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The Evolution and Feasibility of Transcatheter Aortic Valve Replacement in Patients at Low Surgical Risk: A Review

TAVR in Low-Risk Patients

By Aditya Sengupta, MD; Sophia L. Alexis, MD; Gilbert H. L. Tang, MD, MSc, MBA

Author & Funding Disclosures

Dr. Tang is a physician-proctor for Edwards Lifesciences and Medtronic.

Abstract

This past decade has witnessed the evolution of Transcatheter Aortic Valve Replacement (TAVR) as the preferred treatment for symptomatic severe aortic stenosis in patients who are at an intermediate, high, or extreme risk for surgery. Four landmark clinical trials now provide strong evidence that TAVR is non-inferior, and perhaps even superior, to surgery at short- and mid-term follow-up. However, issues such as new-onset left bundle branch block and permanent pacemaker implantation continue to plague outcomes after TAVR, and the long-term durability of the implanted bioprostheses have yet to be determined before TAVR can be universally adopted.

Introduction

Since its first clinical application in 2002, Transcatheter Aortic Valve Replacement (TAVR) has evolved dramatically and has surpassed Surgical Aortic Valve Replacement (SAVR) as the standard of care for patients with severe symptomatic aortic stenosis who are at an intermediate or higher risk for surgery[1-12]. Trial data now suggest that TAVR with a balloon-expandable or self-expanding transcatheter heart valve (THV) is at least as safe and effective as SAVR in patients at low surgical risk[13-16]. Here, we critically assess the data from the recent low-risk TAVR studies in the context of its evolving clinical indications. Outstanding issues, including long-term adverse events and durability, are also discussed.

Landmark Low-Risk Trials

Four landmark trials comparing TAVR with SAVR in patients at low surgical risk are discussed below (Table 1).

Table 1. Summary & Comparison of Low-Risk TAVR Trials

Trial (Ref)	Design	Patients (N)	Risk Stratification	Primary Outcome	Key Secondary Outcomes
PARTNER 3[13]	1:1 Randomization, Transfemoral SAPIEN 3 THV vs. SAVR	503 TAVR 497 SAVR	STS-PROM < 4%	Composite of Death, Stroke, or Rehospitalization at 1 Year: 8.5% in TAVR vs.15.1% in SAVR, Absolute Difference -6.6 Percentage Points, 95% CI -10.8 to 02.5, P < 0.001 for NoninferiorityHR 0.54, P = 0.001 for Superiority	30-Day TAVR vs. SAVR ~ Stroke Rate: 0.6% vs. 2.4%, P = 0.02 Death or Stroke: 1.0% vs. 3.3%, P = 0.01 New-Onset AF: 5.0% vs. 39.5%, P < 0.001
Evolut Low Risk[14]	1:1 Randomization, Medtronic CoreValve/ Evolut R/Evolut PRO THV vs. SAVR	734 TAVR 734 SAVR	STS-PROM < 3%	Composite of Death or Disabling Stroke at 2 Years: 5.3% TAVR vs. 6.7% SAVR, Difference -1.4, Bayesian Credible Interval for Different, -4.9 to 2.1, Posterior Probability of Noninferiority > 0.999	30-Day TAVR vs. SAVR ~ Disabling Stroke: 0.5% vs. 1.7%; Bleeding Complications: 2.4% vs. 7.5%; AKI 0.9% vs. 2.8%; AF 7.7% vs. 35.4%; Moderate/ Severe AR 3.5% vs. 0.5%, PPM 17.4% vs. 6.1%
MedStar Low Risk TAVR[33]	Prospective, Multicenter Feasibility Trial, Transfemoral SAPIEN 3 or CoreValve Evolut R THV vs. SAVR	200 TAVR vs. 200 Historical Propensity-Score Matched, Site-Specific Isolated SAVR Patients (from STS Database)	STS-PROM < 3%	Zero All-Cause Mortality at 30 Days	30 Days: 0 Disabling Stroke, 5.0% PPM, and 14.0% HALT; 1 Year: 3.0% Mortality, 2.1% Stroke, 7.3% PPM; Valve hemodynamics were not impacted by HALT
NOTION (6-Year Outcomes)[36]	1:1 Randomization, Medtronic 1st Generation CoreValve THV vs. SAVR	139 TAVR vs. 135 SAVR Randomized; 6-Year Follow-Up: 50 TAVR vs. 50 SAVR	TAVR vs. SAVR, Mean STS-PROM: 3.0 ± 1.7% vs. 3.0 ± 1.6%	6-Year All-Cause Mortality, TAVR vs. SAVR: 42.5% vs. 37.7% (P = 0.58)	6-Year SVD, TAVR vs. SAVR: 24.0% vs. 4.8% (P < 0.001); Endocarditis: 5.9% vs. 5.8% (P = 0.95); BVF: 6.7% vs. 7.5% (P = 0.89)

The results of four landmark low-risk trials are summarized here. AF = Atrial Fibrillation; AKI = Acute Kidney Injury; AR = Aortic Regurgitation; BVF = Bioprosthetic Valve Failure; CI = Confidence Interval; HALT = Hypoattenuated Leaflet Thickening; HR = Hazard Ratio; NORDIC = Nordic Aortic Valve Intervention; PARTNER = Placement of Aortic Transcatheter Valves; PPM = Permanent Pacemaker; SAVR = Surgical Aortic Valve Replacement; STS-PROM = Society of Thoracic Surgeons-Predicted Risk of Mortality; SVD = Structural Valve Deterioration; TAVR = Transcatheter Aortic Valve Replacement; THV = Transcatheter Heart Valve.

The PARTNER 3 & Evolut Low-Risk Trials

The Placement of Aortic Transcatheter Valves (PARTNER) 3 Trial evaluated the noninferiority and superiority of the Edwards SAPIEN 3 THV (N = 503) versus SAVR (N = 497) in low-risk patients (Society of Thoracic Surgeons Risk of Mortality, or STS-PROM, <4%). The composite endpoint of death from any cause, stroke, or re-hospitalization at one year was significantly lower with TAVR. While the vast majority of the 30-day safety end points were similar between the two treatment arms, the rates of new-onset atrial fibrillation (AF) at 30 days, death or stroke at 30 days, and length of hospitalization were significantly lower with TAVR[13].

Similarly, the Evolut Low-Risk Trial tested the non-inferiority of the Medtronic self-expanding THV (N = 725) against surgery (N = 678) in low-risk patients. Here, three different self-expanding prostheses were used for TAVR due to their availability during the study period (CoreValve, Evolut R, or Evolut PRO). Compared to the PARTNER 3 trial, this study had a longer follow-up period of two years with regards to the composite primary endpoint of death or disabling stroke (5.3% vs. 6.7%, posterior probability > 0.999 for noninferiority). Furthermore, at 30 days, TAVR patients had a lower incidence of AF and life-threatening bleeding, but a higher incidence of at least moderate aortic regurgitation (AR)[14].

Both trials demonstrated that TAVR is at least as efficacious and safe as SAVR in low-risk patients at 1-2 years. In particular, new permanent pacemaker (PPM) implantation, at least moderate paravalvular leak (PVL), and coronary artery obstruction occurred with equal frequency in both arms of the PARTNER 3 study. This is in contrast to previous trials where the aforementioned complications occurred more frequently with SAVR as compared to TAVR[10,17-24]. Furthermore, both studies showed low rates of aortic valve re-intervention at one year with TAVR (0.6% in PARTNER 3, 0.7% in Evolut). As expected, new left bundle-branch block (LBBB) and mild PVL favored SAVR. Of note, TAVR in the Evolut Trial resulted in a higher incidence of PPM implantation (17.4% at 30 days and 19.4% at one year) than SAPIEN 3 TAVR (6.6% at 30 days and 7.5% at one year); the design differences between a balloon-expandable and self-expanding valve may partly explain this discrepancy.

There were a number of limitations common to both studies, the most obvious of which was the lack of follow-up beyond 12-24 months (note that the recently published FinnValve trial, with follow-up of up to three years, corroborate the aforementioned findings)[25]. Structural valve deterioration (SVD), along with the implications of PVL and patient-prosthesis mismatch, will have to be assessed[26-28]. In particular, the Evolut Trial demonstrated a lower rate of severe patient-prosthesis mismatch at one year in the TAVR group (1.8% vs. 8.2%), albeit larger valve areas; the long-term sequelae of this finding will need to be ascertained, especially since severe patient-prosthesis mismatch occurred less frequently compared to prior studies[29,30]. Furthermore, a stronger selection bias may have occurred in the PARTNER 3 trial since a third of screened patients were excluded for various anatomical reasons. In contrast, this rate was approximately 15% in the Evolut trial[31].

These results may also not be universally applicable. For one, bicuspid valvulopathy was an exclusion criterion in both studies, whereas bicuspid disease accounts for approximately 50% of all

AVRs[32]. The vast majority of patients had ejection fractions (EF) >60%, none had severe multi-valvular disease, and women were a minority in both studies (28.9% to 36.2%). Nevertheless, the outcomes from both trials constitute the next step forward in the evolution of TAVR and represent a monumental advance in the treatment of Severe Symptomatic Aortic Stenosis.

Low-Risk TAVR (LRT) Trial

The LRT trial prospectively compared TAVR (N = 200) in low-risk patients (STS-PROM 1.8 ± 0.5%) to a historical control cohort of SAVR patients from the STS database[16]. No patients reached the primary endpoint of all-cause mortality at 30 days. At one year, mortality, stroke, and PPM implantation rates were 3.0%, 2.1%, and 7.3%, respectively. Greater than mild PVL was seen in 1.5%. The improvements in aortic valve area (AVA) and mean gradient (MG) seen at 30 days persisted to one year[33].

In addition to validating the outcomes of the PARTNER 3 and Evolut trials, the LRT study provides a degree of generalizability to low-risk TAVR patients in the United States[10, 11, 34]. Moreover, the LRT study had remarkably low stroke rates at one year.

However, this was not a randomized study, and data are limited to a 12-month period. Interestingly, there was a relatively high rate of leaflet thrombosis post-TAVR, a finding that was comparable to data from the SAVORY (Subclinical Aortic Valve Bioprosthesis Thrombosis Assessed with Four-Dimensional Computed Tomography) and RESOLVE (Assessment of Transcatheter and Surgical Aortic Bioprosthetic Valve Thrombosis and Its Treatment with Anticoagulation) observational registries[35]. This is discussed in greater detail below.

Nordic Aortic Valve Intervention (NOTION) Trial

The NOTION Trial was the first randomized study that compared TAVR with the CoreValve bioprosthesis to trial SAVR in low-risk patients (STS-PROM 3.0 ± 1.7%)[15]. At six years, there was no difference in all-cause mortality. The MG was lower and the effective orifice area (EOA) was larger after TAVR; these differences persisted through all six years of follow-up ($p < 0.001$). SVD was significantly higher in the SAVR arm mainly due to higher post-procedure MGs, but there were no differences in bioprosthetic valve failure (BVF) rates[36].

Even though the outcomes of the NOTION Trial were favorable and comparable to previous high- and intermediate-risk studies, a number of key limitations deserve special attention[37]. First, the indications for new PPM implantation were not entirely clear; coupled with the use of an older generation, non-repositionable self-expanding valve and older deployment techniques, this may partially explain the unusually high rate of PPM implantation (43.7% post-TAVR vs. 8.7% post-SAVR at 5-years, $p < 0.001$)[38]. The implications of the dramatically higher incidence of SVD post-SAVR are also unclear, and the results have to be interpreted with caution. As Tang et al. point out, a disproportionately greater number of larger valves were used in the TAVR arm since echocardiography (rather than CT) was used for sizing. These larger valves also tend to have lower baseline MGs[39]. Lastly, given that mortality and BVF rates were similar between the two groups (and validated by a lack of clinical differences in the CoreValve US pivotal trial), there remain unanswered questions regarding the validity of the SVD definition used in this study[37].

Outstanding Issues & Future Directions

Several issues remain that need to be addressed as TAVR is expanded to low-risk patients.

Stroke

One of the major shortcomings of TAVR after the original PARTNER Trial was the significantly higher rate of stroke with transcatheter therapy[23]. In the early development of TAVR, this was attributed to inexperienced operators and larger delivery systems. The current stroke rates in high-risk patients are decreasing, and stand in stark contrast to those shown in the low-risk trials[13,14,33]. The advent of cerebral protection devices has aided in reducing the stroke risk. For instance, Ndunda et al. performed a meta-analysis in 1,330 patients using the Sentinel Cerebral Protection System (Claret Medical Inc., Santa Rosa, CA, USA) and discovered that it conferred a decrease in clinical stroke at 30 days[40]. In contrast, SAVR stroke rates may never be quite as low given the risks associated with cardiopulmonary bypass, post-operative AF, manipulation of a calcified aorta, and debridement of diseased valves[41].

Paravalvular Leak

Five-year data from the NOTION Trial showed a significant difference in TAVR versus SAVR with mild PVL in 45.9% vs. 16.7% and moderate PVL in 7.1% vs. 0%. The clinical implication of this is still unclear as both groups had similar NYHA functional class and all-cause mortality, even for patients with moderate regurgitation at three months, by the end of the study[43]. One-year results from PARTNER 3 and Evolut showed no significant difference in outcomes in patients with up to mild PVL[13,14].

Conduction Abnormalities

Conduction abnormalities are a well-known complication of TAVR[44]. For instance, Nazif et al. found a 15.4% rate of LBBB at hospital discharge in 1,179 patients at intermediate risk from the PARTNER II Trial and S3i Registry. These patients had a significantly higher mortality at two years[45]. Currently, prophylactic PPM implantation is not merited since ~ 40% of LBBB resolves at one month.

While the PARTNER 3 Trial did not show a difference in PPM insertions, new LBBB at one year was almost three times as high in the TAVR group[131]. In contrast, there was a higher PPM implantation rate in the Evolut Low Risk Trial, but we do not know how many of these patients remained pacer-dependent at one year; the incidence of new LBBB was not reported[13]. The NOTION Trial was able to correlate pacemaker implantation with a difference in mortality of 38.2% versus 21.7% at five years[43]. Though we have not yet solved how to completely avoid this complication, minimizing valve manipulation, avoiding over-sizing, and implanting at higher depths can decrease conduction disturbances[46].

Coronary Reaccess

Careful consideration of coronary height and aortic root dimensions is paramount when choosing the appropriate THV device. Valve positioning is also key, particularly in younger patients in whom reintervention for progressive CAD is probable. Recent evidence suggests that unlike SAVR, the THV orientation relative to native aortic valve commissures appear random, and in >50% of cases, a THV commissure has overlap with one or both coronaries[47]. Understanding native aortic root anatomy and THV features will facilitate the ability to perform coronary reaccess[48]. In addition, depending on the valve type, the initial THV orientation at deployment may or may not impact the final orientation[49,50]. Tang et al. recently reported that crimping the SAPIEN 3 valve at various orientations relative to the delivery catheter had no significant difference in the incidence of severe neo-commissural overlap with the coronaries[49]. On the other hand, having the "Hat" marker of the Evolut catheter facing the outer curve or center front position during initial deployment significantly reduced severe overlap[50]. Newer THVs such as the JenaValve (JenaValve Inc., Irvine, CA) and J-Valve (JC Medical, China) that require commissural alignment for deployment may make coronary reaccess easier. This issue will be important as TAVR expands to younger and lower-risk patients, or those with moderate CAD that may progress with time.

Durability

It is well documented that the longevity of bioprosthetic valves is directly proportional to age. In low-risk patients, we do not yet have robust data, but after five years, re-intervention was necessary in 3/145 in the TAVR group (for PVL) and 1/135 in the SAVR group in the NOTION Trial[43]. In contrast, we do have longer-term data in intermediate/high-risk patients. In 8-year data collected from 990 patients in eight Italian centers using CoreValve, reintervention occurred only 13 times at >30 days[51]. In the 19 patients that survived at the Vancouver center that reported 10-year follow-up, there was 89.5% freedom from reintervention with 76.5% freedom from moderate to severe SVD[52]. Valve durability will be an important issue in younger patients, where redo-TAVR may be limited by the initial THV type and root anatomy[49].

Subclinical Leaflet Thrombosis

Most patients with subclinical leaflet thrombosis are asymptomatic. Often overlooked, it is likely caused by reduced leaflet motion or blood flow in the neo-sinuses that are surrounded by the native aortic valve leaflets[53]. In the PARTNER 3 and Evolut trials, there was no difference in amount of valve thrombosis at 30 days for TAVR versus SAVR. In the LRT study, 14.0% of patients had subclinical leaflet thrombosis at one month[13,14,33]. Even though there was a trend towards a higher stroke rate in patients with hypoattenuated leaflet thickening, the actual event rates were very low (1 vs. 4 strokes) and the trial was not adequately powered to detect differences[33].

Interestingly, Chakravarty et al. found an association between subclinical leaflet thrombosis and cerebrovascular events. In their study of 890 patients, 13% of TAVR valves versus 4% of surgical valves had subclinical leaflet thrombosis with resultant increased rates of all strokes or transient ischemic attacks[35]. Fortunately,

prevention/resolution was possible with anticoagulation, but the question of when to initiate such therapies to improve hemodynamics remains unanswered.

Valve Reintervention

For young patients who may need multiple aortic valve interventions, questions remain regarding the feasibility of redo-TAVR and the ability to extract the THV surgically without replacing the aortic root. TAVR-in-SAVR is approved for high- or extreme-risk patients and is a relatively simple procedure, but comes with a higher risk of coronary obstruction[49,54]. In patients with small surgical valves, balloon valve fracture may be feasible in certain bioprostheses[54]. These choices must be weighed carefully, especially since re-operative SAVR is safe with low mortality in low-risk, younger patients[42]. In failing THVs, redo-TAVR has seldom been described. In contrast to TAVR-in-SAVR, the THV stent frame in redo-TAVR is typically higher than surgical valves with an associated higher risk of coronary obstruction. To this end, Tang et al. have devised a classification scheme using angiographic data describing the aortic root anatomy relative to valve positioning and stent frame dimensions to determine the feasibility of redo-TAVR[49]. Furthermore, because THV orientation relative to native commissures tends to be random and the native aortic valve leaflets become barriers to the coronary orifices, leaflet management techniques, such as Bioprosthetic or native Aortic Scallop Intentional Laceration to prevent Iatrogenic Coronary Artery obstruction during TAVR (BASILICA), may not adequately reduce coronary obstruction risk in redo-TAVR[55].

Endocarditis

Rates of prosthetic valve endocarditis (PVE) after TAVR and SAVR have reportedly been similar, around 1.5% within a year. In 20,006 patients who underwent TAVR, Regueiro et al. discovered a 1.1% incidence per person-year of PVE with mean time to diagnosis of 5.3 months post-implantation. Younger age was a risk factor (although this study took place with a higher risk cohort). Eighty-two percent were treated with antibiotics alone and 14.8% required surgical intervention (10.8% were transcatheter valve explantations)[56]. In another study, based on the FinnValve Registry 6,463 consecutive patients who underwent TAVR and SAVR were found to have no significant difference in risk (3.4/1,000 person-years vs. 2.9/1,000 person-years) over an 8-year observational time period[57]. Yeo at al. similarly found younger age as an independent risk factor when looking at 41,025 patients with TAVR (OR 0.92, 95% CI 0.89 to 0.95), and so did Kolte et al. in an evaluation of 29,306 TAVR patients. Larger stent posts, groin access, involvement of pacemaker leads (given higher rate of implantation), and decreased sterility outside of a main operating room could be possible reasons[58,59].

Conclusion

TAVR is rapidly becoming an appealing option for a younger, low-risk population that may not wish to undergo surgery. Given recent trial data, estimated surgical risk no longer directs the dichotomy between TAVR and SAVR. As this paradigm shifts, issues such as new conduction abnormalities, coronary reaccess, structural valve deterioration and long-term durability all need to be discussed with the patient. Appropriate patient selection based on clinical and anatomic factors is of the utmost importance when considering candidacy for TAVR versus SAVR.

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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 bioprosthetic 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, blistering, or peeling of skin, 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.

Important Labeling Information for Geographies Outside of the United States

Indications: The Melody™ TPV is indicated for use in patients with the following clinical conditions:

- Patients with regurgitant prosthetic right ventricular outflow tract (RVOT) conduits or bioprostheses with a clinical indication for invasive or surgical intervention, OR
- Patients with stenotic prosthetic RVOT conduits or bioprostheses where the risk of worsening regurgitation is a relative contraindication to balloon dilatation or stenting

Contraindications

- Venous anatomy unable to accommodate a 22 Fr size introducer sheath
- Implantation of the TPV in the left heart
- RVOT unfavorable for good stent anchorage
- Severe RVOT obstruction, which cannot be dilated by balloon
- Obstruction of the central veins
- Clinical or biological signs of infection
- Active endocarditis
- Known allergy to aspirin or heparin
- Pregnancy

Potential Complications/Adverse Events: 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.

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

The Melody Transcatheter Pulmonary Valve and Ensemble II Transcatheter Delivery System has received CE Mark approval and is available for distribution in Europe.

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710 Medtronic Parkway
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Gilbert H. L. Tang, MD, MSc, MBA
Corresponding Author
Surgical Director, Structural Heart Program Mount Sinai Health System
Department of Cardiovascular Surgery
1190 Fifth Avenue, GP2W, Box 1028
New York, NY, USA
T. 212.659.6800 F. 212.659.6818
gilbert.tang@mountsinai.org

Aditya Sengupta, MD

Cardiothoracic Surgery Resident
Icahn School of Medicine at Mount Sinai
Mount Sinai Health System
New York, NY, USA

Sophia L. Alexis, MD

Cardiothoracic Surgery Resident
Icahn School of Medicine at Mount Sinai
Mount Sinai Health System
New York, NY, USA

A Melody for the Elderly

By Aphrodite Tzifa, MD, FRCPCH; Dimosthenis Avramidis, MD; Dimitra Loggitsi, MD, PhD; Konstantinos Spargias, MD, PhD

Transcatheter implantation of pulmonary valves for treatment of Right Ventricular Outflow Tract dysfunction was first reported in 2000[1]. Since then, over 10,000 patients have received transcatheter therapy with a Melody percutaneous valve for failed pulmonary conduits. The vast majority of these patients have been children or young adults, mostly because Complex Congenital Heart Disease surgery started taking place after the 1970's.

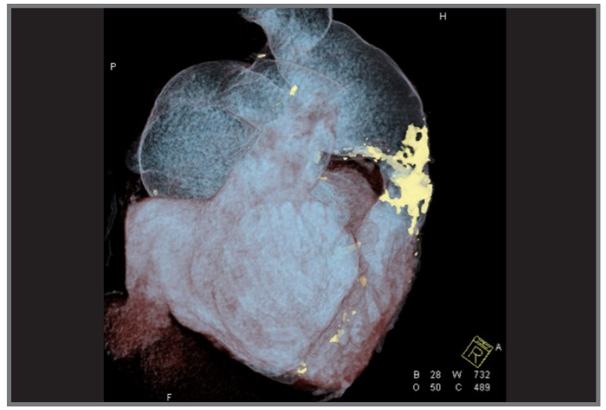


Figure 1. Transparent Volume-Rendering image (VRT) - Lateral RVOT view with demonstration of the heavily calcified homograft.

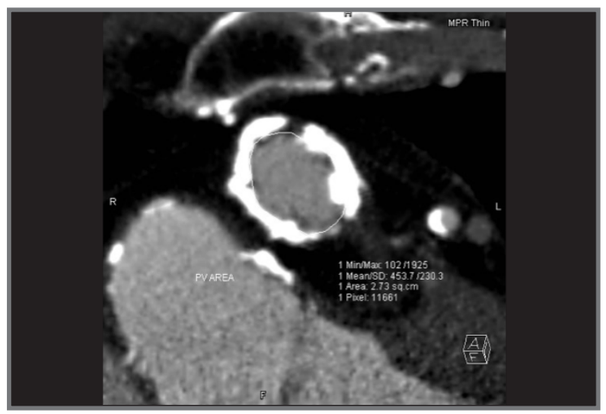


Figure 2. CT angiographic image with planimetric measurement of the effective area of the calcified pulmonary homograft.

However, older patients who have received a pulmonary conduit for other indications, such as the Ross procedure for Aortic Valve Disease, may present with conduit failure at a more advanced age. A contributing factor to the latter is also the fact that the pulmonary homograft longevity is superior in the Ross setting rather than in other Congenital Heart Disease entities[2].

We report the case of an 81-year-old patient who presented with pulmonary homograft dysfunction and received transcatheter valve therapy in the pulmonary position with the use of a 22mm Melody valve inside a 31-year old pulmonary homograft. To the best of our knowledge, this is the oldest patient to date who has received transcatheter pulmonary valve implantation therapy.

The patient presented with aortic stenosis at the age of 50 years and underwent a Ross operation in 1986 by Professor Donald Ross. His homograft was noted to be calcified and stenosed 14 years later, but due to good clinical condition, the patient had refused a re-operation. He remained under frequent follow-up and became symptomatic with clinical signs of pedal oedema and ascites, requiring multiple hospitalisations, one year before the patient was referred for transcatheter therapy.

Non-invasive imaging with CT and MRI showed a heavily calcified and stenosed homograft (Figures 1,2), with the coronary arteries at a safe distance from the area of interest (Figure 3a, b). Echocardiographic peak Doppler derived pressure gradient across the pulmonary homograft was 60mmHg and pulmonary regurgitant fraction as assessed by MRI phase contrast flows was 28%. Right ventricular ejection fraction was 55% and RVEDV measured 115ml/m^2. Due to advanced age and multiple vascular operations, the patient also underwent an MRI assessment of his femoral veins to delineate the vascular anatomy and to choose the entry point for insertion of the 22Fr Melody Ensemble system. The procedural steps were the usual with pre-implantation of a covered stent followed by implantation of a 22mm Melody valve. Although the 31-year old homograft was heavily calcified, the stent and valve were implanted without any disruption to the calcified homograft wall. After valve implantation, haemodynamic assessment revealed an RV-PA pressure gradient drop from 40mmHg to 5mmHg, whilst MPA angiogram showed no residual pulmonary valve regurgitation.

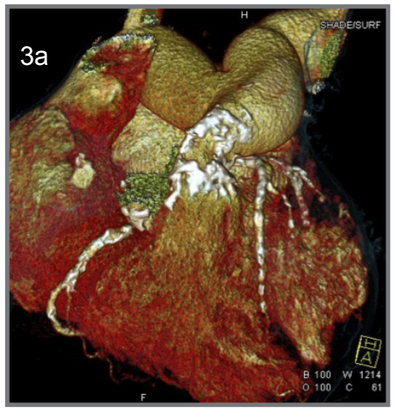
The patient did not need admission to the ICU and was discharged home from the ward after 48 hours. He improved significantly post-procedure, and at 1-month follow-up, his ascites had therapy resolved completely, whilst diuretic decreased from a combination of three

drugs to just 20mg of Furosemide once a day.

Discussion

Transcatheter valve implantation has become routine therapy for elderly patients with Aortic Valve Disease[3] and for selected congenital patients with pulmonary or Tricuspid Valve Disease[4]. Moreover, reports of hybrid or transcatheter implantation of valves in the mitral position have been on the rise[5]. The benefit of a transcatheter approach versus open-heart revalvulation is greater in multi-operated patients with significant co-morbidities or in patients of advanced age. Valve-in-valve therapy in the pulmonary position has received approval when a homograft or conduit has already been implanted during previous surgery and has become dysfunctional. The life-span of a pulmonary homograft is usually between 10-20 years, as they most frequently get stenosed, regurgitant or both, due to calcification.

Our report depicts the wide age span that transcatheter valve therapy in the pulmonary position may be suitable for. It also highlights the need for close collaboration between Adult and Congenital Cardiologists, as patients who might benefit from transcatheter pulmonary valve therapy can be found even amongst the elderly. This is particularly important as modern transcatheter therapies are continuously expanding their potential applications and, on the other hand, the congenital population is growing older.



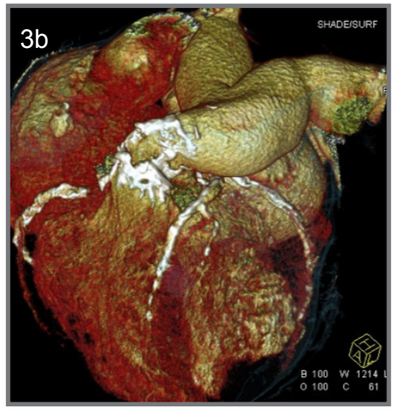


Figure 3. 3D-CT angiographic assessment of the coronary arteries in relation to the pulmonary homograft, anterior (3a) and left lateral (3b) view.

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Aphrodite Tzifa, MD, FRCPCH

Director of Department of Congenital Heart Disease
Mitera Hospital, Hygeia Hospital Groups
Athens, Greece
T. +302106869788
A.Tzifa@btinternet.com

Dimosthenis Avramidis, MD

Department of Congenital Heart Disease
Mitera Hospital, Hygeia Hospital Groups
Athens, Greece

Dimitra Loggitsi, MD, PhD

Department of Radiology
Mitera Hospital, Hygeia Hospital Groups
Athens, Greece

Konstantinos Spargias, MD, PhD

Division of Transcatheter Valve Therapies
Hygeia Hospital
Athens, Greece

Medical News, Products & Information

Compiled and Reviewed by Kate Baldwin and Tony Carlson

B. Braun Interventional Systems Expands its Congenital and Structural Heart Portfolio With the EmeryGlide MR Conditional Guidewire From Nano4Imaging

B. Braun Interventional Systems Inc. (BIS), a company dedicated to providing innovative solutions in the field of congenital and structural interventional cardiology, today announced it has signed an exclusive US distribution agreement with Nano4imaging for their EmeryGlide™ guidewire.

The EmeryGlide MR conditional guidewire is the latest cutting-edge addition to BIS' congenital and structural heart portfolio. "We are excited to collaborate with Nano4imaging to bring to the U.S. market this compelling product and procedural innovation to perform MRI guided interventions," said Dave Mittl, B. Braun Interventional Systems Corporate Director of New Business Development. "Our team continues to invest its resources into being at the forefront of providing clinicians with clinically relevant innovations in the area of congenital and structural heart care."

The EmeryGlide is an MR conditional guidewire that enables MRI guided cardiac catheterizations. Under defined conditions, the wire can be used in combination with MR compatible products for the introduction or placement of diagnostic catheters or other interventional devices. The EmeryGlide is the only MR conditional guidewire available in the United States.

"We are glad that with B. Braun Interventional Systems as a strong new partner, our EmeryGlide will find its way to the U.S. pediatric market with the ability to extend to other interventional MRI applications," commented Christoph Manegold, CEO, Nano4imaging USA, LLC.

Real-time magnetic resonance imaging (MRI) guidance enables excellent soft tissue visualization and does not use ionizing radiation to perform diagnostic and interventional cardiac catheterizations, a particularly important consideration in congenital heart defect patients who often need multiple procedures throughout their lifetime, including X-ray-dependent cardiac catheterization. In addition to reduced X-ray exposure for patients and clinicians, MRI enables additional and more detailed imaging, which in many cases improves diagnostics.

"Cardiac catheterization in the MRI suite has been primarily limited to diagnostic procedures due to lack of MRI compatible guidewires and other interventional equipment. The availability of the EmeryGlide guidewire in the United States, the only 510(k) cleared MR conditional guidewire, has enabled me and some of my other iCMR colleagues to advance catheters to places that were previously not possible, especially in complex congenital heart disease patients," said Dr. Suren Reddy from UT Southwestern/Children's Medical Center, Dallas. "This guidewire has the potential to significantly advance the field of MR guided cardiac catheterizations and interventions."

Dr. Madhav Swaminathan Elected President of the American Society of Echocardiography

Madhav Swaminathan, MD, MBBS, MMCi, FASE, has taken the helm as President of the American Society of Echocardiography (ASE). His presidency, which will last one year, marks the first time that an anesthesiologist has been elected to head ASE in its 44-year history.

Dr. Swaminathan addressed the members of the Society at their annual business meeting and shared his excitement for leading ASE for the next year. He said, "ASE has taken an unprecedented step of tapping the first anesthesiologist as its president. It is a bold statement about celebrating diversity. I look forward to leading the Society that has opened its arms to everyone who is interested in cardiovascular ultrasound. In addition to guiding ASE into a new strategic plan beginning in 2020, I am committed to building a network of leaders that supports the well-being of the entire cardiovascular ultrasound community."

Dr. Swaminathan is Board-Certified in Anesthesiology and Perioperative Transesophageal Echocardiography. He is Vice Chair for Faculty Development, Duke Anesthesiology, and Professor of Anesthesiology, Duke University School of Medicine. He joined the faculty at Duke in 2002 and rose rapidly to the rank of professor with tenure, winning teaching and community service awards along the way. Administratively, he served as Director, Perioperative Echocardiography Service from 2004-2014, where he transformed Duke's research in echocardiography, developed new echo educational initiatives, and brought practitioners of cardiovascular ultrasound together. In his role as the vice chair for faculty development, he is responsible for nurturing the faculty with the vision, mentorship, opportunities, and infrastructure they need to be leaders in changing the face of perioperative medicine. His research interests focus on diastolic dysfunction as well as kidney outcomes after cardiac surgery. He has published over 160 papers in peer-reviewed journals and has written several editorials and book chapters,and is a co-editor of a popular textbook on perioperative echocardiography.

In 2015, Dr. Swaminathan was named the 16th Feigenbaum Lecturer at the ASE Scientific Sessions. This was the first time an anesthesiologist was given this honor, which is awarded to a young investigator in recognition of their significant contributions to research in the field of cardiovascular ultrasound and their potential to continue at a high level of achievement. Dr. Swaminathan has held many significant roles on ASE committees, including chair of the Membership Committee and chair of the Council on Perioperative Echocardiography

Madhav Swaminathan, MD, MBBS, MMCi, FASE, has taken the helm as President of the American Society of Echocardiography (ASE).

(COPE). He has also served on the Industry Relations Committee, Education Committee, and as co-chair and chair of the Perioperative Echocardiography track for ASE's Scientific Sessions from 2011-2015. He currently serves on the editorial board of CASE, ASE's cardiovascular imaging case reports journal. He has participated on other writing groups and taskforces, including Governance, Public Relations, and Non-Traditional Users.

Dr. Swaminathan is active in a number of other professional societies, including the American Medical Association, the Society of Cardiovascular Anesthesiologists, the American Heart Association, the Association of University Anesthesiologists, and the International Anesthesia Research Society.

He attended college in India, earning an MBBS with distinction at Delhi University. He completed residencies and fellowships in anesthesia and cardiac anesthesia at Catholic University of Louvain, Belgium, the Royal Victoria Hospitals Trust, Belfast, UK, and Duke University, Durham, NC. He has also received a Master of Management in Clinical Informatics from Duke University in 2016.

Dr. Swaminathan served as ASE's vice President and President-Elect prior to ascending to President. Joining him as new members of the 2019-2020 Executive Committee are Vice President, Raymond Stainback, MD, FASE, Texas Heart Institute, Baylor St. Luke's Medical Center, Houston, TX; and Secretary, Matt Umland, ACS, RDCS, FASE, Aurora Healthcare, Aurora, WI.

Continuing ASE officers include: President-Elect, Judy Hung, MD, FASE, from Massachusetts General Hospital, Boston, MA; Council Representative, Wyman Lai, MD, MPH, FASE, CHOC Children's Hospital, Orange, CA; and Treasurer, Carol Mitchell, PhD, RDMS, RDCS, RVT, RT(R), ACS, FASE, University of Wisconsin Hospital, Madison, WI, and Immediate Past President, Jonathan R. Lindner, MD, FASE, of Oregon Health & Science University, Portland, OR.

In addition to the new officers, the ASE membership has elected the following new board of directors members to two-year terms: Piers Barker, MD, FASE, Duke University Medical Center, Durham, NC (Pediatric Council Steering Committee Chair); Alina Nicoara, MD, FASE, Duke University Medical Center, Durham, NC (Perioperative Council Steering Committee Chair); Alan S. Pearlman, MD, FASE, Seattle, WA (Past President); Peter Rahko, MD, FASE, University of Wisconsin, Milwaukee, WI; Jennifer Schaaf, BS, ACS, RDCS, FASE, The Christ Hospital Health Network, Cincinnati, OH; Vandana Sachdev, MD, FASE, National Institute of Health, Bethesda, MD; and Cathy West, MSc, DMU (CARDIAC), AMS, EACVI CHD, FASE, Royal Brompton Hospital, London, UK (International). Geoffrey Rose, MD, FASE, Sanger Heart & Vascular Center, Charlotte, NC, will also serve on the board after being reappointed for his exceptional service.

Edwards PASCAL Transcatheter System Receives CE Mark

PRNewswire – Edwards Lifesciences Corporation (NYSE: EW), the global leader in patient-focused innovations for Structural Heart Disease and Critical Care monitoring, today announced the Edwards PASCAL transcatheter valve repair system has received a CE Mark for the treatment of patients with mitral regurgitation.

"Mitral valve disease is complex, varied and prevalent, and patients are in significant need of multiple safe and effective therapies to treat debilitating symptoms that can lead to a high rate of mortality," said Bernard J. Zovighian, Edwards' Corporate Vice President, Transcatheter Mitral and Tricuspid Therapies. "The introduction of the PASCAL system to clinicians and patients in Europe provides a differentiated, minimally-invasive therapy to address the needs of patients with mitral regurgitation."

The PASCAL system is designed for effective reduction of mitral regurgitation while respecting the native anatomy. It features contoured, broad paddles to maximize coaptation of the mitral leaflets, and a central spacer that fills the regurgitant orifice area. The delivery system allows for independent leaflet capture and the ability to optimize leaflet position.

"The PASCAL system is uniquely designed for optimized valve leaflet capture and coaptation, and to help operators achieve their ultimate goal of safe and effective mitral regurgitation reduction for their patients," said Konstantinos Spargias, THV Director, Hygeia Hospital, Greece, and an investigator in the multi-national prospective CLASP Study.

The PASCAL system is one of multiple transcatheter repair or replacement therapies designed to address mitral and tricuspid valve diseases that are under development by Edwards. It represents the culmination of 20 years of innovation by Edwards to develop a novel, differentiated and advanced platform for patients in need. The company is building upon a long history of knowledge, experience and commitment to advance transformative therapies and develop a robust body of clinical evidence.

The PASCAL system is not approved in the United States; the CLASP IID U.S. pivotal trial is currently enrolling patients with symptomatic primary mitral regurgitation.

Dr. Spargias is a consultant to Edwards Lifesciences.

Geneva Health Solutions Hits Critical Milestones Driving Growth; Predicts Cardiac Data Explosion in 2019

Geneva Health Solutions (GHS), the leading cloud-based technology platform and service for managing data from implantable cardiac devices, announces triple-digit revenue growth in 2018, an indicator of the explosive growth of implantable cardiac device data expected in 2019. This year, GHS has also tripled its client base and workforce, quadrupled the number of devices being monitored through its service and increased its revenue more than ten-fold.

"Data deluge from implanted cardiac devices has hit critical mass for cardiac practices, physicians and staff, and our ability to become an extension of their team and implement an effective remote monitoring program is truly improving patient care," said Yuri Sudhakar, CEO of Geneva Health Solutions. "Armed with actionable information every day, cardiologists can pro-actively reach out to patients with device issues and arrhythmias like atrial fibrillation and heart failure diagnostics well in advance of a significant health problem."

The GHS patent-pending platform aggregates cardiac device data from all major implantable cardiac device manufacturers' remote monitoring portals and in-office checks. The GHS remote monitoring service helps providers manage the incoming data and alerts, improves patient compliance and has significant clinical benefits including the early detection of device issues and arrhythmias as well as a reduction in hospitalizations, and thus patient care costs.

Significant Milestones for 2018 Include:

- Forty-four New Cardiology Sites in 2018 – Geneva Health Solutions' client list has grown from 16 clinics to over 65 cardiology sites in one year, with 45 of those sites also using the Geneva Health Solutions Remote Monitoring Service.
- Improved Remote Monitoring Pathway Financials – GHS eliminates workflow inefficiencies, optimizes reimbursement, and provides device clinic resource support to ensure clinics can properly implement the remote monitoring standard of care. With the GHS service, cardiology providers have experienced over a 70% improvement in the profitability for the standard of care by optimizing reimbursement and reducing costs.
- Increased Patient Outreach – Today, more than 30,000 are being monitored by the GHS Remote Monitoring Service, a 4x growth from last year. GHS has become an extension of the device clinic, assisting overextended clinic staff, improving patient adherence and compliance as well as mitigating liability.
- Geneva University Founded in 2018 – Geneva University is a rigorous training program in data analytics and preparation for cardiac device technicians to help them achieve the highest standards in cardiac remote monitoring.
- Employee Growth – In response to the company's unprecedented growth, GHS nearly tripled its employee count this year. More than 40 new cardiac device

specialists were added to the Geneva team.
- Specialty Expansion for Children with Cardiac Devices – GHS has also boosted its impact in pediatric cardiac care through contracts with Nemours Health's Dupont Hospital for Children and Pediatric Cardiology Center of Oregon to help monitor children with cardiac devices.

www.genevahealthsolutions.com

Texas Children's Hospital Again Ranks Among the Best Children's Hospitals Nationally by US News & World Report

Texas Children's Heart Center and Pulmonology Rank 1st Nationwide

Texas Children's Hospital is proud to consistently be recognized as a leader in pediatric care by U.S. News & World Report, tying for third overall in their 13th annual Best Children's Hospitals rankings. Again, Texas Children's is named as the best place in the country for children in need of both pediatric cardiology and heart surgery, as well as pulmonary care. Additionally, six of the hospital's subspecialties rank in the top three and all rank within the top 10.

For more than a decade, no other pediatric hospital in the state ever achieved an overall ranking as high as Texas Children's. For more information, visit texaschildrens.org/best.

Ranked Among the Top 10 in All Subspecialties

In addition to ranking pediatric hospitals overall, US News also ranks the top 50 pediatric hospitals across 10 major subspecialties each year. Texas Children's is one of only 10 children's hospitals across the country to achieve the Honor Roll designation, and the only hospital in the state of Texas awarded this distinction.

With the partnership of academic affiliate Baylor College of Medicine, Texas Children's is a distinguished leader and resource for health and hope to children and their families. The hospital earns the U.S. News Honor Roll distinction by ranking as one of America's best in:

- #1 Cardiology and heart surgery
- #1 Pulmonology
- #2 Gastroenterology and GI surgery
- #2 Nephrology (kidney disorders)
- #3 Cancer
- #3 Neurology and neurosurgery
- #6 Urology
- #7 Neonatology (tied for 7)
- #8 Diabetes and endocrinology
- #10 Orthopedics

Global Leader in Pediatric Heart Care

For more than 60 years, the integrated, multidisciplinary team at Texas Children's Heart Center has combined cutting-edge technology with a compassionate and family-centered approach to care. Annually, nearly 1,000 surgeries and more than 1,300 cardiac catheterization procedures are performed in the new, state-of-the-art Lester and Sue Smith Legacy Tower, the home of Texas Children's Heart Center, where a team-based approach brings experts in every aspect of cardiac care to the bedside.

Texas Children's Heart Center cardiologists, congenital heart surgeons, cardiac anesthetists and cardiac intensivists are world-renowned leaders in the field and work together to treat some of the rarest and most complex heart cases from Houston, across Texas, the U.S. and around the world. The multidisciplinary team strives to provide unparalleled care at every point from diagnosis through treatment and follow-up, in order to achieve the best possible care for each patient.

Areas of special expertise of the Heart Center include: cardiac catheterization, congenital heart surgery, electrophysiology, adult congenital heart disease, cardiac nursing, cardiac critical care, coronary artery anomalies, pulmonary vein stenosis, Marfan syndrome and connective tissue disorders, and one of the largest cardiac transplant and ventricular assist device programs in the world.

The Destination for Children with Lung Disease

Offering services to treat children dealing with any breathing problem, Texas Children's pulmonary team manages a wide range of common and rare pediatric lung disorders. With more than 16,000 outpatient visits annually, the hospital has

Texas Children's Heart Center and Pulmonology is ranked 1st nationwide.

numerous specialty clinics focused on severe asthma, cystic fibrosis, pulmonary hypertension, lung transplant clinic, tracheostomy and ventilator, aerodigestive multispecialty clinics, sleep disorders, and more.

The hospital's pulmonary team offers a wide array of specialized programs. Texas Children's Cystic Fibrosis (CF) Care Center is the only accredited pediatric CF center in Southeast Texas. Its Pulmonary Hypertension Program is one of the few programs in the U.S. dedicated to treating children; because of this, Texas Children's has extensive experience in the diagnosis and treatment of infants, children and teens with this rare condition. Additionally, Texas Children's has one of the largest and most successful pediatric lung transplant programs in the world and is one of only two institutions worldwide that performs an average of 10 pediatric lung transplants each year. With a typical wait time of four to six months for new lungs, Texas Children's transplants children from all areas of the United States. As a result of these programs and others, Texas Children's is also one of the largest training programs of future pediatric lung specialists.

www.health.usnews.com/best-hospitals/pediatric-rankings

CONGENITAL CARDIOLOGY TODAY

Founder & Senior Editor
Tony Carlson
Tony@cct.bz

Editor-in-Chief
Kate Baldwin
Kate@cct.bz

Co-Founder & Medical Editor
John W. Moore, MD, MPH
Dr.John@cct.bz

Editor-in-Chief Emeritus
Richard Koulbanis

Staff Editor
Loraine Watts

Staff Editor & Writer
Virginia Dematatis

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Do not implant the Nit-Occlud PDA into patients who have endocarditis, endarteritis, active infection, pulmonary hypertension (calculated PVR greater than 5 Wood Units), thrombus in a blood vessel through which access to the PDA must be obtained, thrombus in the vicinity of the implantation site at the time of the implantation or patients with a body weight < 11 lbs. (5kg). An angiogram must be performed prior to implantation for measuring length and diameter of the PDA. Only the pfm medical implantation delivery catheter should be used to implant the device. Administration of 50 units of heparin per kg bodyweight should be injected after femoral sheaths are placed. Antibiotics should be given before (1 dose) and after implantation (2 doses) to prevent infection during the implant procedure. Do not implant the Nit-Occlud PDA in an MR environment. Do not pull the Nit-Occlud coil through heart valves or ventricular chambers. Contrast media should not be injected through the implantation catheter. The catheter must not be connected to high pressure injectors. Patients may have an allergic response to this device due to small amounts of nickel that has been shown to be released from the device in very small amounts. If the patient experiences allergic symptoms, such as difficulty in breathing or swelling of the face or throat, he/she should be instructed to seek medical assistance immediately. Antibiotic prophylaxis should be performed to prevent infective endocarditis during first 6 months after coil implantation. Potential Adverse Events: Air embolism, Allergic reaction to drug/contrast, Apnea, Arrhythmia requiring medical treatment or pacing, Arteriovenous fistula, Bacterial endocarditis, Blood loss requiring transfusion, Chest pain, Damage to the tricuspid or pulmonary valves, Death, Embolization of the occluder, requiring percutaneous or surgical intervention, Endarteritis, False aneurysm of the femoral artery, Fever, Headache/ Migraine, Heart failure, Hemolysis after implantation of the occluder, Hypertension, Hypotension or shock, Infection, Myocardial infarction, Occluder fracture or damage, Perforation of the heart or blood vessels, Stenosis of the left pulmonary artery or descending thoracic aorta, Stroke/TIA, Thromboembolism (cerebral or pulmonary), Valvular Regurgitation, Vessel damage at the site of groin puncture (loss of pulse, hematoma etc.).
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