>
<td>Evanston Northshore Hospital (Evanston, IL)</td>
</tr>
<tr>
<td>Olaf Franzen</td>
<td>University Heart Center Hamburg (Hamburg, Germany)</td>
</tr>
<tr>
<td>Yun Ching Fu</td>
<td>Taichung Veterans General Hospital (Taichung, Taiwan)</td>
</tr>
<tr>
<td>David Gao</td>
<td>Shanghai Children's Medical Center (Shanghai, China)</td>
</tr>
<tr>
<td>Eulogio Garcia</td>
<td>Hospital Clinico San Carlos (Madrid, Spain)</td>
</tr>
<tr>
<td>Marc Gewillig</td>
<td>University of Lueven (Lueven, Belgium)</td>
</tr>
<tr>
<td>Matt Gillespie</td>
<td>Children's Hospital of Philadelphia (Philadelphia, PA)</td>
</tr>
<tr>
<td>Omer Goktekin</td>
<td>Bezmialem Vakif University (Istanbul, Turkey)</td>
</tr>
<tr>
<td>Steven Goldberg</td>
<td>University of Washington (Seattle, WA)</td>
</tr>
<tr>
<td>William Gray</td>
<td>Columbia University (New York, NY)</td>
</tr>
<tr>
<td>Eberhard Grube</td>
<td>Heart Center Siegburg (Siegburg, Germany)</td>
</tr>
<tr>
<td>Jeff Harrisberg</td>
<td>Pediatric Cardiology (Gauteng, South Africa)</td>
</tr>
<tr>
<td>William E. Hellenbrand</td>
<td>Yale University (New Haven, CT)</td>
</tr>
<tr>
<td>James Hermiller</td>
<td>The Care Group (Indianapolis, IN)</td>
</tr>
<tr>
<td>Howard Herrmann</td>
<td>University of Pennsylvania (Philadelphia, PA)</td>
</tr>
<tr>
<td>David Holmes</td>
<td>Mayo Clinic (Rochester, MN)</td>
</tr>
<tr>
<td>Name</td>
<td>Institution</td>
</tr>
<tr>
<td>--------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Horst Sievert</td>
<td>CardioVascular Center</td>
</tr>
<tr>
<td></td>
<td>Sankt Katharinen Hospital</td>
</tr>
<tr>
<td></td>
<td>(Frankfurt, Germany)</td>
</tr>
<tr>
<td>Frank Silvestry</td>
<td>University of Pennsylvania Hospital</td>
</tr>
<tr>
<td></td>
<td>(Philadelphia, PA)</td>
</tr>
<tr>
<td>Paul Sorajja</td>
<td>Minneapolis Heart Institute Foundation</td>
</tr>
<tr>
<td></td>
<td>(Minneapolis, MN)</td>
</tr>
<tr>
<td>Christian Spies</td>
<td>Queen's Heart Physician Practice</td>
</tr>
<tr>
<td></td>
<td>(Honolulu, HI)</td>
</tr>
<tr>
<td>Gregg Stone</td>
<td>Columbia University</td>
</tr>
<tr>
<td></td>
<td>(New York, NY)</td>
</tr>
<tr>
<td>Corrado Tamborino</td>
<td>University of Catania</td>
</tr>
<tr>
<td></td>
<td>(Catania, Italy)</td>
</tr>
<tr>
<td>Vinod Thourani</td>
<td>Emory University</td>
</tr>
<tr>
<td></td>
<td>(Atlanta, GA)</td>
</tr>
<tr>
<td>Jonathan Tobis</td>
<td>UCLA Medical Center</td>
</tr>
<tr>
<td></td>
<td>(Los Angeles, CA)</td>
</tr>
<tr>
<td>Murat Tuczu</td>
<td>Cleveland Clinic Foundation</td>
</tr>
<tr>
<td></td>
<td>(Cleveland, OH)</td>
</tr>
<tr>
<td>Zoltan Turi</td>
<td>Robert Wood Johnson</td>
</tr>
<tr>
<td>Alec Vahanian</td>
<td>Bichat University Hospital</td>
</tr>
<tr>
<td></td>
<td>(Paris, France)</td>
</tr>
<tr>
<td>Joseph J. Vettukattil</td>
<td>Spectrum Health</td>
</tr>
<tr>
<td>Kevin Walsh</td>
<td>Our Lady's Hospital</td>
</tr>
<tr>
<td>John Webb</td>
<td>St. Paul Hospital Vancouver</td>
</tr>
<tr>
<td></td>
<td>(British Columbia, Canada)</td>
</tr>
<tr>
<td>Brian Whisenant</td>
<td>Intermountain Medical Center</td>
</tr>
<tr>
<td>Matthew Williams</td>
<td>Mount Sinai Medical Center</td>
</tr>
<tr>
<td>Neil Wilson</td>
<td>University of Colorado</td>
</tr>
<tr>
<td>Evan Zahn</td>
<td>Cedars Sinai Medical Center</td>
</tr>
</tbody>
</table>
NEW TECHNOLOGY

207 Feasibility of Fully Automated Motion Compensated Overlay for Transcatheter Aortic Valve Implantation
Nick Assink, Maria-Louisa Izamis, Olivier Nempont, Marco Verstege, Cherif P. Sahyoun, Alexander Haak,
John D. Carroll, John C. Messenger, Gerhard Schymik, Navid Madershahian, Thorsten C. Wahlers,
Peter Eshuis

ORIGINAL SCIENTIFIC ARTICLE

212 Current Interventional Management Strategies for Coronary Arteriovenous Fistulae
Awad Al-Qahtani, MD1, Ayman Zakaria, MD2, Ziyad M. Hijazi, MD, MPH, FACC, MSCAI3*

222 Patent Foramen Ovale Closure for Recurrent Stroke Prevention: A Network Meta-Analysis of Randomized Controlled Trials
George S. Mina, Demiana Soliman, Kalgi Modi

CASE REPORTS

228 Retrieval of a Partially Deflated Balloon: A Novel Approach
Stephen Nageotte, Cheryl Takao

234 Transcatheter Repair of Anterior Mitral Leaflet Perforation in a Patient with Mechanical Aortic Valve Using Antegrade and Retrograde Approaches
Reda Abuelatta, Hesham Naeim, Ahmad AlAhmadi, Saleh Al Ghamdi, Osama Amoudi, Ibraheem AlHarbi,
Abdelfatah Elasfar

240 Left Main Protection and Emergency Stenting During TAVR with Self-Expandable Valve
Marko Noc, Branko Cveticanin, Saibal Kar, Oscar A. Mendiz
Feasibility of Fully Automated Motion Compensated Overlay for Transcatheter Aortic Valve Implantation

Nick Assink, MSc¹, Maria-Louisa Izamis, PhD², Olivier Nepomuc, PhD³, Marco Verstege, PDEng⁴, Cherif P. Sahyoun, PhD⁴, Alexander Haak, PhD⁴, John D. Carroll, MD⁴, John C. Messenger, MD⁴, Gerhard Schymik, MD⁵, Navid Madershahian, MD⁶, Thorsten C. Wahlers, MD⁶, Peter Eshuis, PhD,¹*  
¹ Philips Healthcare, Best, The Netherlands  
² Philips Research, Eindhoven, The Netherlands  
³ Philips Research, Paris, France  
⁴ Division of Cardiology, University of Colorado Hospital, Aurora, Colorado, USA  
⁵ Municipal Hospital Karlsruhe, Karlsruhe, Germany  
⁶ Department of Cardiac and Thoracic Surgery, Cologne University Heart Center, Cologne, Germany

Abstract

Background: Automated motion compensation of aortic root overlay on fluoroscopy during transcatheter aortic valve implantation (TAVI) could ensure accurate device positioning at minimal contrast cost, thereby reducing complication rates.

Objectives: To describe the feasibility of software that automatically compensates for cardiac and respiratory motion on X-ray, which may allow greater device control during TAVI.

Methods: Twenty four TAVI cases (25,607 frames) from four independent institutions using either the Medtronic CoreValve (n=8) or Edwards Sapien valve (n=16) were post-processed with the software. For each case, the algorithm applied three steps: (i) Generation of an anatomical roadmap using X-ray (Vascular Outlining, or VO) or 3D segmentation of CT data, (ii) Correlation to pigtail catheter, and (iii) Real-time motion compensation.

Results: VO motion compensation was activated 84% of all frames yielding a relative displacement error of -1.09 ± 2.65 mm. Similarly, CT-aided motion compensation was activated 84% of frames yielding a relative displacement error of -0.77 ± 2.92 mm.

Conclusions: We have shown feasibility of the first fully automated motion compensation method for real-time continuous visualization of the target aortic anatomy during TAVI procedures. Our method has the potential to improve valve positioning accuracy and reduction in deployment variability.

Key Words
Aortic stenosis • TAVI • TAVR • Imaging modalities • Non-invasive imaging

Introduction

With over 250,000 procedures conducted worldwide in the last decade, transcatheter aortic valve implantation (TAVI) has gained widespread acceptance for the treatment of aortic valve disease [1]. As outcomes continue to improve, TAVI is expected to be performed in younger, lower-risk patients [2] and will grow the number of procedures further. Correct positioning of the artificial valve is crucial for TAVI outcome [3]. Current implantation of prosthetic aortic valves
outside the optimal depth range still occurs in 21% of the cases [4], resulting in high-degree atrioventricular block (10-30%) and paravalvular leak (4-35%) [5]. We have created a fully-automated software that enables anatomical roadmap overlays on live fluoroscopic images compensated for cardiac and respiratory motion without workflow disruptions, which may allow for greater control over valve placement. This paper describes how our technology works and reports on the results of the feasibility study performed.

**Method**

Our algorithm comprises three steps:

i. **Anatomical roadmap generation.** Angiograms with contrast injections are automatically identified and the frame best opacifying the aortic root is selected by the algorithm, upon which two types of anatomical roadmaps are generated:

1. Vascular Outlining (VO): The outline of contrast is detected in the X-ray image (Figure 1a).
2. Computed Tomography (CT) aided: The automatic CT segmentation [6, 7] is registered to the angiographic image (Figure 1b).

ii. **Correlate anatomical roadmap to pigtail catheter.** The pigtail catheter is routinely locked in an aortic valve cusp and its motion reflects overall aortic valve motion. The software searches for the pigtail catheter (Figure 1c) and sets the spatial relation with respect to the anatomical roadmap (Figure 1d). This correlation process is performed for all angiograms producing a series of references (Figure 1e).

iii. **Live motion compensation.** Each live fluoroscopic image is filtered to enhance pigtail-like objects, which is then matched to the references (Figure 1f).

---

**Figure 1.** The three steps of motion compensation: i. Anatomical roadmap generation: (Panel A) Vascular Outlining (VO) based on the angiographic image, (Panel B) Computed-Tomography (CT) segmentation registered to the angiographic image. ii. Correlate anatomical roadmap to pigtail catheter: (Panel C) The reference map for the pigtail is extracted, (Panel D) The spatial relation between the pigtail reference map (blue) and the anatomical roadmap (red) is set. iii. Live motion compensation: (Panel E) The pigtail reference map best matching the current pigtail shape is selected, (Panel F) Live fluoroscopic image is filtered (left) and matched to the pigtail reference map (right), (Panel G) Fluoroscopic view of the matching result, (Panel H) The transformation is applied to the anatomical roadmap resulting in a dynamic motion-compensated roadmap, either VO (blue) or CT (red).
frames yielding a relative displacement error of -1.09 ± 2.65mm and 2.24mm absolute displacement error. CT-aided motion compensation was activated 84% of all frames yielding a relative displacement -0.77 ± 2.92mm and 2.22mm absolute displacement error.

The relative and absolute displacement error increased for the larger and hence more obstructive CoreValve and also increased when the pigtail catheter was positioned in the more obstructive middle position (Table 1). Overall VO and CT-aided motion compensation demonstrated similar performance.

**Discussion**

We have used the pigtail catheter as a contrast-independent landmark for motion compensation during TAVI without any need for software interaction. To our knowledge, only one approach has successfully tracked the aortic valve plane by using the calcifications on the aortic valve as contrast-independent landmarks [8]. A clinical trial correlated this approach with a promising reduction in the incidence of conduction disorders [9]. The feasibility of the approach was limited by the need to manually annotate the calcifications after every repositioning of the C-arm. Additionally, not every patient may have sufficient visible calcifications [10]. All currently available CT fusion solutions provide static overlays only.

Of the two motion compensation methods evaluated: VO has the advantage of requiring only a well-contrasted aortic root angiogram representing the current aortic anatomical situation. CT-aided motion compensation provides a richer 3D view, with the ability to integrate pre-procedural planning in the live roadmap.

---

**Table 1. VO and CT-aided motion compensation results.**

<table>
<thead>
<tr>
<th>Valve type</th>
<th>Pigtail catheter cusp position</th>
<th>Number of cases</th>
<th>Frames with activated MC (%)</th>
<th>Relative displacement error (mm)</th>
<th>Absolute displacement error (mm)</th>
<th>Frames with activated MC (%)</th>
<th>Relative displacement error (mm)</th>
<th>Absolute displacement error (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoreValve</td>
<td>Lowest</td>
<td>8</td>
<td>82</td>
<td>-1.10±2.61</td>
<td>2.00</td>
<td>85</td>
<td>-1.13±2.91</td>
<td>2.15</td>
</tr>
<tr>
<td>Sapien</td>
<td>Lowest</td>
<td>4</td>
<td>87</td>
<td>0.09±2.56</td>
<td>1.97</td>
<td>98</td>
<td>-0.15±2.45</td>
<td>1.50</td>
</tr>
<tr>
<td></td>
<td>Middle</td>
<td>12</td>
<td>89</td>
<td>-1.24±2.72</td>
<td>2.71</td>
<td>80</td>
<td>-0.09±3.02</td>
<td>2.48</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>24</td>
<td>84</td>
<td>-1.09±2.65</td>
<td>2.24</td>
<td>84</td>
<td>-0.77±2.92</td>
<td>2.22</td>
</tr>
</tbody>
</table>
A major limitation of the study design was the post-processing of data. Actual clinical use of motion compensation is needed to determine the impact of the motion compensated anatomical roadmap on valve positioning. Another limitation of the technology is its dependence on the pigtail catheter maintaining its position locked in one of the aortic valve cusps. It is important not to lose this position as the device is advanced, as the relationship between the pigtail and the valve plane is assumed constant. Whereas this is common in clinical practice during valve positioning, the pigtail is typically pulled in the last phases of deployment, implying that the motion compensated overlay may not be used for guidance if any final adjustments are required. Further studies are warranted to examine whether these limitations are clinically acceptable. Of note, the live overlay is automatically disabled when detecting pigtail retrieval, to avoid erroneous guidance.

The implications of this work are perhaps greatest for enhancing the learning curve amongst new operators and for physicians performing TAVIs on lower-risk patients with potentially fewer X-ray-visible anatomic landmarks. Prospective studies of impact of this technology on contrast usage and positioning accuracy are warranted.

Conclusion

We have shown feasibility of the first fully automated motion compensation method for real-time continuous visualization of the target aortic anatomy during TAVI procedures. Our method has the potential to improve valve positioning accuracy and reduction in deployment variability and contrast usage.

Conflict of Interest

• Nick Assink – Master student located at Philips Healthcare
• Maria-Louisa Izamis – Employee of Philips Healthcare
• Olivier Nemport – Employee of Philips Healthcare
• Marco Verstege – Employee of Philips Healthcare
• Cherif P. Sahyoun – Employee of Philips Healthcare
• Alexander Haak – Employee of Philips Healthcare
• John D. Carroll – Research funding and in-kind support from Philips Healthcare
• John C. Messenger – Research funding and in-kind support from Philips Healthcare
• Gerhard Schymik – In-kind support from Philips Healthcare
• Navid Madershahian – In-kind support from Philips Healthcare
• Thorsten C. Wahlers – In-kind support from Philips Healthcare
• Peter G. Eshuis – Employee of Philips Healthcare

References

Abstract

Coronary arteriovenous fistulae are uncommon abnormal connections between one of the coronary arteries and a heart chamber or another blood vessel, usually pulmonary vasculature or other venous vessels. Clinically significant fistulae may lead to ischemia of the segment of the myocardium perfused by the affected coronary artery. Therefore, closure of such fistulae is indicated. Transcatheter closure if feasible is recommended and can be achieved using different occlusion devices. This paper discusses the clinical classification of fistulae and the interventional approach to eliminate such fistulae with some case examples. The availability of new coils and catheters render the interventional approach safe and effective.

Key Words
Coronary fistula, Coil occlusion, Congenital heart disease, Interventional therapies

Coronary artery fistula is defined as an abnormal connection between one of the coronary arteries and a heart chamber or another blood vessel, usually pulmonary vasculature or other venous vessels. It is estimated to account for 0.2-0.4% of total congenital cardiac anomalies [1]. In 1908 Maude Abbott published the first pathological account of this condition [2].

Bjork and Crafoord in 1947 performed the first successful surgical closure of a coronary fistula in a patient with a preoperative diagnosis of patent ductus arteriosus [3].

In general, most coronary artery fistulae are small and do not cause any symptoms. Most are clinically undetectable and are found incidentally on echocardiography performed for other reasons or in adults undergoing coronary angiography performed for an unrelated cause. Most fistulae resolve spontaneously without causing any complications. Only those fistulae that are about three times the size of a normal caliber of a coronary artery may cause symptoms or complications and require management. Symptoms may include the following:

- Dyspnea on exertion
- Angina
- Fatigue
- Palpitations

Due to steel phenomenon, large fistulae may lead to ischemia of the segment of the myocardium perfused by the affected coronary artery. The mechanism is related to the diastolic pressure gradient and runoff from the coronary vasculature to a low-pressure receiving cavity/vessel. If the fistula is large, the intracoronary diastolic perfusion pressure progressively diminishes.
Prior to the era of echocardiography, the right coronary artery was considered to be the major site of origin of the fistulae (40-60%), followed by the left anterior descending (30-60%) then circumflex and a combination thereof. However, currently, we believe more fistulae originate in the left anterior descending artery. The right side of the heart (ventricle, pulmonary arteries, right atrium, coronary sinus, etc) is the major drainage (termination) site of most fistulae (90%) [4, 5].

Prior to 1990’s, surgical ligation was considered the treatment of choice with external ligation of the fistula preferred if possible. However, if the fistula is posteriorly located behind the heart, internal closure of the termination site on cardiopulmonary bypass offered a safe alternative [6]. Recurrence rate after surgical closure is about 10% [7].

Since the report by Reidy et al. [8], percutaneous closure in the cardiac catheterization laboratory has become the most common option for management of large fistulae. To enable successful and safe closure, it is imperative to define the anatomy of the fistula by selective coronary angiography. Detachable balloons, coils, devices, and vascular plugs all have been used successfully to close coronary fistulae [9, 10].

The purpose of this paper is to discuss the management decisions and details of transcatheter closure techniques.

Management Decisions

As mentioned above, small fistulae in an asymptomatic patient need not be closed. However, if the fistula is large or if the patient is symptomatic, closure is recommended. The decision process in managing fistulae depends on: site of origin of the fistula (proximal vs distal) [11], size of the fistula, patient’s symptoms, presence of any complication caused by the fistula (angina, heart failure, endocarditis, rupture, etc), age of the patient, the anatomy of the fistula and presence of other indications to undergo an invasive procedure. The current recommendations by the AHA/ACC guidelines [12] include for Class 1: patients with continuous murmur should undergo exact delineation of the origin and termination of the fistula by either echocardiography or CT/MRI; patients with large fistulae should undergo closure (surgical or percutaneous) after delineation of the exact anatomy and finally, small-moderate fistulae with complications (ischemia, arrhythmias or ventricular dysfunction of unexplained etiology) should undergo closure. Last but not least, the approach of elimination of the fistula (surgical vs. transcatheter) depends on the expertise of the physicians involved in the management of the patient.

Proximal Fistulae

If small in size with no symptoms, observation is recommended and no medications. However, if the fistula is medium or large with or without symptoms, closure is recommended (surgical vs. transcatheter) followed by antiplatelets for at least one year.

Distal Fistulae

If small in size with no symptoms, observation is recommended with no medications. However, if medium in size with or without symptoms one has two options: closure followed by antiplatelets for one year or observation while receiving antiplatelets indefinitely. If the fistula is large with symptoms, closure is recommended, 6 hours post-closure, heparin should be started to keep PTT at 1.5 times normal while warfarin is started. Patients should be discharged home on Warfarin to keep INR around 2.5 for a period of 6-12 months [11]. Also, these patients should receive antiplatelets indefinitely. If the fistula is large with no symptoms, one has two options: either observation while receiving antiplatelets indefinitely or closure. If fistula is closed, one should treat as large fistula with symptoms.

Another important factor in the decision-making process is the size of the patient.
acetate (PVA) embedded within them to increase thrombogenicity. Steel was the initial material used for coils then came Platinum and different alloys that made them softer, more radio-opaque and non-ferromagnetic enabling future MRI follow-ups [14]. The methods of coil delivery had evolved over the last five decades in response to the need for a safer and more controllable deployment as well as to solve the technical problems encountered in old methods. Among the early methods were the pushable, injectable and liquid coils delivered by pushing wires or injecting saline or contrast after loading the coils in the delivery catheters [14]. The first detachable coil was described in 1977. Current detachable coils are deployed by a variety of mechanisms including mechanical, by electrolysis, and by hydrostatic means. The disadvantage of the mechanical detachment is that there is often friction between the coil and the microcatheter, during embolization through tortuous vessels, this friction can limit delivery, or the coil can rotate or flip at detachment [14]. Deployment of coils can be done by a wide range of catheters, the current assortment of microcatheters widely used may not be all well suited for several anatomic variants, including excessive vascular tortuosity. The most commonly used microcatheters for coiling are Excelsior SL-10 and 10-18 (Stryker, Kalamazoo, MI, USA), Echelon 10 and 14 (Medtronic, Minneapolis, MN, USA) and Headway 17 (Microvention TERUMO, Tustin, CA, USA). As mentioned above, these catheters are readily available in radiology departments engaged in aneurysm coiling. The proper coil for embolization should be sized 20 to 30% larger than what the target vessel measures on pre-deployment angiogram to prevent distal embolization or migration. Placement of an undersized coil risks its distal embolization away from the intended location. Attempting to place an oversized coil may result in the coil not forming the intended shape or even straightening in the vessel [14]. In general, dense packing of the target vessel is recommended to achieve complete embolization. The key to inducing complete thrombosis is cross-sectional occlusion which can be done by different techniques [15]. A scaffold technique involves initially deploying a higher radial force coil followed by a
softer coil or an anchoring technique where a distal coil is anchored in a branch vessel then packed proximally [15]. This prevents distal migration and results in a tighter coil pack. An inflated compliant occlusion balloon may be used distal to the coil delivery catheter to prevent unwanted distal embolization, especially in high-flow fistulae. Then the balloon can be deflated and withdrawn after the deployment of the first coil that acts as a future basket for further coils [14].

6. The Amplatz family of devices have been used for percutaneous closure of fistulae. The muscular device, the Duct occlude and the vascular plugs (I, II, IV) all have been used successfully for the closure of these fistulae [16-20]. The advantage of the plugs over the conventional devices is the need for a smaller sheath/catheter for deployment, thus making retrograde delivery possible. For deployment of devices (muscular VSD device or the PDA device), perhaps the best approach is to form an arteriovenous wire loop and deployment of the device from the venous side (see example below). However, for the vascular plugs, it is possible to deploy them from the retrograde approach using the corresponding guide catheter or small delivery sheath.

7. Finally, we want to emphasize the importance of anticoagulation and antiplatelet therapy post device/coil closure of fistulae. As discussed above [11], in some patients intravenous heparin has to be initiated about six hours after closure and bridging to Warfarin and antiplatelet therapy thereafter. This is extremely important to avoid the unfortunate complication of thrombus propagation proximal to the devices/coils [21].

Techniques

Fistulae can be closed either in a retrograde fashion (approach from the arterial system) or from the venous side (direct access if possible or after establishing an arteriovenous wire loop). Each technique has its own merits.

Retrograde approach

Access should be obtained via the right femoral artery and vein. We usually insert a 4-5Fr sheath in the artery in children and 6Fr in adults. For the vein, a corresponding size can be used. On occasions, we also obtain access in the contralateral femoral artery. We do this if we use a 4-5Fr diagnostic coronary catheter for closure. The purpose of this is to perform control angiography for assessment of the position of coils/devices prior to release. However, if we use a guide catheter, one may not need additional access. After a careful hemodynamic assessment is performed, selective coronary angiography is performed in the affected coronary artery. Usually, we perform at least two angiograms in different orthogonal views. The purpose of the angiograms is to delineate the exact anatomy of the fistula (origin, course, termination and viable myocardial branches). If the flow is brisk due to the size of fistula, one may need to balloon occlude the fistula with an end-hole balloon catheter advanced over a wire into the fistula and injection via this catheter after removal of the wire. We find this technique to be helpful in delineating the termination site and also in delineating the myocardial branches distal to the balloon (see case below).

Case example:

Four year young female child presented with continuous murmur heard shortly after birth. Echocardiography revealed the presence of moderate-large sized coronary artery fistula arising from the left anterior descending artery (LAD) and terminating in the right ventricle. She has been followed conservatively until age four years, when it was decided to close it on an elective basis. Her weight was 16.4 kg. A 4Fr sheath was inserted in the right femoral artery and 6Fr in the right femoral vein. Selective left coronary angiography was performed using a 4Fr JL diagnostic catheter (Figure 1A). Then a 150cmx6cm Excelsior SL-10 Microcatheter (Stryker, Kalamazoo, MI, USA) was inserted inside the JL. The Transend floppy tip guidewire, 0.016” (Stryker, Kalamazoo, MI, USA) was used to navigate the tortuosity of the coronary artery until the wire reached to the right ventricle (Figure 1B). Then over this wire, a 4Fr balloon-tipped catheter was exchanged and positioned in the distal coronary artery. With balloon inflation, hand injection delineated the fistula better (Figure 1C). Then over the same wire, the balloon-tipped catheter was exchanged for the JL and then the Excelsior Microcatheter was fed over this wire all the way to the dis-
Figure 1. Selective Left Main Coronary Artery Angiograms in a 4 yr. young female child with left anterior descending (LAD) coronary artery to right ventricle (RV) fistula. **Panel A.** Dilated LAD terminating with a fistula to the RV (arrow). **Panel B.** Diagnostic JR catheter in left main and an 0.016” Transend guide wire all the way to RV (arrow). **Panel C.** A 4Fr. Balloon tipped catheter was advanced in LAD. Balloon inflated to block flow (arrow) and this delineated fistula better. **Panel D.** Cine fluoroscopy of the Excelsior Microcatheter in fistula. Two radio-opaque markers delineating position of the Microcatheter (arrows). **Panel E.** Cine fluoroscopy after deployment of first Target detachable coil (arrow) [8mmx20cm]. **Panel F.** Cine fluoroscopy after 4 additional Target detachable coils were deployed (arrow) [second coil was also 8mmx20cm, 3rd and 4th coils were 4mmx8cm and last coil was 6mmx20cm]. **Panel G.** Angiogram just after the deployment of the five coils revealed no flow distal to coil. **Panel H.** Final angiogram shows flow stopped proximal to coils.
Case example:
We previously have published this case [17]. 12 days young female baby, 2.4 kg presented in florid congestive heart failure due to a very large left main coronary (LMC) artery to the right ventricle fistula. Her right femoral artery was occluded due to a prior cardiac catheterization. Access was achieved from the left femoral artery 4Fr, left femoral vein 4Fr, and right internal jugular vein 8Fr. The initial hemodynamic assessment revealed systemic pulmonary artery pressure and infinite Qp:Qs ratio. Angiography in the left main coronary artery revealed the presence of huge LAD to right ventricle fistula (Figure 2A, B). The fistula was crossed easily from the arterial side using a 0.035” floppy tip guidewire. The wire was advanced all the way to the main pulmonary artery and snared using a 4Fr, 10mm gooseneck snare (Microvena) and was exteriorized from the right jugular vein (Figure 2C, D) creating an arteriovenous wire loop. An 8Fr. Mullins sheath was advanced over this wire from the jugular vein through the right ventricle into the fistula and into the distal LAD. The first device used was a 12mm Amplatzer muscular VSD device (AGA Medical, Plymouth, MN) (Figure 2E). A total of 7 Flipper coils (five of them were 5mmx8cm, and two were 5mmx-10cm) were deployed from the arterial side to create a nest behind the VSD device (Figure 2F, G). Repeat angiogram still revealed significant residual shunt (Figure 2H). Due to the heavy contrast load used (7ml/kg), the procedure was terminated. The baby remained stable without a rise in troponin or lactate but remained intubated with the continued moderate residual flow by echocardiography. Therefore, two days later the baby was brought back to the catheterization laboratory and a right carotid artery cut down was used and an 8Fr. sheath was inserted. A 10/8 mm Amplatzer Duct Occlud (AGA Medical) (Figure 2I) and a 9mm Gianturco Grifka Vascular Occlusion Device (Cook Medical) (Figure 2J) were deployed proximal to the coils and muscular VSD device. Repeat angiography revealed good devices positions and minimal residual flow (Figure 2K, L). Repeat hemodynamics revealed that the pulmonary artery pressure dropped to 40% systemic and the Qp:Qs ratio decreased to 2.7:1. The baby was extubated two days later. She was transferred back to referring institution on 4mg/kg aspirin orally. She was...
Case Example:
A 76-year-old gentleman was referred to us due to symptoms of increased shortness of breath. He was known to have a circumflex to pulmonary artery fistula for ten years prior to this procedure. He was a previous smoker. Pulmonary function test revealed a mild form of chronic obstructive pulmonary disease. Cardiac catheterization was performed via the right femoral artery using 7Fr. sheath and right femoral vein using 6 Fr. sheath. Hemodynamics revealed slightly elevated pulmonary artery pressure with a mean of 26mmHg and Qp:Qs ratio of 1.4:1. Angiography at one month revealed complete closure of the fistula and normal cardiac function.

The direct access technique
If the fistula could not be crossed from the arterial side to close retrogradely or to create wire loop, one may attempt to cross directly from the venous side (fistula exit) [22]. The following case illustrates this technique.
phy in the left main coronary artery revealed normal LMC and LAD. The circumflex origin was very narrow and very tortuous. At mid circumflex, a fistula arose and drained to the right pulmonary artery (RPA). The fistula size was double the size of the circumflex (Figure 3A). Angiography in the right coronary artery revealed normal artery with minimal coronary artery disease; however, the distal branch (posteromedial coronary artery) drained via smaller channels and connected with the circumflex fistula and all drained to the RPA (Figure 3B). Multiple attempts to cross the fistula from the LMC artery failed. Therefore, a 5Fr. JR catheter was used from the venous side to the RPA and crossed the exit site of the fistula (Figure 3C). A 0.016” guidewire (Transend) was used to navigate the fistula. The wire and a 150cmx6cm Excelsior SL-10 Microcatheter were advanced all the way to the origin of the fistula from the circumflex. The wire was removed and a total of eight Target detachable coils were deployed in mid-distal fistula (1st coil: 12mmx30cm; 2nd coil: 10mmx30cm; 3rd and 4th coils: 9mmx20cm; 5th, 6th and 7th coils: 4mmx8cm and 8th coil: 3mmx4cm) showing filling of the circumflex (Figure 3D, E, F). Repeat angiography revealed complete closure of fistula (Figure 3G). The patient had recovered overnight and a repeat echocardiography the next day revealed complete closure of the fistula. He was discharged home after 24 hours from the procedure on his medications of warfarin and aspirin.
Follow-up

It is mandatory to follow patients with coronary arteriovenous fistulae life-long. Such patients may be at increased risk for acute or late-onset coronary thrombosis [21-26]. Patients with distal fistulae with dilated proximal conduit are especially at increased risk for such complications. We propose that such patients receive life-long antiplatelet therapy. The issue of anticoagulation needs to be taken into consideration as discussed above. Further, these patients need to undergo coronary imaging every few years based on symptoms or even periodic CT coronary angiography. Other factors may increase the risk of coronary thrombosis such as smoking, diabetes, hypertension, and hyperlipidemia. Patients with fistula drainage to the coronary sinus may be at higher risk of coronary thrombosis [27]. To best understand the long-term sequelae of coronary fistulae closure, there is an ongoing registry by the CCISC (Congenital Cardiovascular Interventional Study Consortium) collecting data on these patients.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

References

10. Qureshi SA. Coronary arterial fistulas. Orphanet J Rare Dis. 2006;1(51):51(page 1-6)


Cite this article as: Al-Qahtani A, Zakaria A, Hijazi ZM. Current Interventional Management Strategies for Coronary Arteriovenous Fistulae. Structural Heart Disease. 2018;4(5):212-221. DOI: https://doi.org/10.12945/j.jshd.2018.043.17
Abstract

Background: Patent foramen ovale (PFO) has been shown to be associated with recurrent strokes. Randomized controlled trials (RCTs) evaluating the benefit of transcatheter closure of PFO over medical therapy in patients with cryptogenic stroke showed inconsistent results.

Objectives: We aimed by performing network meta-analysis to evaluate three different treatment strategies for stroke prevention, namely, PFO closure, antiplatelet therapy and oral anticoagulation.

Methods: We searched PUBMED and Cochrane database for RCTs comparing PFO closure to medical therapy in patients with PFO and cryptogenic stroke. Three different strategies were evaluated; PFO closure, antiplatelet therapy alone and oral anticoagulation. A Bayesian network meta-analysis was performed to calculate odds ratios (OR) and 95% credible intervals (CrI). The outcome of this study was recurrent stroke events at the longest follow up period reported.

Results: We included 4 RCTs with a total of 2821 patients. There was significant reduction of recurrent strokes with PFO closure when compared to antiplatelet therapy alone (OR 0.29, CrI 0.07-0.84). On the other hand, there were no statistically significant differences between PFO closure and oral anticoagulation (OR 0.52, CrI 0.1-1.92) or between anticoagulation and antiplatelet therapy (OR 0.55, CrI 0.13-2.14).

Conclusion: In patients with PFO and cryptogenic stroke, transcatheter PFO closure is associated with significant reduction in recurrent strokes when compared to antiplatelet therapy alone. This benefit was not statistically significant when PFO closure was compared with the use of oral anticoagulation.

Key Words
Patent foramen ovale • Stroke • Network meta-analysis

Introduction

The presence of patent foramen ovale (PFO) has been shown to be associated with increased incidence of stroke. [1–3] Therefore, PFO closure has the potential of prevention of recurrent stroke events in patients with PFO and cryptogenic stroke. Randomized controlled trials (RCTs) that evaluated the benefit of transcatheter PFO closure in recurrent stroke prevention showed inconsistent results. [4–9]. One of the differences between those trials is that oral anticoagulation was permitted in the medical therapy arm in some of the trials, [4, 6, 9] which could have contributed to the discrepancy in the results. Hence, in the current study we aimed by performing network meta-analysis to compare three different strategies for recurrent stroke prevention, namely, PFO closure, antiplatelet therapy alone and oral anticoagulation.
Methods

We searched PubMed and Cochrane Central Register of Controlled Trials for trials comparing PFO closure to medical therapy from inception through October, 2017. Only studies in the English language or studies with an English translation were included. Citations were screened at the title/abstract level and relevant citations were retrieved as full reports. References from the included studies were also manually searched for relevant studies.

Studies were eligible for inclusion if they were randomized controlled trials that compared PFO closure to medical therapy in patients with cryptogenic stroke and PFO. If the medical therapy arm in any study included patients on antiplatelets and/or oral anticoagulation, the study was included only if recurrent stroke was reported separately for each group of patients. Studies were excluded if they were non-randomized trials or if outcomes of patients on antiplatelets and patients on oral anticoagulation were not reported separately. Moreover, patients who received PFO closure plus anticoagulation and patients who did not receive any antithrombotic therapy in any of the included studies were excluded from the final analysis.

The outcome of the present study was recurrent strokes at the longest follow up period reported in each study. In the CLOSURE I trial,[6] the outcome included was recurrent strokes or transient ischemic attacks. Data were independently extracted from the included trials by the first and second authors (G.M. and D.S.) on a pre-specified data sheet. Any discrepancy was discussed until there was complete agreement on all the results in the final data sheet.

Network meta-analysis was performed using a Bayesian Markov chain Monte-Carlo model. [10] Dichotomous outcome variables were compared with odds ratios (OR) and 95% credible intervals (CrI). The more conservative random effect model was adopted for final interpretation of the results. Vague (non-informative) priors for between-study heterogeneity were applied to the random effects analyses. Analyses using the fixed effect model was also performed and was only shown in the forest plot diagram. Three chains with different starting variables were used. To achieve convergence, a burn-in phase of 10,000 simulations was performed then 20,000 simulations were performed for the final analyses. Convergence was confirmed by assessing whether the Monte Carlo error is less than 5% of the standard deviation of the effect estimates or between study variance and by visual inspection of Gelman Rubin graphs. [11, 12] The heterogeneity between trials was determined from the median between-trial variance $\tau^2$. A $\tau^2$ estimate of 0.40 was interpreted as a high degree of heterogeneity. [13] Consistency between direct and indirect evidence was assessed by plotting the posterior mean deviance of the individual data points in the inconsistency model against their posterior mean deviance in the consistency model. Consistency was suggested when each data point had a posterior

<table>
<thead>
<tr>
<th>Trial name</th>
<th>Mean age (years)</th>
<th>Female (%)</th>
<th>PFO closure device</th>
<th>Medical therapy</th>
<th>Follow up duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLOSE [5]</td>
<td>44</td>
<td>42</td>
<td>All available devices</td>
<td>aspirin, clopidogrel or aspirin/dipyridamole</td>
<td>Coumadin or direct oral anticoagulants</td>
</tr>
<tr>
<td>CLOSURE I [6]</td>
<td>46</td>
<td>48</td>
<td>STARFlex Septal Closure System</td>
<td>Aspirin</td>
<td>Coumadin</td>
</tr>
<tr>
<td>REDUCE [7]</td>
<td>45</td>
<td>40</td>
<td>HELEX and Cardioform Septal Occluders</td>
<td>aspirin, clopidogrel or aspirin/dipyridamole</td>
<td>N/A</td>
</tr>
<tr>
<td>RESPECT [8]</td>
<td>46</td>
<td>45</td>
<td>Amplatzter PFO Occluder</td>
<td>aspirin, clopidogrel or aspirin/dipyridamole</td>
<td>Coumadin</td>
</tr>
</tbody>
</table>
The process of citation screening and publication selection according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow chart is demonstrated in Figure 1. Initial screening was performed on 148 articles. Five trials were then fully retrieved for review and four trials were included in the final analyses. Two trials compared PFO closure to antiplatelet therapy and/or oral anticoagulation [6, 8], one trial compared PFO closure to antiplatelet therapy alone [7], and one trial compared antiplatelet therapy one time to PFO closure and a second time to oral anticoagulation [5]. Characteristics of trials included in our study are shown in Table 1.

mean deviance contribution close to one. [12, 14] All statistical analyses were performed using WinBUGS 1.4 (MRC Biostatistics Unit, Cambridge, UK) [15] and the Microsoft Excel-based tool (NetMetaXL). [12]
The network included a total of 2821 patients. PFO closure was performed in 1332 patients, 1070 patients received antiplatelet therapy alone and 419 patients received oral anticoagulation alone (Figure 2A). There was significant reduction of recurrent strokes with PFO closure when compared to antiplatelet therapy alone (OR 0.29, CrI 0.07-0.84). On the other hand, the reduction in recurrent stroke when PFO closure was compared to oral anticoagulation was not statistically significant (OR 0.52, CrI 0.1-1.92). Moreover, the difference between oral anticoagulation and antiplatelet therapy in recurrent stroke reduction was also non statistically significant (OR 0.55, CrI 0.13-2.14). Heterogeneity assessment by τ² was 0.9. Network com-

Figure 2. Panel A. Diagram of different treatment arms for recurrent stroke prevention. Panel B. Forest plot of mixed treatment comparisons showing statistically significant reduction of recurrent strokes with PFO closure only when compared to antiplatelet therapy. Both fixed and random effect models are shown.
Comparisons of different treatment modalities are shown in Figure 2B. Plotting the posterior mean deviance of the individual data points in the inconsistency model against their posterior mean deviance in the consistency model suggested reasonable consistency between direct and indirect evidence.

Discussion

The present study is a network meta-analysis comparing three different strategies for recurrent stroke prevention in patients with PFO and cryptogenic stroke, namely, PFO closure, antiplatelet therapy and oral anticoagulation. The main finding of our study is that PFO closure is associated with significant reduction in recurrent strokes when compared to antiplatelet therapy alone.

Trans catheter PFO closure has been compared to medical therapy in randomized trials to evaluate the benefit in recurrent stroke prevention in patients with cryptogenic strokes. In the CLOSURE I [6] and the PC [4] trials as well as the early results of the RESPECT trial, [9] there was no significant benefit of PFO closure over medical therapy. However, when PFO closure was compared to antiplatelet therapy alone in the REDUCE [7] and CLOSE [5] trials, there was significant reduction in recurrent stroke events in patients who underwent PFO closure. Hence, the inclusion of patients on anticoagulation in the medical therapy arm might have contributed to the absence of difference between PFO closure and medical therapy.

A recent updated meta-analysis comparing PFO closure to medical therapy, whether antiplatelets or oral anticoagulation, PFO closure was associated with significant reduction in recurrent strokes. [16] In our study, however, we aimed to evaluate the benefit of PFO closure compared to antiplatelet therapy and oral anticoagulation separately. Based on the results of our study, there is clear benefit of PFO closure over antiplatelet therapy alone. On the other hand, when compared to oral anticoagulation, the benefit of PFO closure is less evident and needs further investigation.

There are limitations to our study that should be considered. There was marked heterogeneity between the results of the trials. However, we used the more conservative random effect model for interpretation of the results. Another limitation is the exclusion of the PC trial as outcomes were not reported separately for patients on antiplatelets and patients on anticoagulation in that trial. A third limitation is that we were unable to perform subgroup analysis based on factors like age, atrial septal aneurysm and shunt size that might have an impact on recurrent strokes. A fourth limitation is that the only outcome evaluated was recurrent strokes because there were no sufficient data on other outcomes that was stratified based on medical therapy used. Finally, the number of patients in the oral anticoagulation arm is small. Therefore, the results pertaining the use of anticoagulation should be taken with caution and more trials are needed to validate our findings.

In conclusion, when compared to antiplatelet therapy alone, PFO closure is an effective treatment strategy for recurrent stroke prevention in patients with PFO who had a cryptogenic stroke. This benefit was not statistically significant when PFO closure was compared with the use of oral anticoagulation.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

References


Retrieval of a Partially Deflated Balloon: A Novel Approach

Stephen Nageotte, MD, MBA*, Cheryl Takao, MD
Division of Cardiology, Department of Pediatrics, Children’s Hospital of Los Angeles, Los Angeles, California, USA

Abstract

A rare complication of balloon dilation in the catheterization laboratory is the inability to deflate the balloon catheter. In the literature, methods described for deflating the balloon all involve puncture or rupture of the balloon while it is within the patient. Here we present a case in which a novel approach was used in order to puncture and deflate the balloon outside of the patient. We further looked at how balloons rupture when overinflated and the potential risks associated with doing this inside of a patient.

Case Presentation

A 3-year-old female with a history of tetralogy of Fallot with Pulmonary Atresia status-post full repair presented with significant continued branch Pulmonary Artery (PA) stenoses. Her past medical history included being an ex-28 week premature infant, chronic lung disease, central sleep apnea, and right femoral vein thrombosis. She had two previous cardiac surgeries (a modified Blalock-Taussig shunt (BTS) in the neonatal period; central pulmonary arterioplasty and VSD repair with 14mm RV to PA conduit at 9 months of age). She also had three previous catheterizations which included angioplasty of left (L)PA and right (R) PA, as well as implantation of a Valeo 9mm x17mm stent (Bard Peripheral Vascular, Tempe, AZ) in the LPA, mounted on a 7mm balloon. Despite this, she had evidence of continued branch PA stenosis with RPA peak gradient of 43 mmHg and LPA peak gradient of 46 mmHg by echocardiogram. She was referred to the catheterization laboratory to evaluate her branch PAs with possible angioplasty and/ or stent implantation.

In the catheterization laboratory, access was first obtained in the right internal jugular vein with a 4 Fr sheath and the left femoral vein with a 6 Fr sheath, as the patient had a history of right femoral vein occlusion. Initial hemodynamics showed the RV pressure to be 82% of the systemic pressure and there was significant intimal proliferation within the LPA stent down to 4.1mm compared to 6.7mm distally. A 0.018” Platinum Plus Guidewire (Boston Scientific Corp., Marlbor-
ough, MA) was positioned from the RIJ sheath into the distal LPA across the LPA stent. The initial short RIJ sheath was exchanged for a 63 cm long 4 Fr sheath (Cook Medical, Bloomington, IN), positioned across the LPA stent. A 7mm x 2cm Sterling Balloon (Boston Scientific Corporation, Marlborough, MA) was advanced through the long sheath, over the wire and positioned within the LPA stent. The balloon was inflated several times until it was positioned well within the stent. After the balloon was inflated a fourth time, however, the balloon catheter could not be fully deflated and could not be housed in the 4 Fr sheath (Figure 1). Of note, we had previously resheathed the balloon by using an inflate-deflate method involving applying positive and then negative pressure to the balloon while pulling the balloon into the sheath to keep the sheath in the pulmonary artery.

Because the balloon could not be resheathed, the sheath, balloon and Platinum Plus wire were all pulled into the right atrium to straighten the curve. Negative pressure was applied many times to the balloon with no success in deflation. The 6 Fr sheath in the LFV was exchanged for an 8 Fr 90cm long sheath in an attempt to snare and cover the deflated balloon. The distal tip of the Platinum Plus wire was snared in the right atrium through this 8 Fr sheath and the balloon was pulled into this larger sheath. Unfortunately, the balloon could not be completely pulled into the 8 Fr sheath, but the profile of the balloon extruding from the sheath was nearly the same width as the 8 Fr sheath (Figure 2). The 8 Fr sheath, snare, balloon, Platinum Plus wire and 4 Fr sheath were then pulled down and out of the left groin with part of the balloon uncovered by the sheath (Figure 3). The partially inflated balloon was exposed and punctured with a needle and deflated manually. It could then be pulled back into the 4 Fr RIJ long sheath and safely removed (Figure 4).

Discussion

The inability to deflate an angioplasty balloon is a known, albeit uncommon, complication of balloon dilation procedures [1]. This complication was first
described in the early literature for the balloon atrial septostomy procedure [2-6]. In some cases, successful deflation of the balloon was eventually achieved by use of the stiff end of a wire advanced either through the second lumen of the balloon catheter or through a second end-hole catheter. With the wire held in position just past the tip of the catheter, the balloon was pulled back onto the wire in order to puncture the balloon [2,5]. In other cases, the balloon was punctured by a fine needle introduced percutaneously, either transhepatically or through the chest wall [3,4]. Both of these approaches have significant risks associated with them. With the first approach, there is the risk of vessel/cardiac damage from the wire. With the latter, there are obvious risks through transcutaneous needle access of the balloon of damage to the heart and surrounding structures. According to Hijazi et al., when a balloon septostomy catheter does not deflate, the first thing to do is to pass a guide wire in the balloon lumen to clear any obstruction. This maneuver was not performed in our case. If this does not work, an injector should be connected to the balloon and 3-5 cc of contrast injected under pressure using 300 psi in order to rupture the balloon [7]. With this approach, rupture of the balloon at high pressure has the risk of embolization of the balloon fragments [8]. Finally, if this does not work, one can try using the stiff end of a guide wire through a second catheter [7].

In order to test the technique of balloon rupture, we overinflated a series of balloon catheters ex vivo to see at what pressure the balloons burst and how they tore. First, we manually burst a series of balloons by slowly over-inflating the balloon with a BasixTouch inflation device (Merit Medical, South Jordan, UT) until the balloon burst. It should be noted that balloon rupture mechanisms are subject to variations due to balloon materials system fatigue. Table 1 lists the sizes and types of balloons tested as well as the burst pressures and type of hole or tear created. During manual over-inflation, all Sterling balloons as well as the Opta Pro, Palmaz Blue and Valeo balloons had longitudinal tears. The Dorado Balloon burst with a pinhole tear in the proximal balloon. The Atlas Gold Balloon did not burst, but the high pressure created a connection between the wire lumen and the balloon lumen within the catheter. This balloon remained unable to deflate. We additionally burst a Miller-Edwards Balloon Septostomy Catheter (Edwards Life sciences, Irvine, CA).
Next, we tested the balloon bursts in the manner Hijazi et al. proposed using a pressure injection. When we did this in the manner described, the power burst pressures are listed in Table 2. The manual burst pressures are shown in Table 1.

At 6 mL of fluid and at a pressure of 6 atm, the balloon burst and the fragment completely ruptured off of the catheter (Figure 5)(Table 1).

### Table 1. Manual burst pressures.

<table>
<thead>
<tr>
<th>Size (mm x cm)</th>
<th>Type</th>
<th>Burst (atm)</th>
<th>Burst (psi)</th>
<th>Listed Burst (atm)</th>
<th>Type of hole/ tear</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 x 2</td>
<td>Sterling</td>
<td>26</td>
<td>382</td>
<td>14</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>5 x 2</td>
<td>Sterling</td>
<td>27</td>
<td>397</td>
<td>14</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>6 x 2</td>
<td>Sterling</td>
<td>24</td>
<td>353</td>
<td>14</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>7 x 2</td>
<td>Sterling</td>
<td>27</td>
<td>397</td>
<td>14</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>16 x 2</td>
<td>Atlas Gold</td>
<td>35</td>
<td>514</td>
<td>18</td>
<td>Hole between wire and balloon lumens</td>
</tr>
<tr>
<td>8 x 2</td>
<td>Opta Pro</td>
<td>17</td>
<td>250</td>
<td>10</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>7 x 2</td>
<td>Dorado</td>
<td>27</td>
<td>397</td>
<td>22</td>
<td>Proximal Pinhole</td>
</tr>
<tr>
<td>6 x 1.7</td>
<td>Palmaz Blue</td>
<td>22</td>
<td>323</td>
<td>10</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>7 x 1.8</td>
<td>Valeo</td>
<td>27</td>
<td>397</td>
<td>14</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>Miller-Edwards BAS balloon</td>
<td></td>
<td>6</td>
<td>88</td>
<td></td>
<td>Complete rupture of balloon</td>
</tr>
</tbody>
</table>

Atm= atmospheres; psi= pounds per square inch

### Table 2. Power burst pressures.

<table>
<thead>
<tr>
<th>Size (mm x cm)</th>
<th>Type</th>
<th>Burst (atm)</th>
<th>Burst (psi)</th>
<th>Listed Burst (atm)</th>
<th>Type of hole/ tear</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 x 2</td>
<td>Sterling</td>
<td>27</td>
<td>401</td>
<td>14</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>6 x 2</td>
<td>Sterling</td>
<td>33</td>
<td>481</td>
<td>14</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>8 x 2</td>
<td>Sterling</td>
<td>33</td>
<td>484</td>
<td>18</td>
<td>Hole between wire and balloon lumens</td>
</tr>
<tr>
<td>9 x 2</td>
<td>Sterling</td>
<td>33</td>
<td>484</td>
<td>18</td>
<td>Hole between wire and balloon lumens</td>
</tr>
<tr>
<td>12 x 2</td>
<td>Atlas Gold</td>
<td>33</td>
<td>484</td>
<td>18</td>
<td>Hole between wire and balloon lumens</td>
</tr>
<tr>
<td>6 x 2</td>
<td>Opta Pro</td>
<td>25</td>
<td>364</td>
<td>10</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>9 x 1.7</td>
<td>Valeo</td>
<td>20</td>
<td>300</td>
<td>12</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>9 x 1.7</td>
<td>Valeo</td>
<td>21</td>
<td>309</td>
<td>12</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>10 x 1.7</td>
<td>Valeo</td>
<td>21</td>
<td>309</td>
<td>12</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>5 x 2</td>
<td>Dorado</td>
<td>37</td>
<td>537</td>
<td>24</td>
<td>Proximal pinhole</td>
</tr>
<tr>
<td>6 x 2</td>
<td>Dorado</td>
<td>37</td>
<td>537</td>
<td>24</td>
<td>Proximal pinhole</td>
</tr>
<tr>
<td>7 x 2</td>
<td>Tyshak Mini</td>
<td>26</td>
<td>383</td>
<td>4</td>
<td>Longitudinal</td>
</tr>
<tr>
<td>16 x 5.5</td>
<td>BIB</td>
<td>Outer- 11;</td>
<td>Outer- 167;</td>
<td>5/5</td>
<td>Longitudinal</td>
</tr>
</tbody>
</table>

| Inner- 25     | Inner -370  |            |            |                    |                                 |
kept auto-stopping due to the peak pressure limit of 300 psi. When we changed the peak pressure limit to 600 psi, we were able to burst the balloons. Table 2 similarly lists the sizes and types of balloons tested as well as the burst pressures and type of hole or tear created, again keeping in mind that balloon rupture mechanisms are subject to variations due to balloon materials system fatigue. Unfortunately, not all burst pressures were captured. Both Dorado balloons developed pinhole tears in the proximal balloon. Additionally, the Atlas Gold as well, as one Sterling balloon, developed a hole between the wire and balloon lumens. However, these balloons did eventually deflate (Table 2).

In our patient, by covering the balloon with the larger sheath, the balloon was able to be positioned outside of the body where it could be punctured. Multiple factors contributed to the success of this technique and may not be applicable in many other situations. In our case, the balloon was not stuck fully inflated to its maximal diameter and thus could be safely pulled back into the right atrium. If there was a structure proximal to the balloon that was narrower than the partially inflated balloon, it could not have been pulled safely into the right atrium, making our technique more difficult. In the selection of the size of the second venous sheath, careful attention needed to be paid to the size of the partially deflated balloon. While our intent was to fully pull the partially inflated balloon into the larger sheath, luckily the exposed balloon was nearly the exact size of the sheath, making it safe to remove from the vessel orifice partially exposed. An even larger sheath could have been used to fully cover the balloon. This technique could not be performed if the angioplasty was being performed on the arterial side. Finally, if the balloon did not partially deflate, it could not have been pulled out of the stent and would have obstructed flow to the LPA. In this scenario, one of the other techniques to rupture the balloon in its position could be employed.

**Conclusion**

We report a novel approach to removal of a balloon that could not be fully deflated. Utilizing this method does not involve puncture or rupture of the balloon while it is still inside the patient. A second venous access point opposite to the site where the balloon catheter enters often can straighten the balloon catheter and assist in its retrieval — the largest size sheath that can be placed safely should be considered to fully cover the balloon. While there are limitations to this approach, removal of a partially deflated balloon in this manner offers a safe alternative to the traditional removal techniques. As new balloon catheters emerge, it is important to know how they will rupture if one plans to rupture the balloon within the patient as there may be a risk of balloon embolization, pinhole balloon rupture or creation of a connection between the wire and balloon lumens. If the patient is stable, it may be worthwhile to first attempt balloon...
rupture outside of the patient with the same type of balloon. However, it should be noted that in vivo rupture mechanics of the balloon can differ when they are subjected to the stresses of use during catheterization. Perhaps more important than the specifics of this technique, is the notion that when faced with difficult clinical situations, the interventional cardiologist needs to think outside the box.

References

8. Vogel JH. Balloon embolization during atrial septostomy. Circulation 1970;42;155–156. DOI: 10.1161/01.CIR.42.1.155

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Transcatheter Repair of Anterior Mitral Leaflet Perforation in a Patient with Mechanical Aortic Valve Using Antegrade and Retrograde Approaches: Case Report

Reda Abuelatta, MD1, Hesham Naeim, MD1,2, Ahmad AlAhmadi, MD1, Saleh Al Ghamdi, MD1, Osama Amoudi, MD1, Ibraheem AlHarbi, MD1, Abdelfatah Elasfar, MD1,3*

1 Adult Cardiology Department, Madinah Cardiac Center, Madinah, Saudi Arabia
2 Cardiology Department, Alazhar University, Cairo, Egypt
3 Cardiology Department, Tanta University, Egypt

Abstract

Mitral leaflet perforations after surgical aortic valve replacement may be iatrogenic or due to endocarditis. We present a 20-year-old female who underwent surgical mechanical aortic valve replacement 8 months prior to this presentation for bicuspid severe aortic valve stenosis. She presented with acute decompensated heart failure with dyspnea and New York Heart Association (NYHA) functional class of III-IV. Transthoracic (TTE) and transesophageal echocardiography (TEE) demonstrated severe mitral regurgitation (MR) through an anterior mitral leaflet perforation. The patient refused surgical repair and percutaneous closure of the perforation was decided and performed using both antegrade and retrograde approaches. In this report, we emphasize the details and challenges of the procedure.

Key Words
Mitral leaflet perforation, Mechanical aortic valve, Catheter-based Mitral valve interventions

Introduction

Anterior mitral leaflet perforation complicating bicuspid aortic valve has been reported and are mostly iatrogenic or related to infective endocarditis [1]. For patients with clinical symptoms, surgical re-intervention is generally the accepted approach [2]; however, reoperation after aortic valve replacement may be associated with an increased risk of mortality and morbidity. Very few sporadic cases of percutaneous closure of perforated anterior mitral leaflet have been reported [3-5]. We describe a case of successful percutaneous closure of an anterior mitral leaflet perforation in a patient who previously had a mechanical aortic valve replacement. We present this case to emphasize the role of double antegrade and retrograde approaches through both femoral arterial and venous accesses and the challenges of the procedure.

Case Report

History

A 20-year-old female was diagnosed with bicuspid aortic valve (AV) and severe aortic stenosis (AS) complicated by infective endocarditis and mechanical AV
replacement was done. Eight months later, she presented to our center with progressive SOB with NYHA class III-IV. Cardiovascular examination revealed 4/6 holosystolic murmur at the apex. Transthoracic echocardiography revealed severe mitral incompetence (Figure 1A). Transesophageal echocardiography (TEE) showed 5x5mm anterior mitral leaflet (AML) perforation through the A2 segment with moderate pulmonary hypertension (estimated systolic pulmonary artery pressure of 50 mmHg). The aortic valve showed a mean gradient of 18 mm/Hg across the AV with no valvular or paravalvular leaks. The left ventricular ejection fraction (LVEF) was 55% and the left ventricular end systolic diameter was 46 mm. Several blood cultures were taken and they showed no bacterial growth. As the patient refused redo surgery, she was referred for a possible percutaneous closure of AML perforation.

Procedure

The procedure was performed under general anesthesia with three-dimensional TEE guidance (PHILLIPS iE33 Cardiovascular Ultrasound, USA) and perioperative prophylactic antibiotics were given. The challenges were crossing the defect in the A2 segment, selecting the appropriate device and the AML behavior after device deployment. Very low transseptal puncture was intended to create a straight tract without tension on the AML during closure. We anticipated that crossing the defect from the LA side will be extremely difficult due to leaflet’s movement away from and parallel to the crossing wire with each heartbeat. In addition, crossing through the mechanical aortic valve may carry the challenge of hemodynamic instability or mechanical disruption of the valve. Arterial and venous femoral accesses were secured and heparin was given. Transseptal access was done; tip deflectable catheter (Agilis St Jude) 8.5 F was introduced.
A Tourque Vue 6F sheath (St Jude Amplatzer) crossed the atrial septum to the AML perforation and was forwarded to the ascending aorta, crossing the mechanical aortic valve with extreme caution as harm may affect the AML, creating more injury or disrupting the mechanical aortic valve. The device chosen for closure needs to be light enough not to affect the AML mobility and needs to be fixed away enough from the closure line to avoid creating new MR through the normal MV orifice. We selected an atrial septal defect closure device (Amplatzer septal occluder, St Jude) size 4 mm with the large disc (16mm) designed to be in the LV side for better stability. During and after crossing the defect, monitoring with real-time 3D-TEE imaging was for effective negotiation in the LA cavity and through the anterior mitral leaflet perforation (Figure 1B, 1C).

With the help of 2 dimensional (2D) TEE at a 120-degree angle with slight clockwise rotation, the mechanical AV and the AML perforation were visualized at the same view helping to cross the defect. Real-time 3D imaging was used to monitor device implantation. Retrograde crossing using cut pigtail catheter and 0.035" Terumo glide wire across one orifice of the aortic valve was successful, avoiding the central slit orifice (Figure 1D). The cut pigtail, with a suitable curve, successfully passed to the LV cavity then was carefully pulled back to the level of the AML, and the wire was easily oriented through the hole of the AML. This step ended by snaring the wire in the LA forming the complete arteriovenous (AV) loop (Figure 1C). A Tourque Vue 6F sheath (St Jude Amplatzer) crossed the atrial septum to the AML perforation and was forwarded to the ascending aorta, crossing the mechanical aortic valve with extreme caution as harm may affect the AML, creating more injury or disrupting the mechanical aortic valve. The device chosen for closure needs to be light enough not to affect the AML mobility and needs to be fixed away enough from the closure line to avoid creating new MR through the normal MV orifice. We selected an atrial septal defect closure device (Amplatzer septal occluder, St Jude) size 4 mm with the large disc (16mm) designed to be in the LV side for better stability. During and after crossing the defect, monitoring with real-time 3D-TEE imaging was
Discussion

Mitral leaflet perforations are generally rare and mostly due to infective endocarditis [1, 6]. Other causes can be iatrogenic and would have occurred during surgery for the aortic valve, or due to autoimmune diseases like systemic lupus, erythematosus, or antiphospholipid syndrome [7]. During aortic valve surgery, anterior mitral leaflet perforation can happen due to the fibrous continuity between the anterior mitral leaflet and the aortic valve [8]. Furthermore, the middle of the anterior mitral leaflet corresponds to the anatomical location of the commissure between the left and non-coronary sinuses of the aortic valve [8]. Because of this close anatomical proximity, either of the two valves may be injured during intervention for the other [8]. In a review of the complications in 475 cases after repair of aortic valve insufficiency done by Dyck et al. [9]; they reported two cases of perforation of the base of the anterior mitral leaflet. In

Follow up

The patient’s clinical course was excellent as she had significant symptomatic improvement with NYHA class I and her follow-up echocardiography showed no residual MR, no diastolic mitral valve gradient and estimated systolic pulmonary artery pressure of 35 mmHg after 6 months following the procedure (Figure 2C and 2D).

Figure 3. Panels A and C. A cartoon showing the location of the anterior mitral leaflet perforation and its relation to the aortic valve, it was 5x5 mm in diameter and 8 mm away from the mitral valve closure line. Panels B and D. Same cartoon showing the ASD closure device in place and its relation to the MV closure line and also relation to aortic valve.
some patients, the mechanism of injury to the mitral valve anterior leaflet is aortic valve regurgitation, with the regurgitant jet being directed towards the mitral valve anterior leaflet, eroding the tissue and leaving the surface more prone to infection [8].

As endocarditis is sometimes associated, infection must be excluded in all patients with leaflet perforation. Perforations in the anterior leaflet may be the only mechanism of mitral regurgitation and if it is large, it may cause severe heart failure and warrant intervention whenever they are diagnosed [1, 2].

In this reported case, multiple blood cultures drawn over two weeks were negative, and no vegetations were seen on TEE. In our case, the perforation may have been either iatrogenic, possibly because of surgical aortic valve replacement, or as a complication of the endocarditis that was diagnosed preoperatively. Surgery is the standard treatment for patients with mitral leaflet perforations [8]; but because of the higher risk related to the redo surgery and the patient’s preference, percutaneous procedure was adopted.

Percutaneous closure carries multiple challenges which include crossing the leaflet perforation, which can be done from either the LA side or the ventricular side, the site of transseptal access, feasibility of crossing and negotiating the mechanical aortic valve, and how much the device can affect the closure mechanism of the mitral valve. We chose a very low septal puncture to avoid stretching the leaflet during manipulation. Then we decided to use either IM catheter or cut pigtail for negotiating the perforation from the LVOT as it was faster and easier. For the mechanical aortic valve, we avoided any excessive tension on the valve and made sure to stay away from the central slit to avoid impairment of both discs simultaneously. The best selection of the closure device was a double disc device with a distance no more than 4mm between the discs, and it is best to have a larger disc towards the high-pressure chamber (LV). Also, there must be enough distance between the edge of the device and the closure line of the mitral valve. We used an atrial septal occluder device size 4 mm with an LV disc of 12 mm and waist thickness of 3 mm. Because of the extreme difficulty of crossing, we preferred keeping a safety wire during device deployment to maintain access in case of accidental loss of the access (Figure 3A-D).

In the study of Velasco S., et al. [3], they used an 8X4-mm Amplatzer Vascular Plug III with no follow up reported. In the study of Raczkiewicz S., et al. [4], they reported using a 6 mm × 3 mm PLD rectangular (Paravalvular Leak Device, Occlutech). They reported five months follow up by transthoracic echocardiography with no residual regurgitation. In the study of Javed U., et al. [5], they used 5mm Amplatzer atrial septal occluder.

In our case, we used an Amplatzer ASD device, however, a small Amplatzer duct occluder II, (5 to 6 mm with a short waist), could be another option since it’s made of micronitinol with a low chance of hemolysis. It can be delivered through a much smaller delivery sheath which could minimize trauma to the mitral valve as well.

Summary

Percutaneous repair of mitral leaflet perforation carries many challenges and is only reserved for appropriately selected patients who have a high risk for surgery or in patients who refuse it. The main challenge during the procedure is the safe crossing through the defect using both the antegrade and retrograde approach. TEE guidance of the procedure is mandatory and real-time 3D is very helpful. Further research is needed to establish mid- and long-term follow up of this approach.

Acknowledgment

We acknowledge Ms. Salma Elasfar from Chatham-kent, ON, Canada, for English language revision.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question
References


Case Report

Journal of Structural Heart Disease, October 2018, Volume 4, Issue 5:240-245
DOI: https://doi.org/10.12945/j.jshd.2018.008.18

Left Main Protection and Emergency Stenting During TAVR with Self-Expandable Valve

Marko Noc, MD, PhD1,2*, Branko Cveticanin, MD1,3, Saibal Kar, MD1,4, Oscar A. Mendiz, MD1,5
1 MC Medicor, Izola, Slovenia
2 Center for Intensive Internal Medicine, University Medical Center, Ljubljana, Slovenia
3 Department of Radiology, General Hospital Izola, Izola, Slovenia
4 Cardiovascular Intervention Center, Cedars-Sinai Heart Institute, Los Angeles, California, United States
5 Interventional Cardiology Department, Cardiology & Cardiovascular Institute. Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina

Abstract

Left main (LM) obstruction is rare but life-threatening complication of transcatheter aortic valve replacement (TAVR) which occurs by displacement of left coronary leaflet toward the ostium or by direct occlusion by the covered skirt of the prosthesis. We report an 88-year old lady with severe aortic stenosis, short distance from annulus to left main origin, shallow/low sinus of Valsalva, and calcification of the left aortic leaflet undergoing TAVR with a self-expandable valve. Instead of recently described “Chimney” stenting with protrusion of a very long stent segment from LM above the prosthesis leaflets and behind the valve frame, a “T-stenting” with stent protrusion only into the left sinus Valsalva was used to secure the LM patency.

Key Words
Emergency left main stenting, TAVR

Introduction

Left main (LM) obstruction is rare but life-threatening complication of transcatheter aortic valve replacement (TAVR) which occurs by displacement of left coronary leaflet over the ostium or by direct occlusion by the covered skirt of the prosthesis [1, 2]. Since this complication may be anticipated if a careful evaluation of aortic computed tomography (CT) scan is performed, LM can be protected up front by placement of a guiding catheter into the LM ostium and advancing a guidewire with undeployed stent into the left anterior descending artery (LAD) [2]. If LM occlusion occurs, the stent can be immediately withdrawn and deployed to reestablish LM patency. Importantly, because of the valve height during the TAVR with a self-expandable valve such as Evolut R (Core Valve Evolut R, Medtronic, Dublin, Ireland), the guiding catheter is located behind rather than above the valve frame. In case of LM occlusion, a "chimney" stenting with protrusion of a very long stent segment from the LM ostium above the prosthesis leaflets and behind the valve frame, has recently been described [3]. We herein present an alternative “T-stenting” strategy with stent protrusion extending only into the sinus of Valsalva toward the valve frame without leaving any stent segment behind the valve frame.

Case report

The patient was an 88-year-old lady with symptomatic severe aortic stenosis (gradient 69/37 mm Hg, AVA 0.4 cm2) and preserved left ventricular ejec-
A 72% patient who was referred for TAVR by the Heart Team because of very high surgical risk (Euroscore II 15.30%, STS 11.06%). Coronary angiography showed diffuse calcification and moderate proximal and mid LAD disease. Pre-procedural CT scan revealed aortic annulus perimeter of 60.1 mm, short distance from annulus to LM origin (6.5 mm), shallow sinuses of Valsalva (average 26.7 mm), a borderline height of left sinus Valsalva (15.1 mm) and a calcified nodule on the left coronary cusp (Figure 1). Because of threatened LM occlusion during valve placement, an EBU 3.5 6 Fr guiding catheter (Medtronic, Dublin, Ireland) was placed via left radial artery to cannulate LM. A .014” BMW guidewire (Abbott Vascular, Abbott

Figure 1. CT measurements of aortic annulus (Panel A), aortic leaflet calcification (Panel B), height of left coronary ostia/left sinus of Valsalva (Panel C) and diameters of sinuses of Valsalva (Panel D).
Park, Illinois, USA) was advanced into LAD followed by placement of undeployed drug-eluting stent Orsiro 3.5x15 (Biotronik, Berlin, Germany). Using the right femoral artery, a 26 mm self-expandable Evolut R valve (Core Valve Evolut R, Medtronic, Dublin, Ireland) was deployed without predilation (Figure 2). Left coronary flow, assessed prior to full deployment, was preserved (Video 1). However, after full deployment, aortography revealed decreased left coronary compared to right coronary flow despite pulling the stent back to the guiding catheter while still maintaining guidewire position (Video 2). Guide injection showed that left leaflet was displaced close to the LM ostium (Video 3). The stent was re-advanced to the LM, protruded proximally close to the valve frame and deployed (Video 4). After placement of an LM stent which extended into the proximal LAD, a haziness was noticed at the distal edge. Stented segment was initially extended with a 2.5x12 Orsiro (Biotronik, Berlin, Germany). Since haziness persisted, additional 2.5x15 mm Orsiro was deployed distally and this resulted in a good angiographic result (Video 5). Aortogram revealed widely patent LM, LAD and circumflex artery with normal flow (Video 6). Except for

Figure 2. Valve deployment to the point of no recapture with the guiding catheter lying behind the valve frame, and guidewire with undeployed stent in the left anterior descending artery.

Video 1. Aortogram before complete valve deployment. Both coronary arteries are well perfused. View supplemental video at https://doi.org/10.12945/jjshd.2018.008.18.vid.01.

Video 2. Aortogram with decreased left compared to right coronary flow after complete valve deployment despite moving of the stent from LAD back to the guiding catheter. View supplemental video at https://doi.org/10.12945/jjshd.2018.008.18.vid.02.

Video 3. Injection through the guiding catheter revealed a mass protruding toward the LM ostium. View supplemental video at https://doi.org/10.12945/jjshd.2018.008.18.vid.03.
Left Main Protection and Stenting During TAVR

Case Report

Noc M. et al.

with its proximal part in a “T-stent” shape. (Figure 3). Twelve months after the intervention, the patient continues to be asymptomatic.

Discussion

Several anatomic factors derived from preprocedural CT scan including low LM ostium, shallow sinuses of Valsalva, severe leaflet calcification with large bulky calcium nodules, high native leaflet length/curved coronary sinus height ratio as well as extreme valve oversizing and “valve-in-valve” procedure, have been identified as high risk features for coronary occlusion during TAVR [2, 4]. A potential risk of coronary occlusion may also be assessed before TAVR using aortic valve predilatation with simultaneous aortogram. If the coronary occlusion is documented, upfront LM protection is mandatory [4]. We did not use this technique because we perform a vast majority of TAVR without predilatation. If we predilate, we always use a small balloon (18-20 mm) to minimize manipulation of the calcified native valve. Predilatation with a smaller balloon would probably underestimate the likelihood of actual LM occlusion during TAVR. Moreover, based on the CT scan, we have already decided to use upfront LM protection. Admittedly, according to CT-derived measurements, a 23 mm rather than 26 mm Evolut R should have been used. Some oversizing with this self-expandable prosthesis was selected because annulus perimeter was at the very upper limit for the 23 mm valve, the native valve was highly calcified, and we have already decided for upfront LM protection.

The optimal strategy for LM protection during TAVR, particularly when using self-expandable Evolut R valve, remains to be defined. The “chimney” technique is generally considered in patients with low sinotubular junction due to potential occlusion of the respective sinus of Valsalva after valve deployment. In our patient, the height of the left sinus of Valsalva was just above the recommended 15 mm. We, therefore, decided for a less complex “T-stenting” and protrude LM stent only above the displaced leaflet and toward the valve frame. Accordingly, the proximal part of the stent was not behind the valve frame. This avoids possible unfavorable interaction between the LM stent and self-expanding valve frame which


Video 5. Post procedural guide injection showed widely patent LM, LAD and left circumflex artery with normal flow. View supplemental video at https://doi.org/10.12945/j.jshd.2018.008.18.vid.05.

Video 6. Final aortogram with comparable left and right coronary flow. View supplemental video at https://doi.org/10.12945/j.jshd.2018.008.18.vid.06.
may also happen after the procedure. We also believe that smaller stent protrusion may facilitate left coronary engagement in the future and may theoretically reduce the risk of stent thrombosis. Of note, using our “T-stenting” technique, we were able to deliver an additional two stents to the LAD through the LM stent without any problems. Retrospectively, we believe that additional LAD stenting was required because there was a distal edge dissection from the initial LM stent which extended into the diffusely diseased proximal and mid LAD. Beside “chimney” and our “T-stenting” techniques, the third option to prevent LM occlusion during TAVR is the recently described "BASILICA" technique with modulating of the native valve leaflet. A single leaflet tear, which would prevent coronary occlusion, is made by leaflet wire traversal and snaring followed by slicing. To our knowledge, this technique has been described so far in only six “valve-in-valve” procedures and one native aortic stenosis. We did not use “BASILICA” because of the lack of experience and fear to increase stroke risk when manipulating with a heavily calcified cusp. However, when discussing any of the herein described LM protection techniques during TAVR, it is important to notice that the number of reported patients is still very limited and long-term efficacy and safety remains to be proven.

Acknowledgements

We are grateful to Natasa Suligoi Cernic, MD for echocardiography and MC Medicor chief medical officer, Metka Zorc, MD, PhD.

Conflict of Interest

Marko Noc and Branko Cveticanin have no relevant conflict of interest. Saibal Kar reports research grant from Edwards Lifesciences and research grants and consultation fees from Abbott Vascular and Boston Scientific. Oscar Mendiz reports proctorship for CoreValve (Medtronic) and consultation fees from Abbott Vascular.

Figure 3. Post procedural computed tomography scan after 3 weeks showing widely patent LM stent protruding toward the valve frame (Panel A) together with three-dimensional reconstruction (Panel B).
References


