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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.

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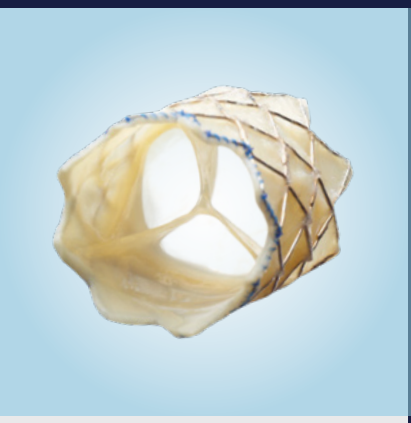

Melody™

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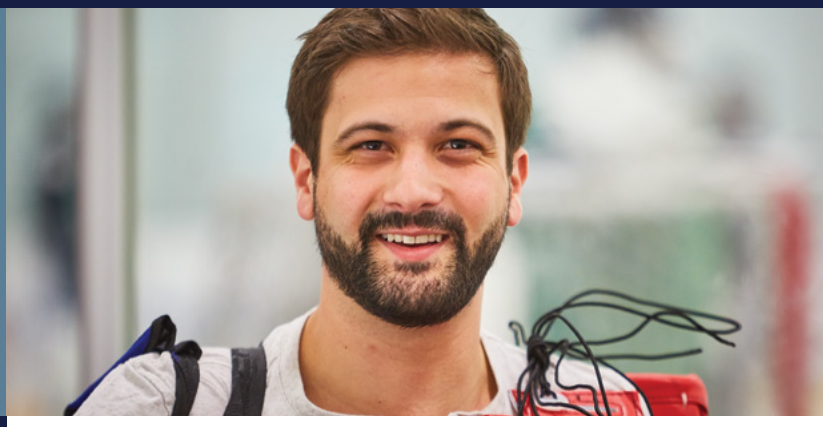

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Melody™ Transcatheter Pulmonary Valve, Ensemble™ II Transcatheter Valve Delivery System

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 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.

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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.

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.

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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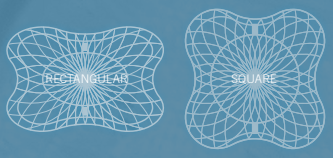

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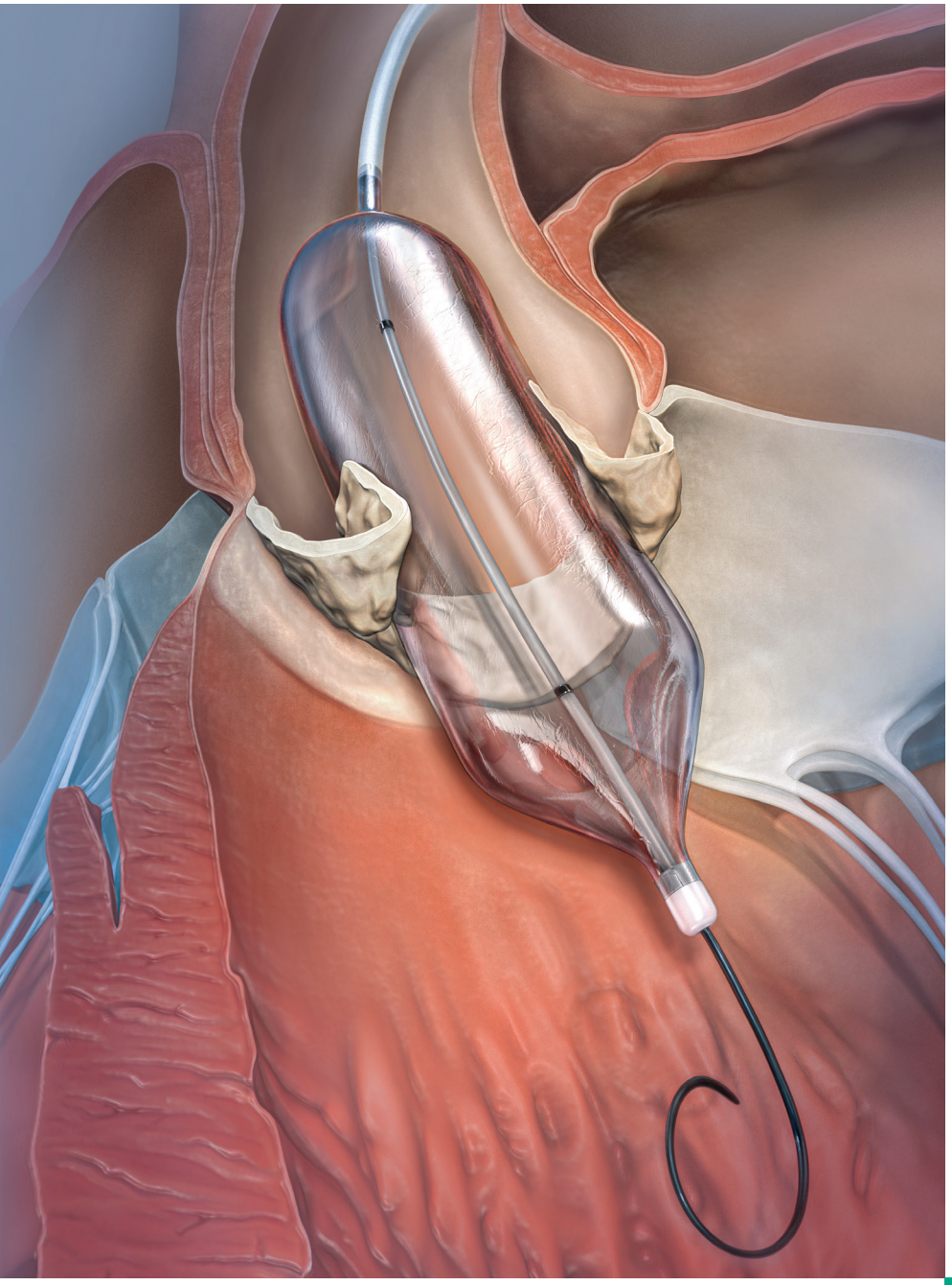

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Endovascular VSD Closure with Lifetech KONAR-Multifunctional Occluder - Novel Device

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Abstract

The aim of this publication is to report the short and mid-term results of the closure of perimembranous and muscular Ventricular Septal Defect (VSDs) with the novel device, Konar-Multifunctional Occluder (MFO).

Introduction: The endovascular closure of Ventricular Septal Defect (VSD) is a well-established procedure. The Konar Multifunctional occluder (MFO) allows closure of large VSDs in an antegrade or retrograde way.

Materials and Method: Since October 2017, the VSD closures were performed in 17 patients with MFO device, including 3 patients weighing less than 5 kg with Associated Complex Congenital Heart Diseases. The Transthoracic Echocardiography (TTE) measurements were as follow: Left orifice: mean of 7.71 mm ±SD (4 to 12.3 mm); Right orifice: mean of 4.69 mm ±SD (2.8 to 7.8 mm); Length: mean of 5.75 mm ±SD (3 to 9.7 mm).

Results: From the scope of 17 patients, 16 procedures were successful and only 1 failed. The mean follow-up was 5.3 months (1 to 11 month). There were no major complications such as complete AV block, hemolysis, etc. No residual shunt was showed in the mid-term follow-up. 2 patients less than 5 kg died afterwards: 1 due to sepsis and the other one after the reoperation of severe restenosis of the pulmonary veins.

Conclusions: VSD closure with the Konar-MF occluder is feasible for both congenital and residual postoperative VSDs. It offers a vast variety of options by allowing different approaches to the VSD occlusion, (antegrade, retrograde and even through the foramen ovale), that had greatly simplified the procedure, giving the device a very substantial advantage, including the closure of large defects in low weight patients.

Key Words

Konar-MFO • MFO • VSD closure • ADO II

Introduction

Ventricular Septal Defects (VSDs) is the second most frequent congenital heart disease. The incidence of VSD is between 1.5 and 3.5/1000 in live birth and 4.5 to 7/1000 in premature babies1. The perimembranous VSD makes 70% of the VSD2 cases.

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Table 1. Different types of MFO catalog numbers with the corresponding delivery sheaths.

Catalog Number		D Disc Diameter (mm)	D2 Waist Diameter LV Side (mm)	D1 Waist Diameter RV Side (mm)	L Waist Length (mm)	Recommended Delivery Sheath (Fr)
	LT-MFO-5-3	10	5	3	4	4F-5F
	LT-MFO-6-4	10	6	4	4	
	LT-MFO-7-5	12	7	5	4	
	LT-MFO-8-6	12	8	6	4	
 with membrane	LT-MFO-9-7	14	9	7	4	6F
	LT-MFO-10-8	14	10	8	4	
	LT-MFO-12-10	16	12	10	4	7F
	LT-MFO-14-12	18	14	12	4	

Although surgical intervention is considered the gold standard for VSD [3-6], VSDs can successfully be closed by catheterization in patients with favorable anatomies and precise indications. Despite this, different complications have arisen where the complete AV block [7, 8], remains the most fearsome, and therefore, it is necessary to be extremely careful with the indication of this procedure, the choice of the device, and even with the vascular access selection.

Different devices have proven to successfully close different types of VSDs, depending on the size, location, and presence or absence of prolapse of the aortic sigmoid. Several devices have been used in VSD closure, such as the PDA Nit-Occlud® coil, Flipper® PDA [9, 10] coil, AMPLATZER™ [11, 12] devices for muscular VSD and Ductus ADO II devices [13, 14].

Regarding vascular access, the arteriovenous loop for the perimembranous VSDs that requires puncture of the femoral artery and the femoral vein was already described by Lock et al [15]. In mid-ventricular and apical VSDs, the arteriovenous loop is performed through the right jugular vein. However, the retrograde approach from the femoral artery can be done by using devices with symmetrical discs that allow easy access and rapid treatment of the VSD [3, 12].

The new Lifetech KONAR-MF™ Multifunctional Occluder (MFO) was developed to allow the occlusions of small to large defects that can be placed through both vascular approaches, anterograde and retrograde.

The purpose of this study is to report the short- and mid-term results of perimembranous and muscular VSDs closure with the use of the new MFO.

Materials and Method

The experience with the new MFO for endovascular closure of VSDs began in October 2017.

Device design

The MFO is a self-expanding occluder consisting of a layer nitinol wire mesh with 144 wires of 0.002" nitinol cables. It has two discs joined by a waist, which is formed by a truncated cone. The base of this cone is attached to the left disc and from the vertex, which is umbilicated, hangs an arm that joins it to the right disc. This arm allows articulation to the right disc. The length of the waist is 4 mm and stretches up to 7 mm.

The left disc or "high-pressure disc" is attached to the base of the truncated cone of the waist, and the right or "low-pressure disc" is attached to the waist arm. Each disc contains a 2.4 mm long hub with a screw so that the device can be positioned retrogradely or anterogradely. Both discs of the device are of equal size. It is a symmetric device.

The base of the cone or "D2" has a diameter of 2 mm greater than the vertex. adding 2 mm on each side to "D2" we obtain the diameter of the left disc or

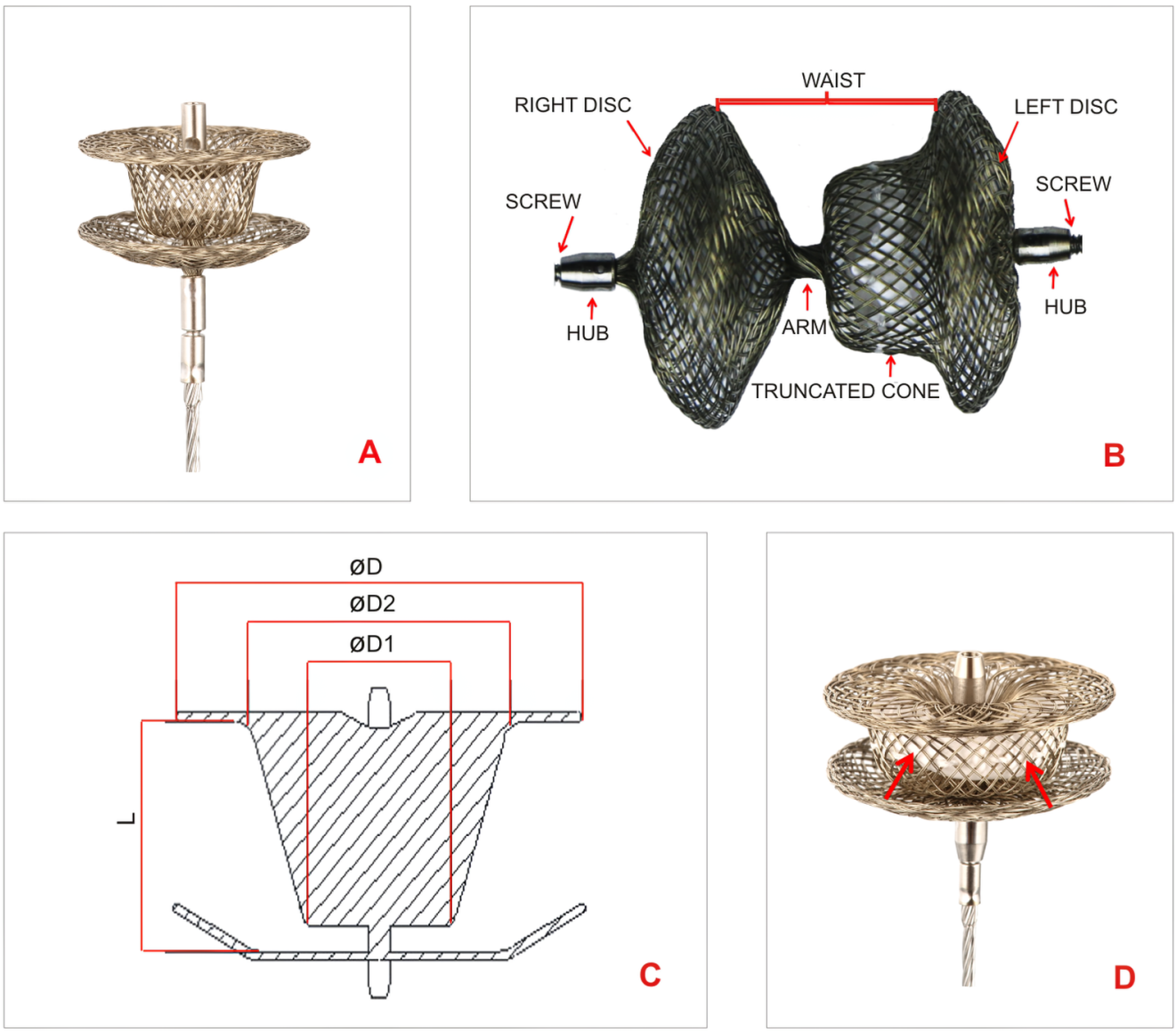

Figure 1. Konar-MFO. ***Panel A.*** The device. ***Panel B.*** The design. ***Panel C.*** Device Components Denomination: ***(Panel D)*** Disc diameter, ***(Panel D1):*** Waist Diameter Right Ventricular side ***(Panel D2):*** Waist Diameter Left Ventricular side. ***Panel D.*** The arrows show the PTFE.

"D", except for the 5-3, 7-5 and 9-7 devices where 2.5 mm must be added on each side.

Devices whose disc diameters "D" is ≥ 14 mm have a PTFE membrane inside (Figure 1).

The delivery system consists of a sheath and a cable (Figure 2). The cable has a thickness of 3 fr and a length of 1,5 m. On one side it has a screw to hold the device and on the other a handle that allows the device delivery maneuver with a counter-clockwise rotation. The delivery sheaths diameter depends on the diameter of the device (Table 1).

All procedures were performed under general anesthesia and patients were anticoagulated with Heparin 100 IU / kg and repeated 50 IU / kg every hour. 7500 IU were used in adults and afterward added 2500 IU more.

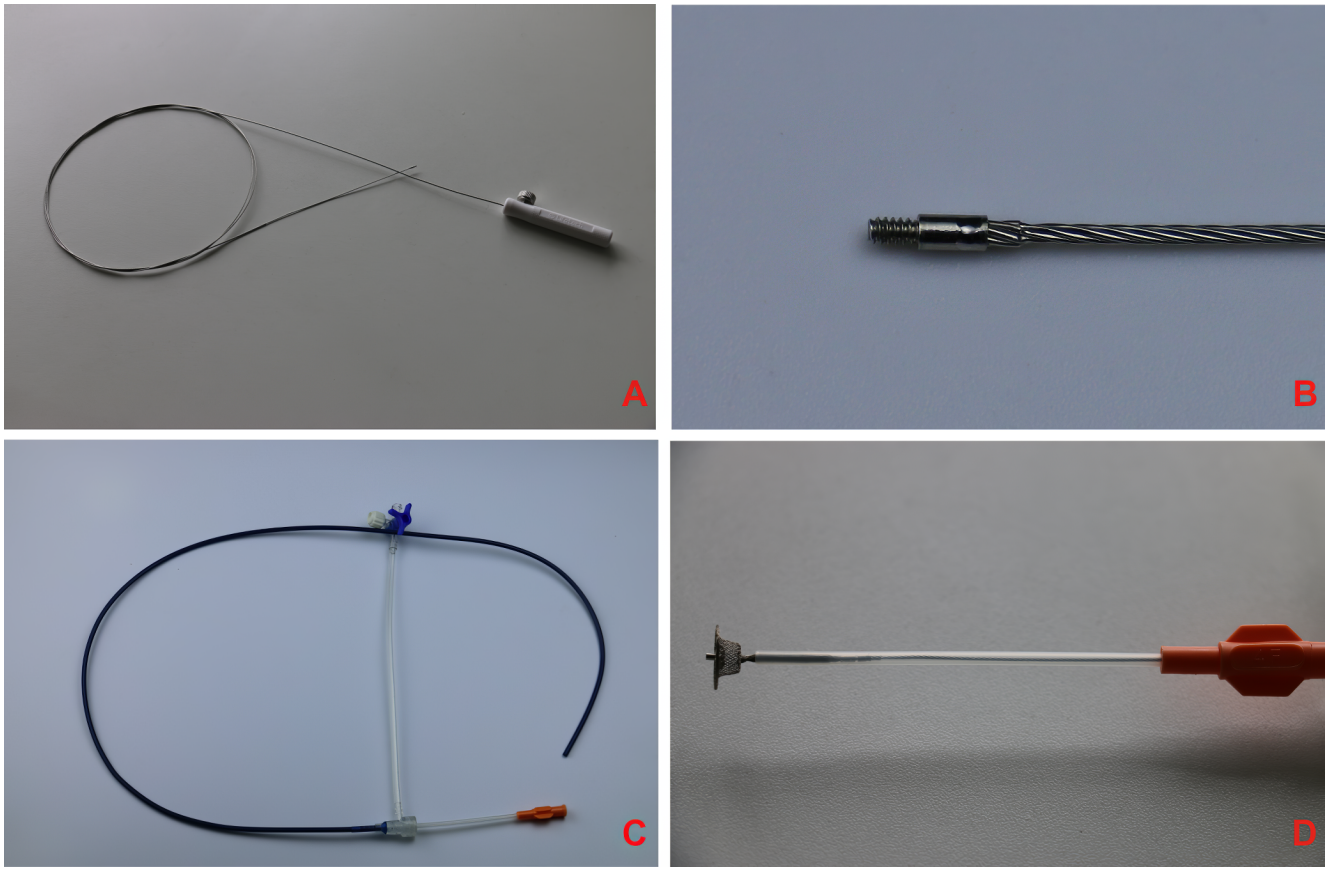

Figure 2. Delivery System. ***Panel A.*** The cable has, on one side a screw to hold the device and on the other side, the handle. ***Panel B.*** The screw that holds the device. ***Panel C.*** The sheath. ***Panel D.*** The loader with the device.

Protocol design

Inclusion criteria

1. Patient > 2.5 kg
2. Perimembranous VSD with aneurism
3. Muscular VSDs with adequate rims
4. Pulmonary/Systemic flow (QP/QS) > 1.5:1
5. Clinical and/or echocardiographic signs of volume overload
6. Pulmonary resistance (PR) ≤7UW
7. History of endocarditis

Exclusion criteria

1. Perimembranous VSDs without aneurysm
2. Muscular VSDs with inadequate rims
3. Not perimembranous or muscular VSD type
4. PR > 7 UW
5. Associate congenital heart disease of exclusively surgical resolution

All previous measurements for the patient selection were made with transthoracic echocardiography (TTE), included the right orifice, the left orifice, and the VSD length.

During the procedure, the patients over 5 Kg, were measured with transesophageal echocardiography (TEE) and under 5kg by transthoracic echocardiography (TTE).

Patients with perimembranous and high muscular VSDs performed 24 hours Holter before the procedure as well as an electrocardiogram (EKG) for those with the prior disorder.

The choice of the appropriate device is related to the TTE measurements of the VSD orifices, the size of the waist and the high-pressure disc of the device. The waist diameter, suggested by the device Company, is 2 mm greater than the maximum diameter of

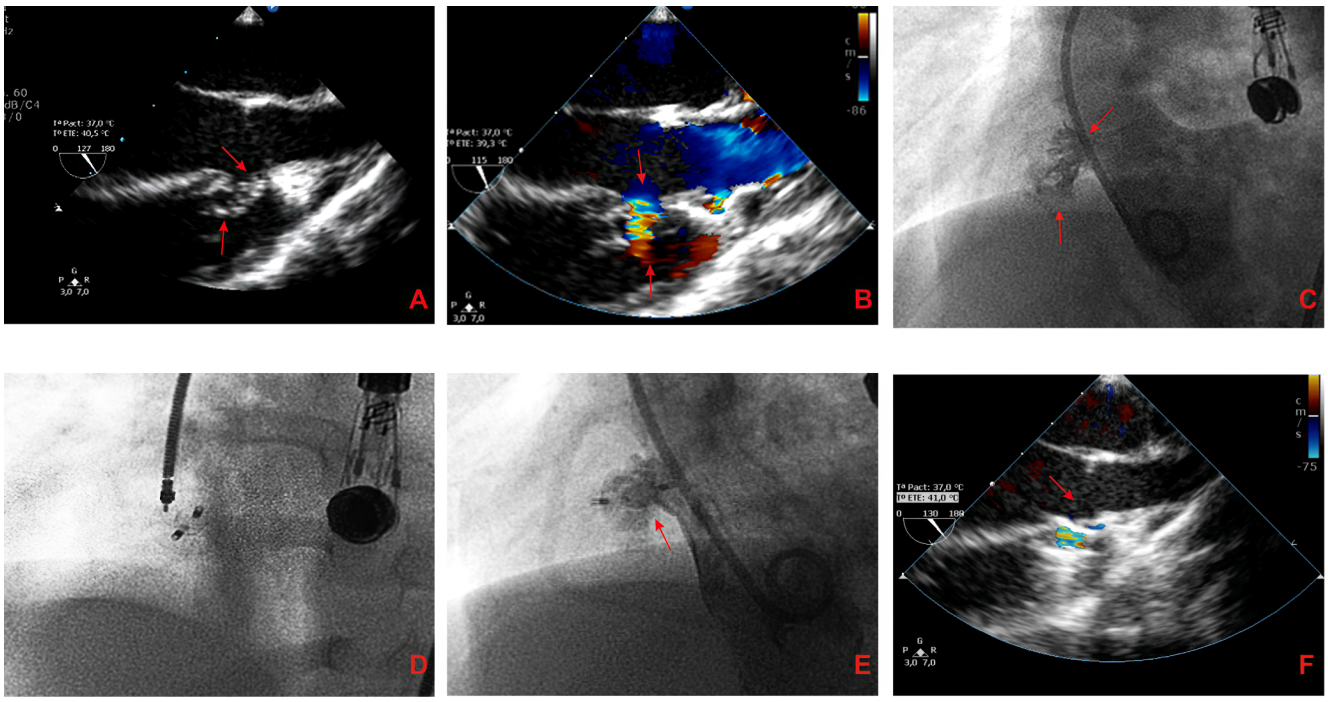

Figure 3. Perimembranous VSD. ***Panel A.*** TEE 120 degrees view. The arrows show the VSD. ***Panel B.*** TEE 120 degrees with Doppler color where the arrow shows the flow of the color through the VSD. ***Panel C.*** Left Ventricular Angiography (4 chambers): the arrow shows the VSD. ***Panel D.*** Retrograde approach positioning of the device. ***Panel E.*** Left Ventricle Angiography (4 chambers): the arrow shows the correct position of the device. ***Panel F.*** TEE 120 degrees view that shows the trivial residual shunt.

the right orifice of the defect. The left disk has a main role in the perimembranous and high muscular VSDs, due to the risk of AV block. In the case of perimembranous VSD with more than one right orifice, the device will need to be placed inside the aneurysm to avoid the conducting system and to occlude all the right orifices. This is achieved with a retrograde approach (Figure 3).

In muscular VSDs, the device has to inevitably lay over the interventricular septum; special care has to be taken in high muscular VSDs due to the direct relationship with the conduct system (Figure 4).

Follow up

- 24 hs: Thoracic X-Ray, EKG and TTE.
- 1 month: EKG and TTE.
- 3 months: EKG, TTE, and 24hs Holter.
- 6 months: EKG and TTE.
- 1 year: Thoracic X-Ray, EKG, TTE and 24hs Holter.

Statistics Analysis

T-Test or Student Test was used in the statistical analysis. Statistical significance is $p < 0.05$.

Results

17 procedures performed on 17 patients: 14 patients > 10 kg and 3 patients <5 kg.

> 10 kg

Sex: 9 males, 5 females; *Age*: median 12.67 years (1.11 to 37 years); and *Weight*: mean 39,96 kg ±SD (12 to 89 kg).

2 patients had complete right bundle branch block prior to the procedure, both postoperative.

VSD type

- Perimembranous VSD with aneurysm: 4 patients. 2 of them had 2 right orifices.

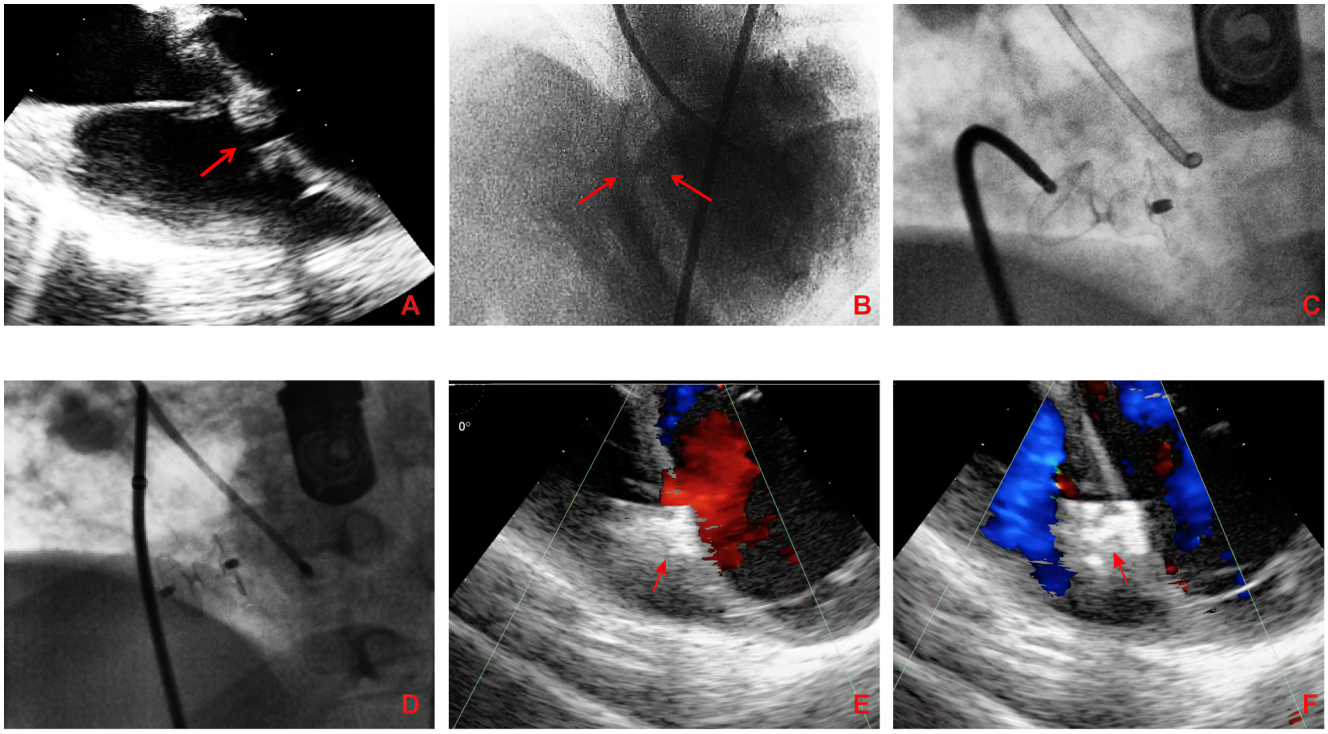

Figure 4. Muscular VSD. ***Panel A.*** TEE 0-degree view. The arrow shows the Muscular VSD. ***Panel B.*** Left Ventricle Angiography (4 chambers): The Muscular VSD is shown by the arrows. ***Panel C.*** MFO Anterograde approach positioning. ***Panel D.*** Left Ventricle Angiography (4 chambers): The device is correctly in place. ***Panels E and F.*** TEE shows no residual shunt.

- Muscular VSD: 8 patients (5 high-muscular and 3 mid-ventricular VSDs). 1 patient had a Ductus Arteriosus associated that was also closed in the same procedure.
- 2 postoperative VSDs: 1 patient had a Perimembranous VSD surgically repaired who suffered from endocarditis and presented with a residual shunt, and 1 patient had Tetralogy of Fallot surgically repaired with a residual VSD and Subtricuspid left ventricle-right atrium shunt.
- 2 postoperative VSDs: 1 patient had a Perimembranous VSD surgically repaired who suffered from endocarditis and presented with a residual shunt; The other patient had Tetralogy of Fallot surgically repaired with a residual VSD and subtricuspid left ventricle-right atrium shunt.

VSD echocardiographic measurements:

- Left orifice: mean 6.92 mm ±SD 2.83.
- Right orifice: mean 4.54 mm ±SD 1.50. 2 patients had more than one right orifice.
- Length: mean 4.82 mm ±SD 3.72.

Hemodynamic data:

- QP/QS: mean 1.65/1 (1.3/1 to 2.2/1).
- Pulmonary pressure: mean 24/11 (20/10 to 40/16).

The device most frequently used was 7-5. The devices employed were: 5-3: 3 devices, 6-4: 2 devices, 7-5: 4 devices, 8-6: 3 devices, 9-7: 1 device and 10-8 1 device.

The mean of the right waist was 5.07mm ±SD 1.52; the mean of the left waist was 7.07mm ±SD 1.52, and the mean length of the waist was 4 mm.

Endovascular VSD closure was successful in 13 out of 14 patients with trivial to no residual shunt. The failed procedure was on a patient who had a high muscular VSD and persisted with severe residual shunt after the implantation of the device. There was an attempt to close the VSD with a bigger device, but the patient presented a transient AV block during the procedure so the decision was taken to surgically close the defect.

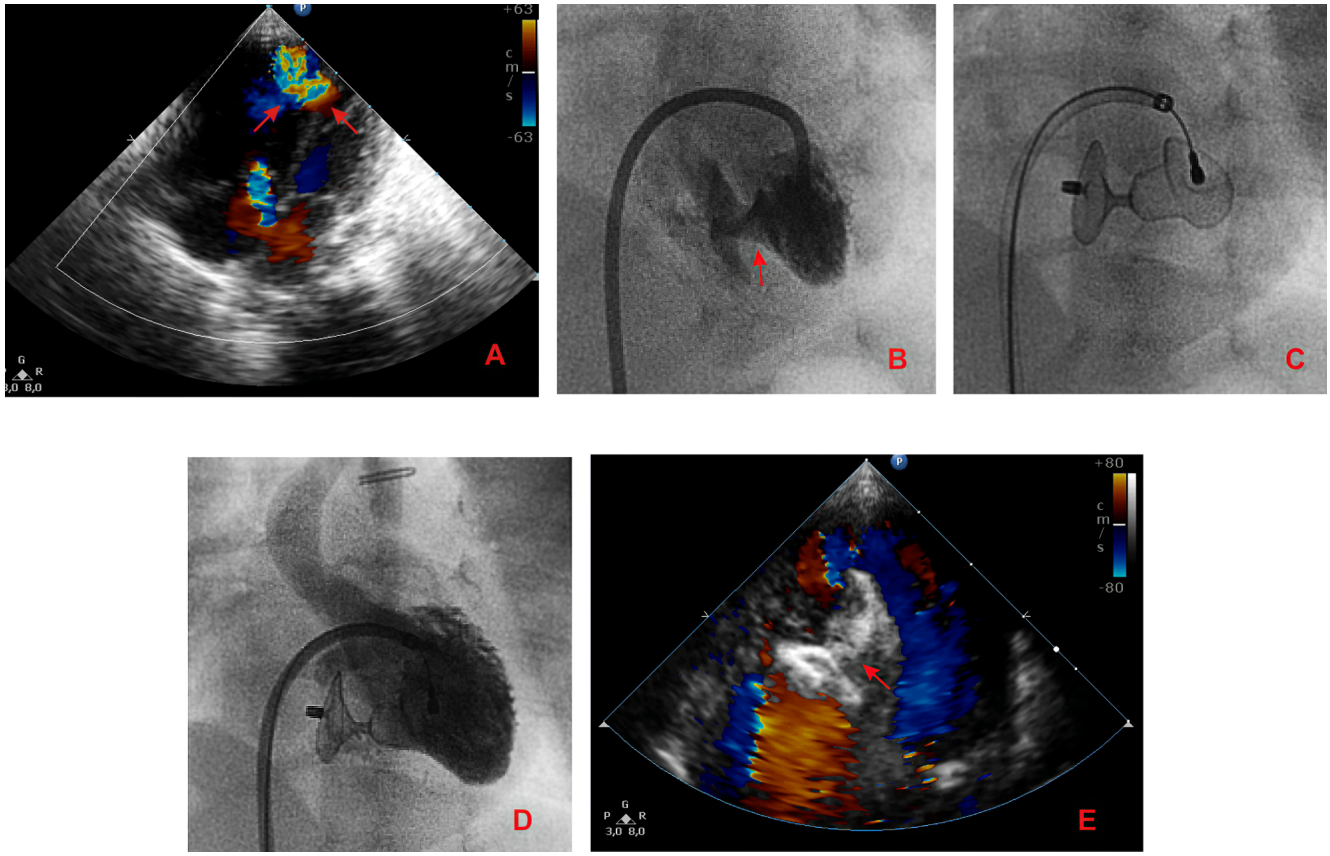

Figure 5. Mid-Muscular VSD. ***Panel A.*** TEE: 4 chambers view shows the Mid-ventricular VSD. ***Panel B.*** Left Ventricular Angiogram: the arrow shows the VSD ***Panel C.*** MFO totally positioned crossing the mitral valve. ***Panel D.*** Left Ventricular Angiogram: a trivial residual shunt can be observed. ***Panel E.*** TEE: 4 chambers view: the arrow shows the trivial residual shunt.

Follow up

The mean follow-up was 5.75 months (1 to 10 months). No complete AV block, hemolysis or mayor complications were observed throughout the follow-up.

< 5 kg

Patients <5 kg had another congenital heart disease associated with severe hemodynamic repercussions. All 3 patients presented with heart failure and pulmonary edema.

The mid-ventricular muscular VSDs were the type of defect.

The associated congenital heart diseases were as follow:

Case 1

1-month-old, 3 kg. Suffered from severe Aortic stenosis and severe Aortic coarctation associated with patent Ductus Arteriosus and a muscular VSD. Aortic valvuloplasty and balloon angioplasty were performed and, 4 days later, the Aortic arch was surgically repaired and the Ductus closed. A week later, the patient remained with heart failure and pulmonary edema, so endovascular occlusion of the VSD was successfully done (Figure 5).

Case 2

3-month-old, 3 kg. Presented with transposition of great arteries and a muscular VSD. After being surgically repaired with arterial switch technique, the patient persisted with residual VSD and severe heart

Table 2. Shows the hemodynamic data, VSD measurements, the devices used and the immediate results.

Case	Left To Right Shunt	Pulmonary Hypertension	Left Orifice	Right Orifice	Length	MFO	Residual Shunt
1	Severe	Severe	8 MM	8 MM	4 MM	10/8	No
2	Severe	Severe	5 MM	7 MM	3 MM	8-6	Mild
3	Severe	Moderate	5 MM	5 MM	3 MM	6-4	No

failure reason why endovascular occlusion of the VSD was performed.

Case 3

5-month-old, 5 kg. The anomaly associated was an obstructed infradiaphragmatic pulmonary venous return. After the surgical repair, the severe pulmonary hypertension persisted so Nitric Oxide was required. After 10 days, the pulmonary pressure decreased and endovascular VSD occlusion was performed. During the Pulmonary vein re-stenosis surgery, the patient died.

Table 2 shows the hemodynamic data, the VSD measurements, the devices used and the immediate result.

Follow up

Case 1

Good clinical condition with Aortic re-coarctation waiting for a new angioplasty.

Case 2

The patients died 15 days after the procedure due to sepsis.

Case 3

The patient developed a progressive severe Pulmonary Vein Stenosis and died during the surgery.

Discussion

VSD closure has historically been surgical [3-6]. After Lock [15] performed the first VSD occlusion by catheterization, different devices and vascular approaches have been proposed.

VSD closure was historically treated through surgery [3-6]. After Lock[15] performed the first VSD occlusion by catheterization, different devices and vascular approaches, such as Nit-Occlud® PDA coil, Flipper® PDA [9, 10] coil and AMPLATZER™ [11, 12] devices for muscular VSD and Ductus ADO II devices [13,14]. have been used to perform the closure.

Few complications were reported, being complete AV block the most feared [7, 8, 17-19].

The endovascular occlusion of perimembranous defects with the MFO device has the same feasibility as other known devices. The MFO great versatility in the vascular access, allow the possibility of closing defects of larger sizes with lower profile sheaths that can be placed through both vascular approaches, anterograde and retrograde, expanding the spectrum of patients who can benefit from the alternative closure by catheterization, among others.

In the short term follow-up, we did not observe in the cohort patients the complete AV block, however, it is a complication that can appear at any time that requires [19] a close follow-up.

In the vascular access, we usually use the antegrade approach for mid-ventricular and apical muscular defects, leaving the retrograde maneuver for the perimembranous and high muscular VSDs. Depending on the circumstances, avoiding the arteriovenous loop can simplify the procedure and reduce the risks associated with this technique. Moreover, avoiding arterial puncture represents a great advantage, especially in small patients. The MFO's great versatility, due to the double hub with screw-in both sides, allows the occlusion of the VSD in an antegrade or retrograde way according to convenience. In complex cases where the placement of the device is challenging, we suggest the use of the antegrade approach.

When using the retrograde approach, the right disc has to be completely open on the right side of the VSD so when it is pulled gently towards the left side, the full occlusion of the right orifice is performed. Later on, the waist and left disc are deployed within the aneurysm, with no differences regarding residual shunt between both approaches.

The patent foramen ovale (PFO) allows reaching through the mitral valve, the left ventricle and catheterizing mid-ventricular and apical VSDs from the cavity. Caution must be placed during the procedure in order to avoid injuries to the mitral valve. The guides must be covered with the catheter at all times and the placement of the sheath through the mitral valve must be done carefully.

Smaller devices contain compact mesh, compare to the larger ones. The PTFE membrane is needed inside the larger occluders to facilitate the closure.

The MFO devices come in different sizes, where the greater diameter of the waist goes from 5 to 14mm and the disc from 10 to 18 mm, enabling the closure of VSDs from 3 mm to 12 mm. To select the adequate device size, the Company suggests that the right waist should exceed the maximum right diameter of the VSD by at least 2 mm. Occasionally the right disc, contributes to the occlusion avoiding the oversize of the device.

In our analysis, the cohort of patients showed that when comparing the right waist of the device with the echocardiographic measurement of the right orifice of the VSD, the mean of the diameters was almost equal. The same result was showed when comparing the left waist of the device with the left diameter of the defect. The result of the analysis of the cohort of patients showed, that the size of the discs had a significant difference with the left waist, which established a linear relationship between the left diameter of the VSD and the size of the discs. The discs device was 4 mm larger than the left orifice of the VSD, concluding that the required size of the disc using the diameter of the left orifice of the VSD should have an additional 4 mm.

Another relevant observation during the analysis for the closure of the perimembranous defects was that the size of the device was ruled by the diameter of the aneurysm, as it had to be placed inside to avoid the AV block, to perform the complete occlusion of the right orifices, sometimes more than one.

The perimembranous VSDs without aneurysm is difficult to be treated with MFO [15-19] since the symmetrical discs might injure the Aortic sigmoids. Eccentric devices can be used for these types of defects where the left disc does not reach the aortic sigmoid valve [22].

Base on our experience, the alternative treatment was able to be offered to patients with very low weight, greater than 2,500 kg [7, 26-28], serious life risk, and did not comply with any requirement needed for other treatments. This group of patients manifests heart failure and acute pulmonary edema due to large defects, greater than 5 mm. Babies with a severe left to right shunt are often symptomatic with failure to thrive and can die from heart failure and respiratory compromise if the medical treatment is insufficient and the closure is delayed. Only patients with mid-ventricular and apical VSD can benefit from MFO for endovascular closure. Patients with high muscular and perimembranous VSDs, especially in patients under 1 year of age, will not be recommended for closure due to the high risk for complete AV block [12]. The low-profile and flexibility of the delivery system is well tolerated by the venous system that allows the crossing through the foramen ovale to LV avoiding the puncture of the arterial, common complication in young children. This is the main reason why Nageswara [26] and Zartner [27] already proposed avoiding arterial puncture in young children.

The postoperative residual VSDs range has been reported between 5 and 25% [30] if reoperation is decided, complications can arise [31]. When residual VSDs are greater than 3 mm and associated with QP / QS over 1.5 / 1, they need to be closed [32, 33]. Base on the information mention before, the endovascular treatment is a suitable option. In our experience, two patients had a residual postoperative VSD and required endovascular closure with no complications in the follow-up. Both patients had post-surgical complete right bundle branch block, so they underwent Holter prior to the procedure that did not show any other type of severe arrhythmia that contraindicated the device occlusion, and they did not present complete AV block during follow-up.

Base on our experience, successful closure was achieved in 92.8% of the cases, without major complications and minimal or no residual shunt. The failed procedure was due to the appearance of transient complete AV block during a reposition maneuver of the device that caused to refer the closure to surgery.

Regarding the group of patients under 5 kg who had severe cardiac diseases, (TCGA with mid-ventricular VSD, critical aortic stenosis with severe aortic coarctation, Total anomalous pulmonary venous connection (TAPVC), the decision was taken to repair the most severe emergent pathology that was putting the patient's life at risk through VSD with the MFO, due to the versatility of the device.

One of the main strengths of this novel device is the presence of a double hub that allows an anterograde or retrograde approach, as well as the low-profile delivery system that allows the closing of large VSDs in low-weigh patients under 5 Kg.

One of the disadvantages of the device in perimembranous VSDs with prolapse of the aortic sigmoid is the symmetrical diameter of the discs that can compromise the function of the aortic valve. As well the length of the right hub (7mm) can injure the tricuspid valve during the device implantation.

This is the first publication of the novel device "MFO" for endovascular VSD closure that is in full development with satisfactory short and mid-term results.

Conclusion

The device increase the possibility of closure of different types of VSD since it allows choosing the antegrade or retrograde approach as well as the closing of a great variety of sizes of VSD and the occlusion of large defects in low-weight patients.

The learning curve of the device, will let us know more details about MFO including the success rate of VSD closure.

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Conflict of Interest

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

Comment on this Article or Ask a Question

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Predictors of Paravalvular Aortic Regurgitation Following Transcatheter Aortic Valve Replacement Using the New Evolut™ PRO System

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Abstract

Background and Objective: The Evolut Pro (EVP) is a novel self-expandable aortic valve. This prosthesis consists of an external porcine pericardial wrap designed to reduce paravalvular leak (PVL), maintaining the benefits of its predecessor. The objective was to assess predictors of PVL using this novel device (d minuscule).

Methods: Twenty-seven consecutive patients with severe symptomatic aortic stenosis undergoing transcatheter aortic valve replacement using the CoreValve EVP bioprosthesis between October 2017 and July 2018, were prospectively recruited.

Patients were divided into two groups according to the presence of PVL: no or trace PVL versus mild or grade II PVL. The groups were compared to identify the demographic, echocardiographic and CT parameters predictive of PVL

Results: Pre-discharge transthoracic echocardiography revealed mild or grade II PVL in 19 cases (70%) (16 patients mild PVL; 3 grade II PVL). There were no patients with grade III or severe (grade IV) PVL. In all patients, the regurgitation was paravalvular. The prosthesis/annulus discongruence (prosthesis diameter – CT mean annular diameter) was significantly related to the occurrence of mild/grade II PVL (4.4±0.9 mm in the mild/moderate PVL group, versus 5±0.5 mm in the group without or trace PVL; p=0.04).

Conclusions: EVP system remains associated with mild or grade II PVL in a significant number of patients. However, hemodynamically significant PVL was not detected in any patient. The prosthesis/annulus discongruence plays a major role in the occurrence of residual PVL.

Key Words

Aortic stenosis • Transcatheter aortic valve replacement • Paravalvular leak • Computed tomography • Echocardiography

Introduction

Transcatheter aortic valve replacement (TAVR) has become standard therapy for patients with severe aortic stenosis who are deemed of at least intermediate risk for surgical valve replacement (SAVR). The current commercially available valves are broadly grouped into balloon-expandable and self-expandable valves [1]. However, there is significant clinical concern regarding the higher incidence of paravalvular leak (PVL) with TAVR as compared to SAVR as this has been associated with poor long-term clinical outcomes [2]. The CoreValve™ system was the first-generation self-expandable valve introduced to the market. The second-generation device was the

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CoreValve™ Evolut™ R System, with a more secure seal protecting against PVL [3, 4]. The latest iteration of this self-expandable valve is named the Evolut Pro system [1]. Based on the prior Evolut™ R platform, this novel valve consists of an external pericardial wrap that ensures a reduction in PVL while retaining other benefits of the previous generation, including a low delivery profile, self-expansion, as well as its ability to recapture and reposition the valve.

The efficacy of the Evolut PRO design has been initially tested by the investigators of the Evolut PRO clinical study [5], conducted as a non-randomized, single-arm prospective registry at eight centers in the USA including a total of sixty well-selected patients. These patients were prospectively followed over 30 days with a primary efficacy endpoint of none or trace aortic regurgitation. The study showed that the Evolut™ PRO system provided excellent hemodynamics and minimal residual aortic regurgitation. There are multiples studies that sought to assess PVL predictors based on anatomical characteristics (defined by computed tomography [CT]) [6-8]. Because Evolut™ PRO is a very new design, apart from the American study [5], there is no additional data available about its safety and efficacy in a "real life" clinical scenario. Moreover, the incidence and determinants of PVL after TAVR with the CoreValve™ Evolut™ PRO remain unknown. We sought to assess predictors of PVL using this novel device.

Methods

Twenty-seven consecutive patients with severe symptomatic aortic stenosis (aortic valve area (AVA) <1 cm^2 or indexed AVA <0.6 cm^2/m^2) undergoing transfemoral TAVI using the Medtronic CoreValve™ Evolut Pro bioprosthesis between October 2017 and July 2018, were prospectively recruited. All patients were previously discussed in a dedicated Heart Team meeting involving cardiac surgeons, interventional cardiologists, experts in cardiac imaging and clinical cardiologists. Our clinical and anatomic selection criteria and device size selection were in accordance with previous recommendations [4]. The prosthesis sizing was based on a combination of echocardiographic and CT measurements but eventually remained at the discretion of the implanting interventional cardiologist. All patients underwent a pre-procedure CT and all images were systematically analyzed using a cardiac application on a dedicated workstation by two independent experienced observers. The best diastolic images at 70 or 80% of the R-R interval were used. The largest (Dmax) and the smallest (Dmin) aortic annulus and left ventricle outflow tract (LVOT) diameters were measured. The mean diameter (Dmean) was derived by averaging the largest and smallest diameter. The circularity of aortic annulus was defined using the eccentricity index using the formula (1 – Dmin/Dmax) [6]. The degree of aortic valve calcification was semi-quantitatively classified as no calcification, mild calcification (small calcium spots), moderate calcification (larger calcium spots), and severe calcification (extensive calcification) as previously described [7]. The "cover index", expressed as a ratio of: ([prosthesis diameter – CT annulus diameter] / prosthesis diameter) x 100, was calculated to assess the congruence between the aortic annulus and the device [8]. Finally, to further explore the value of the difference between prosthesis size and annular size for the prediction of PVL, the difference between the nominal bioprosthesis size and mean CT aortic annulus diameter was assessed [9]. Following a predefined protocol, pre-discharge transthoracic echocardiographic was obtained in all patients. PVL was systematically graded, by an independent experienced operator blinded to angiographic data and procedural results, using multiple parameters including regurgitation color jet density and width, circumferential extent of turbulent regurgitation color jet around the aortic annulus for PVL, descending and abdominal aorta diastolic flow reversal on pulsed wave Doppler, and pressure half- time of aortic regurgitation on continuous wave Doppler signal, as previously defined [10].

For data analysis patients were divided into two groups according to the presence of PVL: no or trace PVL versus mild or grade II PVL. The groups were compared to identify the demographic, echocardiographic and CT parameters predictive of PVL. The data are expressed as the mean ± the standard deviation (SD). The differences between the means were calculated using Student's t-test after assessing normality. The differences in categorical variables were analyzed using Chi-square tests. Univariate analysis was used to identify the most significant predictors of PVL. The

Table 1. Baseline clinical, echocardiographic and CT characteristics.

	All (n=27)	No/trace PVL (n= 8)	Mild/gradeII PVL (n=19)	P value
Patients Characteristics				
Age (years)	85±4.3	83±2.4	86±4.8	0.1
Female	22 (81%)	7 (87%)	15 (79%)	0.6
BSA (mm^2)	1.6±0.1	1.6±0.1	1.6±0.1	0.5
Echo Parameters				
AVA (mm^2)	0.74±0.16	0.72±0.15	0.75±0.17	0.7
Peak gradient (mmHg)	68±21	65±24	69±21	0.6
LVEF (%)	64±13	63±14	64±13	0.9
CT Parameters				
Mean annulus (mm)	23±1.8	22.5±1.7	23.2±1.9	0.4
Annulus área (mm^2)	403±63	387±53	410±67	0.4
Annulus perimeter (mm)	697±114	699±54	697±132	0.9
Mean LVOT (mmHg)	21.9±2.7	20.7±2.5	22.4±2.6	0.1
Eccentricity index	0.22±0.05	0.23±0.06	0.21±0.05	0.5
Cover index	16.6±3.3	18.1±2.1	16±3.6	0.07
Moderate/severe valve calcification	70%	63%	87%	0.4
Prosthesis diameter – CT mean annular diameter (mm)	4.6±0.9	5±0.5	4.4±0.9	0.04

Data are presented as mean ± standard deviation or as number (percentage) of patients. AVA = aortic valve area. BSA = body surface area. LVEF = left ventricle ejection fraction. LVOT = left ventricle outflow tract. NYHA = New York Heart Association; TAVI = Transcatheter aortic valve implantation; PPM = Permanent pacemaker

level of statistical significance was set at $p \leq 0.05$. All statistical analyses were performed using SPSS Statistics version 18.

Results

Baseline clinical, CT and procedural characteristics are shown in Table 1. All 27 patients (mean age, 85±4 years, 81% of females) had severe aortic stenosis (mean AVA, 0.74±0.16 cm^2). An iliofemoral access route was used in all the cases, and 33% of patients required balloon post-dilatation. Left bundle branch block was developed in five cases and a pacemaker was required in 15% of patients due to new conduction system abnormalities. There were no deaths or major adverse cardiac events (MACE) during hospitalization.

Pre-discharge transthoracic echocardiography revealed mild or grade II PVL in 19 cases (70%) (16 patients mild PVL; 3 grade II PVL). There were no patients with grade III or severe (grade IV) PVL. In all patients the regurgitation was paravalvular. Factors associated with the presence of PVL are presented in Table 1. The prosthesis/annulus discongruence (prosthesis diameter – CT mean annular diameter) was significantly related to the occurrence of mild/grade II PVL (4.4±0.9 mm in the mild/moderate PVL group, versus 5±0.5 mm in the group without or trace PVL; p=0.04). However, no significant differences were found using area and perimeter values to calculate prosthesis/annulus discongruence. Moreover, no differences were observed when the body surface area (BSA) was taken into account. Other factors such as eccentricity index, cover index, degree of annular calcification, mean annular

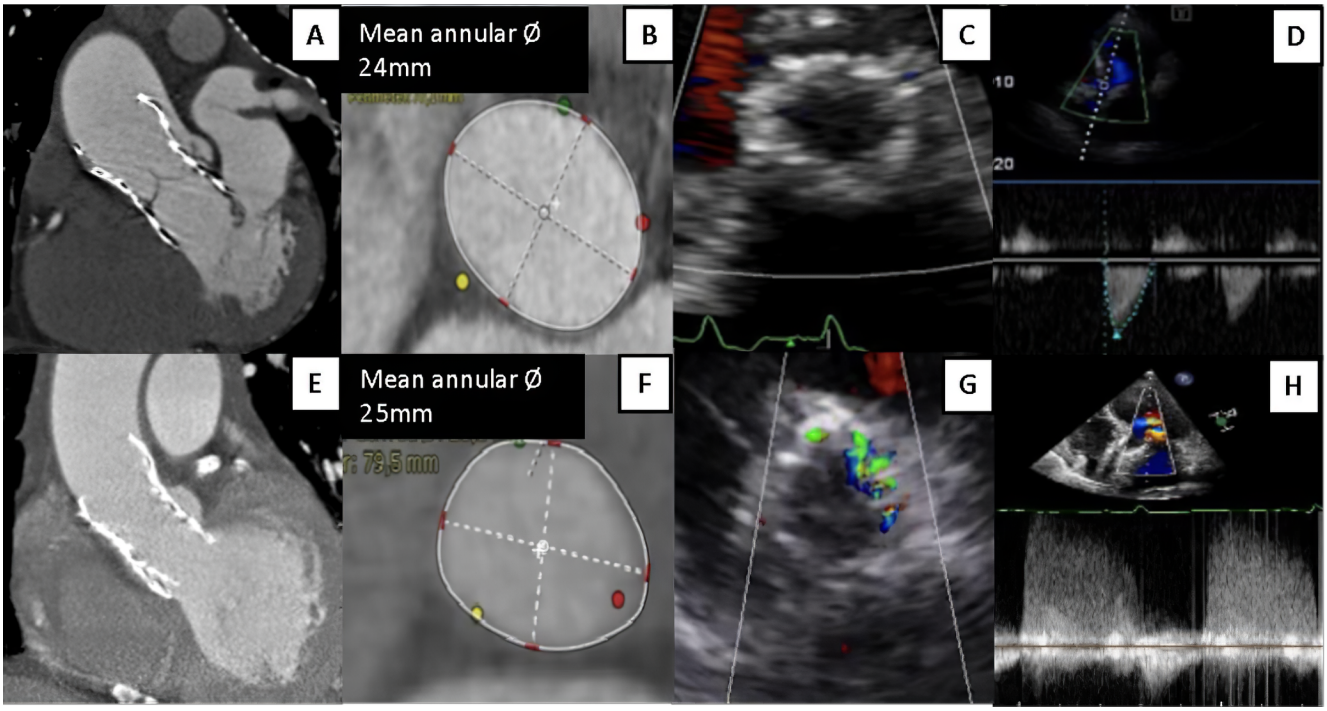

Figure 1. TOP: *Panels A, B, C, D* correspond to a patient without PVL after implantation of an Evolut PRO #29. ***Panel A.*** coronal CT image post TAVR shows mild oversizing with respect to the aortic annulus. ***Panel B.*** oblique transverse CT view showing a mean aortic annular diameter of 24 mm. ***Panel C.*** color Doppler in short axis view at the pre-discharge transthoracic echocardiography with no PVL. ***Panel D.*** Continuous wave Doppler through the aortic valve without any diastolic signal. **BOTTOM:** *Panels E, F, G, H* correspond to a patient with grade II PVL after implantation of a Evolut PRO #29. ***Panel E.*** coronal CT image post TAVR shows that TAVR is not oversized with respect to the aortic annulus. ***Panel F.*** oblique transverse CT view measuring a mean aortic annular diameter of 25 mm. ***Panel G.*** color Doppler in short axis view at the pre-discharge transthoracic echocardiography depicting a color jet around the aortic annulus of grade II PVL. ***Panel H.*** Continuous wave Doppler through the aortic valve with a continuous diastolic signal caused by the PVL.

and LVOT diameter, and baseline aortic regurgitation were not related to the occurrence of significant PVL.

Discussion

This study shows that PVL may still occur after TAVI using the novel CoreValve™ Evolut™ PRO system even when careful sizing, including systematic CT evaluation and technique, is used. In addition, our study demonstrates that the occurrence of mild or grade II PVL is related to a lower degree of oversizing, measured as the disconcordance between prosthesis diameter and mean CT aortic annular diameter (Figure 1). This novel insight may be clinically useful to optimize the implantation of this new device. In the Evolut PRO clinical registry, none to trace PVL was observed in 72.4% of patients while the remaining 27.6% experienced mild PVL at 30 days. There were no patients with moderate or severe PVL [5]. Compared with that study, the only currently available using this valve, our study demonstrated the presence of mild or grade II PVL in 70% of the patients. The different criteria used for PLV assessment (systematic blinded echocardiographic review in our study) and patients characteristics (truly unselected cases in our study) could help to explain this apparently divergent findings.

The presence of significant PVL has been shown to be associated with worse short-term outcomes and increased in-hospital mortality [11]. In fact, the identification of PVL predictors has been widely investigated but with controversial results [12]. Consistent results have been found by other authors with different valve systems. In patients treated with the Edwards

Sapien valve, Detaint et al. reported the occurrence of significant PVL to prosthesis/annulus discongruence [13] and Schultz et al. suggested that improved prosthesis sizing, based on mean annulus diameter on CT, helped to reduce PVL with the Medtronic Corevalve™ [14]. To best of our knowledge, however, this is the first study systematically correlating residual PVL following Evolut™ PRO TAVR with the prosthesis/annulus discongruence. Our findings underscore that appropriate sizing using CT (aiming for mild oversizing) remains critical to avoid residual PVL even with the use of the novel Evolut™ PRO System.

In our experience, the Evolut™ PRO's new design is secure, but it is still associated with a significant incidence of residual mild/grade II PVL, higher than previously reported [4]. Only the prosthesis/annulus discongruence, as measured by CT, was identified as a PVL predictor. Nevertheless, further studies are required to fully define the clinical repercussion of PVL, the clinical utility of assessing prosthesis/annulus discongruence in this setting, and to define other PVL predictors. Because the Evolut™ PRO system is a very new design, only a limited number of patients were included in the present study. Likewise, the potential clinical implications of the degree of PVL detected in our study (mild/grade II) should be established in larger studies.

Conclusion

In conclusion, Evolut™ PRO system remains associated with mild or grade II PVL in a significant number of patients. However, hemodynamically significant PVL was not detected in any patient. The prosthesis/annulus discongruence plays a major role in the occurrence of residual PVL.

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Conflict of Interest

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

Comment on this Article or Ask a Question

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Incremental Prognostic Utility of Myocardial Fibrosis Imaging By Speckle Tracking Echocardiography Post Transcatheter Aortic Valve Replacement

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Abstract

Background: Long-standing aortic stenosis (AS) results in fibrotic changes that often persist after TAVR. Fibrosis in AS preferentially affects the left ventricular (LV) basal segments and can lead to ventricular desynchrony.

Objective: Determine the prognostic utility of strain parameters as measured by speckle-tracking echocardiography in patients undergoing transcatheter aortic valve replacement (TAVR). We hypothesize that basal longitudinal strain (BLS) and mechanical dispersion (MD) measured after TAVR will predict all-cause mortality in severe AS

Methods: 159 patients (51% men, 81±9 years) with severe AS (aortic valve area 0.7±0.2 cm2, mean gradient 46±16mmHg) who underwent TAVR at our institution were retrospectively analyzed. 2D speckle-tracking echocardiography was used to assess myocardial deformation and MD (SD of time from Q/R on the ECG to peak strain in 16 LV segments) immediately after TAVR (median, 1 day). Images were analyzed offline using a vendor-independent software (TomTec).

Results: At 1-year post-TAVR, 28 (17.6%) patients died. Non-survivors demonstrated impaired global longitudinal strain (GLS, -11.2±3% vs -14.2±4%, p=0.001), impaired BLS (-10.9±2% vs -13.3±3%, p=0.001), and pronounced MD (86±33 ms vs 70±26 ms p=0.006) compared to survivors. Baseline multivariable Cox regression model (Figure) included age, STS, NYHA, renal disease, AV mean gradient, and post-TAVR paravalvular leak as significant univariates (model 1, p<0.001). An incremental prognostic value was achieved by adding BLS to model 1+ GLS (p=0.001). Addition of MD to the model 1 + GLS + BLS provided further incremental prognostic increase (p=0.008). For the measurement of GLS, the Interobserver Intraclass Correlation Coefficient was 0.87.

Conclusion: In severe AS, post-TAVR myocardial fibrosis assessed by strain imaging was significantly associated with cardiovascular events. This finding may provide incremental prognostic value in patients with AS.

Key Words

Transcatheter aortic valve replacement • Myocardial fibrosis • Speckle-tracking echocardiography • Basal longitudinal strain • Mechanical dispersion • Mortality

Introduction

Aortic stenosis (AS) is a common valvular heart disease that causes serious myocardial dysfunction [1]. Severe AS is often associated with the development of adverse cardiac symptoms and increased risk of mortality [2]. Untreated symptomatic patients

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have poor outcomes [3]. Transcatheter aortic valve replacement (TAVR) has proven to be an alternative to surgical aortic valve replacement for the treatment of symptomatic severe AS [4].

Randomized clinical trials comparing TAVR with standard-of-care therapies in selected patients with moderate to severe aortic stenosis who are at higher than normal risk for surgical aortic valve replacement have been completed and demonstrated one-year mortality rates for TAVR that were non-inferior and in some cases superior to standard surgical therapies [5-8].

To improve risk stratification in TAVR patients, several studies identified variables associated with poor outcomes. Age, Society of Thoracic Surgery (STS) score, New York Heart Association (NYHA) class, and renal disease were previously identified as prognostic predictors of mortality [9-12]. In addition, paravalvular leak (PVL) and post-procedural renal insufficiency were identified as important risk factors for post-TAVR mortality [13-15].

In long-standing AS, progressive valve narrowing triggers a hypertrophic response that preserves ventricular function for many years. Over time, the development of underlying myocardial fibrosis and myocyte injury leads to progression from hypertrophy to heart failure [16, 17]. Once myocardial fibrosis ensues, it provides a structural substrate for arrhythmogenicity, playing a major role in sudden cardiac death [18]. Moreover, histological studies demonstrated an association between myocardial fibrosis at the time of aortic valve replacement (AVR) and poor long-term outcomes post-valve replacement [19]. Myocardial biopsy is considered the gold standard for assessing myocardial fibrosis, however, it is an invasive procedure that could lead to several complications [20]. Therefore, a need for modern imaging techniques for noninvasive assessment of myocardial fibrosis has emerged.

In this context, two-dimensional speckle tracking echocardiography (2D-STE) is a promising imaging modality that allows the diagnosis of subclinical cardiac impairment including fibrotic changes not detected by conventional echocardiography [21]. 2D-STE provides an assessment of myocardial deformation and left ventricular torsion [22]. Of all the myocardial deformation parameters, global longitudinal strain (GLS) has been shown to be more clinically useful than circumferential or radial strains [23]. In recent studies, GLS had superior prognostic value to left ventricular ejection fraction (LVEF) in predicting cardiac death, urgent valve surgery or hospitalizations due to heart failure [24]. Additionally, GLS has been shown to be an independent predictor of outcomes in patients with severe asymptomatic AS [25].

More recently, regional or basal longitudinal strain (BLS) has been proven to be a superior predictor of future AVR in asymptomatic AS compared to GLS [26, 27]. Additionally, myocardial fibrosis related to long-standing AS can lead to desynchrony and pronounced mechanical dispersion (MD) which has been linked to poor outcomes in these patients [28].

In the early post-TAVR period, a dramatic reduction in the afterload and immediate offloading of the ventricle lead to improvement in strain parameters [29]. However, literature describing the prognostic utility of impaired BLS and MD immediately post-TAVR remains limited. We hypothesize that in addition to GLS, BLS and MD measured immediately post-TAVR will predict all-cause mortality in severe AS.

Methods

Study design and population

This retrospective study was conducted at Rush University Medical Center (RUMC), Chicago, USA. All patients underwent TAVR after evaluation by a multidisciplinary heart team. The study was reviewed and approved by the Institutional Review Board at RUMC. From a total of 187 patients with severe aortic stenosis (aortic valve area < 1 cm^2 , mean gradient > 40 mmHg) who underwent TAVR between January 2012 and March 2018 and had a follow-up echocardiogram performed immediately after TAVR, we excluded patients with incomplete data (n=11), concomitant significant valvular disease (n=10), and poor image quality or arrhythmia at the time of echocardiography (n=7). A total of 159 patients were included in the current study (Figure 1).

Two-dimensional strain imaging

In this study, myocardial strain parameters were measured by 2D-STE using a vendor-independent software (TomTec, Germany) immediately after TAVR

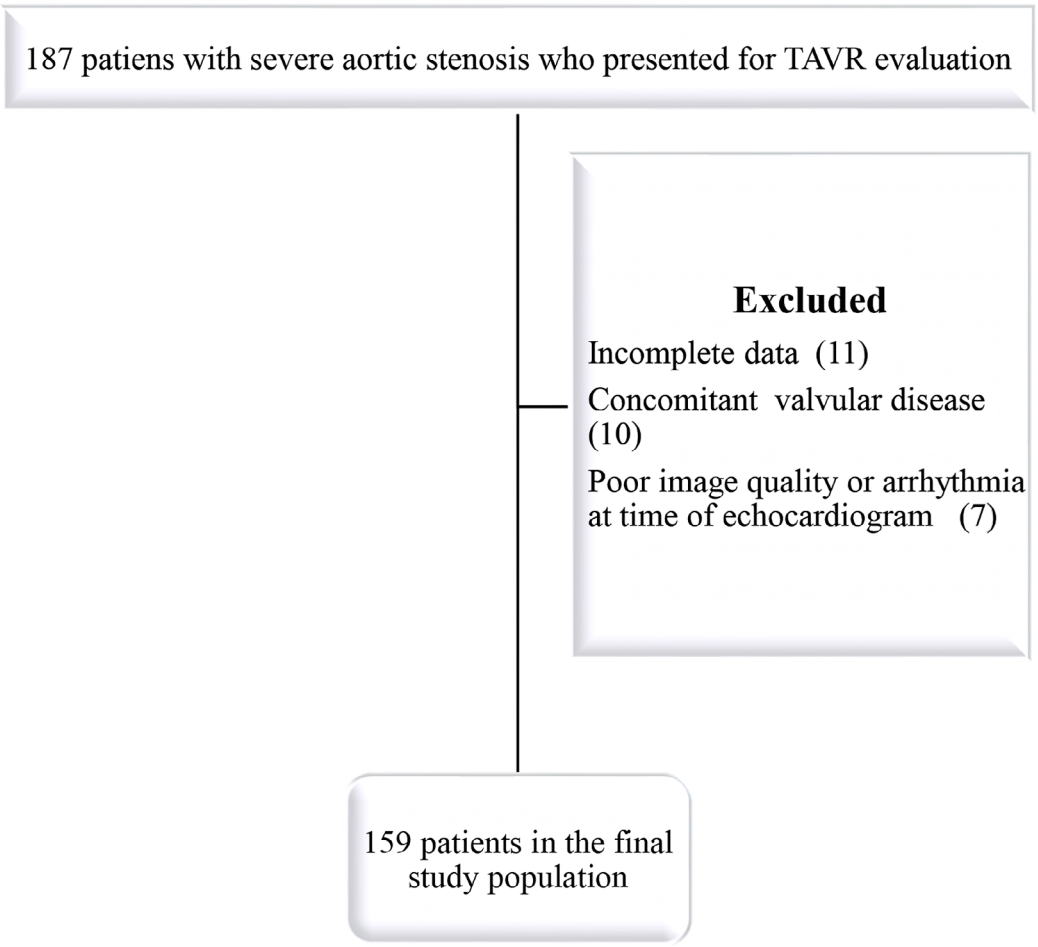

Figure 1. Patient Selection. Flow diagram of screening and exclusion criteria of patients with aortic stenosis.

(median, day 1). Two-dimensional strain analysis was performed on grey-scale images from the three apical views (longitudinal function) with frame rates of 70-90 frame/s and digitally stored for three cardiac cycles. Endocardial border tracking was achieved automatically using two points in the annular region and one point in the apical segments. Tracking quality was visually verified. Segments that failed initial tracking were manually adjusted. Segments that could not be tracked properly after manual adjustment were rejected. Peak systolic values from 16-segment model (6 basal, 6 mid and 4 apical segments) were averaged to obtain GLS (Figure 2). Six basal segments were averaged to obtain BLS. MD was defined as the standard deviation of time to peak strain (time of onset of Q/R wave in electrocardiogram to peak negative longitudinal strain during the cardiac cycle) in 16- segment model.

Statistical analyses

All calculations were performed using SPSS/PC statistical program (version 21, SPSS Inc., Chicago IL, USA). Continuous variables were reported as means ± SD while categorical variables were expressed as numbers or ratios. Comparisons between groups were achieved using unpaired Student's t-test for continuous variables while $\chi 2$ was used to evaluate dichotomous variables. A p-value of less than 0.05 was considered statistically significant. Cox proportionate hazard models were used to determine significant predictors of all-cause 1-year mortality. Multivariate regression analysis included all significant

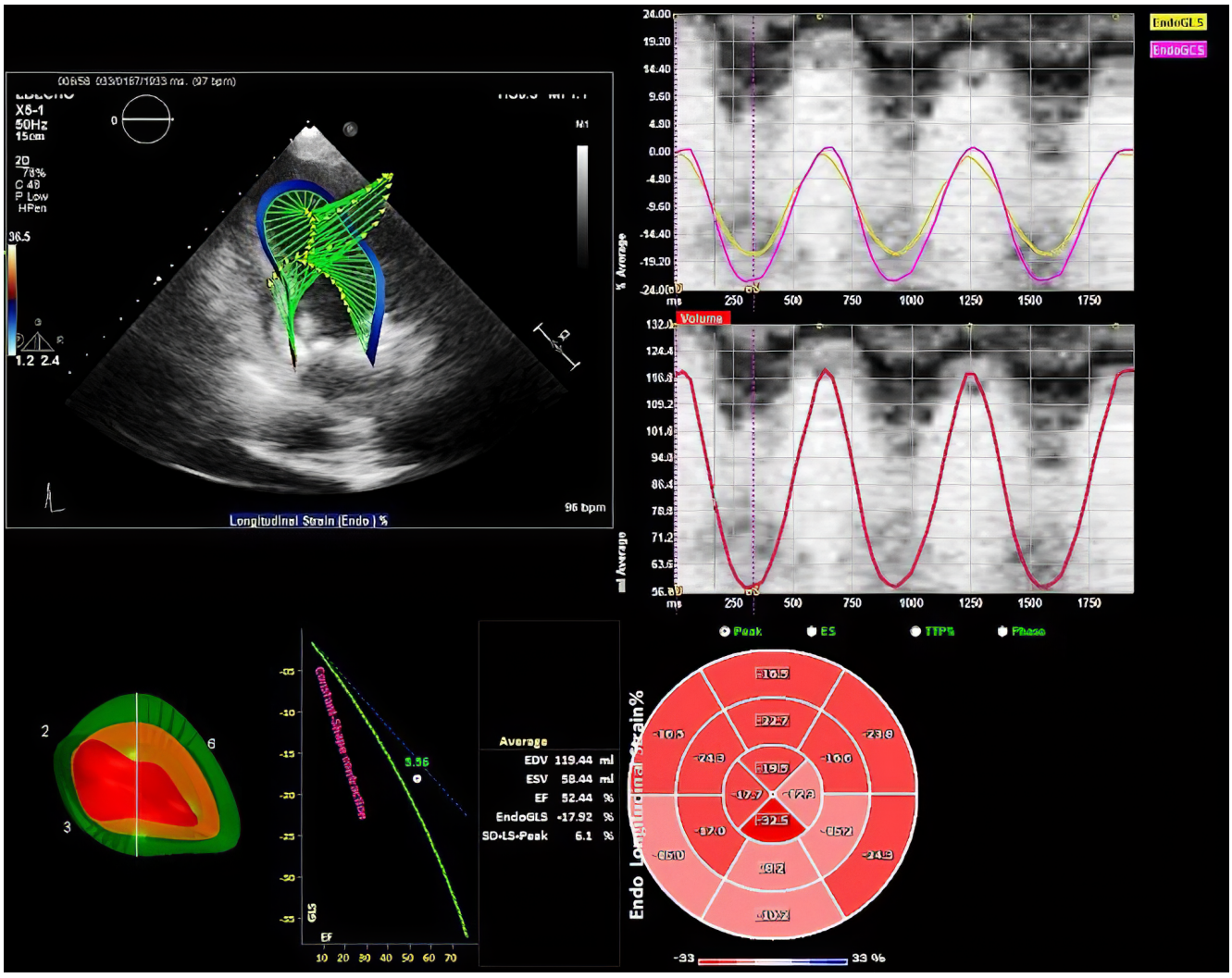

Figure 2. Two-dimensional speckle tracking echocardiography analysis. Strain curves and a color-coded 16-segment bull's eye plot are presented. Color lines indicate regional strain. Values of longitudinal strain are negative ***(sign -)***. Endocardial border tracking in apical four-chamber view can be achieved automatically. Global longitudinal strain can be calculated from 4 chamber views. Model 1 = Age, STS score, NYHA IV, Renal Disease (Cr >2 mg/dL), AV Mean Gradient, post-TAVR PVL.

univariates. To further illustrate the predictive value of strain parameters, cox models with separate addition of GLS, BLS, and MD to baseline model containing significant univariates were constructed. Model discrimination was further assessed using Harrell's C-statistic. Inter- and intra-observer were expressed by intra-class correlation coefficients.

Results

Study population selection is presented in Figure 1. Baseline characteristics stratified according to survival status and total cohort as summarized in Table 1. A total of 159 patients (mean age 80.7±9.1, 49% of women) were included in the study. A total of 28 (17.6%) patients expired one-year post-TAVR.

Cardiovascular risk factors including body mass index (BMI), hypertension, diabetes, hyperlipidemia, and kidney disease were not statistically significant between survivors and non-survivors (Table 1). Non-survivors had higher STS scores (8.1±5.4 vs 5.6±3.7, p=0.004) and more NYHA class IV (28.5% vs 10.6%, p=0.013) (Table 1).

Table 1. Baseline clinical characteristics of all patients.

	All Patients	Survivors	Non-survivors	P-value
N (%)	159	131 (82.4%)	28 (17.6%)	-
Age	80.7±9.1	80.1±9.7	83.5±4.9	0.073
Gender (Female %)	78 (49.0%)	64 (49%)	14 (50%)	0.913
BMI	29.2±7.4	29.7±7.6	27.2±5.7	0.103
NYHA Class IV	22 (13.8%)	14 (10.6%)	8 (28.5%)	0.013
STS score	6.1±4.1	5.6±3.7	8.1±5.4	0.004
Hyper-tension	141 (89%)	115 (88%)	26 (93%)	0.445
Hyper-lipidemia	98 (62%)	78 (60%)	20 (71%)	0.243
Diabetes	67 (42%)	50 (38%)	16 (57%)	0.065
CAD	111 (70%)	89 (68%)	22 (79%)	0.269
Creatinine	1.5±1.3	1.4±1.3	1.6±1.0	0.515
Baseline LVEF, %	55.3±15.4	55.9±15.0	52.2±17.2	0.224
Post-TAVR LVEF, % (Day1)	59±15	61 ±14.5	55±17	0.053
AV mean gradient	46.2±16.4	48.3±16.4	36.3±12.0	0.001
GLS, %	-13.7±4.1	-14.2±4.0	-11.2±3.1	0.001
BLS, %	-12.9±3.2	-13.3±3.2	-10.9±1.9	0.001
MD, msec	72.8±27.8	70.0±25.8	85.8±33.4	0.006

Data are expressed as mean ± SD or as number (percentage). Comparisons were performed using unpaired Student's T tests or $\chi 2$ tests. P-value refers to comparisons between survivors and nonsurvivors.

BMI: body mass index; NYHA: New York Heart Association; STS: Society of Thoracic Surgery; CAD: coronary artery disease; LVEF: left ventricular ejection fraction; AV: aortic valve; GLS: global longitudinal strain; BLS: basal longitudinal strain; MD: mechanical dispersion.

GLS and BLS of non-survivors measured by 2D-STE as shown in Figure 2. Non-survivors demonstrated impaired GLS (-11.2±3% vs. -14.2±4%, p=0.001), impaired BLS (-10.9±2% vs -13.3±3%, p=0.001), and pronounced MD (86±33 ms vs 70±26 ms, p=0.006) compared to survivors.

Univariate analyses showed STS score, NYHA IV, renal disease (defined as baseline creatinine > 2 mg/dl), aortic valve (AV) mean gradient and post-TAVR PVL as significant univariates for 1-year mortality (Table 2). Baseline multivariate Cox regression model included age, STS, NYHA, renal disease, AV mean gradient, and post-TAVR PVL (model 1, p<0.001). Incremental prognostic information was achieved by adding strain parameters as shown in Figure 3. Addition of GLS to model 1 resulted in a significant C-statistic increase (40.6 vs. 34.3, p=0.032). A further incremental prognostic value was achieved by adding BLS to model 1 + GLS (47.5 vs. 40.6, p=0.001). Similarly, addition of MD to model 1 + GLS + BLS resulted in further incremental prognostic value (50.9 vs. 47.5, p=0.008). For the measurement of GLS, the Interobserver Intraclass Correlation Coefficient was 0.87.

Discussion

This retrospective clinical study provides evidence that myocardial strain parameters identified using 2D-STE immediately post-TAVR can be helpful in predicting poor outcomes in patients with AS. We demonstrated that both BLS and MD independently predict 1-year mortality in TAVR patients and provide incremental prognostic information in addition to known prognostic predictors of poor outcomes.

Myocardial fibrosis is an early morphologic change in patients with AS [18, 25, 26]. Two types of myocardial fibrosis were identified, interstitial fibrosis and replacement fibrosis. The interstitial fibrosis is reversible, and the latter is irreversible [27, 28]. Fibrosis affects myocardial diastolic and systolic function and provides a structural substrate for myocardial desynchrony [34]. Therefore, it plays a major role in sudden cardiac death and progression to heart failure [35]. Long-standing AS-related maladaptive myocardial changes resulting in fibrosis and ultimately impaired left ventricular (LV) function may persist after AVR and can affect clinical outcomes [31].

Previous studies developed a robust and definitive risk model to predict the outcomes of TAVR [36-38]. The basic model (model 1) included age, STS score, NYHA IV, renal disease, aortic valve mean-gradient, and post-TAVR PVL had a significant prognostic value in our patients. Various statistical metrics were employed to examine the incremental value of markers beyond model 1 [38-39]. Reviewing marker performances across the metrics, GLS, BLS, and MD emerged as the most promising markers.

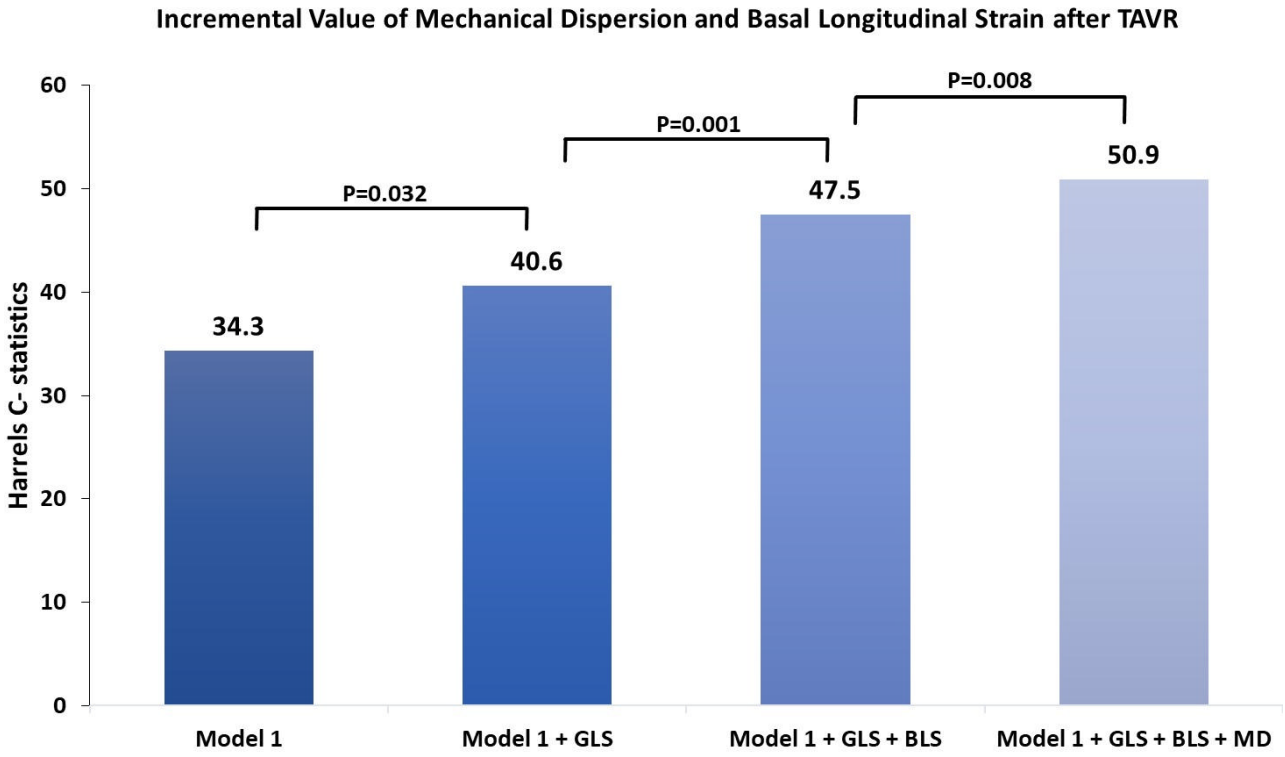

Figure 3. Incremental value of GLS, BLS, and MD post-TAVR. Incremental prognostic information by adding strain parameters. The C statistic values were obtained from the multivariable Cox proportional hazards regression models. Model 1 includes age, STS score, NYHA IV, renal disease (Cr > 2mg/dL), AV mean gradient and post-TAVR PVL as significant univariates. AV: aortic valve; BLS: basal longitudinal strain; Cr: creatinine; GLS: global longitudinal strain; MD: mechanical dispersion; NYHA: New York Heart Association; PVL: paravalvular leak; TAVR: transcatheter aortic valve replacement.

2D-STE is an emerging tool in detecting myocardial dysfunction prior to a clinically significant decrease in LVEF. When assessing for myocardial fibrosis, 2D-STE is cost-effective in comparison to cardiac MRI and less invasive than myocardial biopsy. Impaired pre-TAVR myocardial strain parameters have been linked to adverse outcomes in patients with AS [17]. In this study, we sought to determine if these strain parameters hold a prognostic value even post-TAVR.

Reduction of left ventricular afterload immediately post-TAVR results in improved myocardial strain parameters. In a study done by Delgado et al., a 19% reduction in GLS was noted immediately post-TAVR compared to baseline parameters [40]. In our study, GLS remained an important prognostic variable in multivariate analysis when adjusting for variables in model 1. However, addition of BLS to model 1 + GLS showed a further improvement in incremental prognostic value. This may be explained by the fact that fibrotic changes in AS primarily affect the basal segments and later progress to mid and apical segments [30]. In addition to BLS, MD has also been associated with myocardial fibrosis and heterogeneous myocardial contraction in AS [39]. Studies have shown a moderate correlation between the prevalence of myocardial fibrosis as detected on cardiac MR, and MD measured with 2D-STE [41]. In our study, MD was a significant predictor of all cause 1-year mortality in univariate analyses and remained a significant predictor in multivariate analysis. Additionally, MD resulted in a significant incremental prognostic value when added to model 1 in combination with BLS and GLS. To our knowledge, this is the first study that describes BLS and MD as important prognostic variables immediately post-TAVR. This emphasizes the potential use of 2D-STE in guiding the management of post-TAVR patients.

Table 2. Univariable and multivariate cox regression analysis for predictors of all-cause 1-year mortality.

	Univariate		Multivariate	
Variables	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Age	1.039 (0.99-1.09)	0.094		
Gender (Male)	1.038 (0.49-2.17)	0.922		
BMI	0.954 (0.90-1.01)	0.108		
HTN	0.553 (0.13-2.32)	0.419		
CAD	1.63 (0.67-4.10)	0.269		
Diabetes	2.03 (0.96-4.30)	0.062		
STS score	1.110 (1.04-1.19)	0.003		
NYHA IV	2.92 (1.28-6.63)	0.011		
Renal Disease (Cr>2)	2.31 (1.02-5.24)	0.046		
Baseline LVEF	0.987 (0.96-1.01)	0.260		
Post-TAVR LVEF, % (Day1)	0.978 (0.95-1.01)	0.056		
AV Mean Gradient	0.949 (0.92-0.97)	0.001		
Post-TAVR PVL	2.339 (1.45-3.75)	0.001		
GLS, %	1.21 (1.08-1.34)	0.001	1.12 (1.01-1.24)	0.045
BLS, %	1.29 (1.12-1.47)	0.001	1.21 (1.05-1.40)	0.008
MD, msec	1.02 (1.01-1.03)	0.003	1.02 (1.01-1.04)	0.001
Adjust for: age, STS score, NYHA IV, renal disease, AV mean gradient, post-TAVR PVL				

HR: Hazard ratio; BMI: body mass index; Cr: creatinine; NYHA: New York Heart Association; STS: Society of Thoracic Surgery; CAD: coronary artery disease; LVEF: left ventricular ejection fraction; AV: aortic valve; TAVR: trans-catheter aortic valve replacement; PVL: paravalvular leak; GLS: global longitudinal strain; BLS: basal longitudinal strain; MD: mechanical dispersion.

Conclusion

We demonstrated that post-TAVR BLS and MD are independent predictors of 1-year mortality in patients with severe AS. Our study further demonstrates the incremental prognostic utility of these parameters to known markers of poor out. Early assessment of myocardial strain and mechanical dispersion should be considered as new indices for identifying patients at risk for poor outcomes post-TAVR.

Limitations

Baseline myocardial strain data was not available before TAVR. Therefore, it was not possible to determine whether pre- and post-TAVR strain parameters provide similar or different prognostic information. Another important limitation of our study is the lack of enough data to calculate the delta change in myocardial strain post-TAVR which could be an additional prognostic variable in TAVR patients. Further studies are needed to determine the prognostic implication of this factor. Although internal validation confirmed our results, the differential performance of the markers investigated here needs to be reexamined in larger study populations. More studies are needed to assess whether post-TAVR index-enhanced risk stratification can guide management decisions of post-TAVR patients, alongside with previous models.

Acknowledgments

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Conflict of Interest

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

Comment on this Article or Ask a Question

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Very Late Thrombosis of an Atrial Septal Defect Occluder Device Causing a Massive Splenic Infarction

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Percutaneous occlusion of atrial septal defect (ASD) has emerged as the first approach of treatment in many cardiac centers, because of lower post-procedure morbidity and shorter hospital stay when compared to open-heart surgery. However, there is scarce information on very late complications.

We present a case of a 19-year-old girl who had a very late systemic thrombotic complication. The patient was treated six years before, with the implant of an Occlutech® Figulla® (Helsinborg, Sweden) 33mm device for closing a secundum ASD. The implant was guided by a 2D transoesophageal echocardiogram.

There were no complications during the procedure. The patient was oriented to take DAPT for 6 months after the procedure, but she decided not to take any medication. Interestingly, there were no thrombotic complications during the first six years follow-up.

The Echocardiograms performed at one (TTE), six (TTE) and twelve months (TOE) after the procedure showed a well-implanted device and no residual shunts.

Six years after the procedure, the patient was taking only contraceptive therapy. She has begun abdominal pain of subtle onset and was taken to the ER. An abdominal ultrasound showed low arterial flow in her spleen. An AngioCT was performed, revealing a large splenic infarction. The patient was anticoagulated, first with Low Molecular Weight Heparin and after with Coumadin for one year, keeping the INR target between 2,5 - 3,5.

There were no additional complications. The first TOE showed one mobile thrombus attached to the left disc of the device, and a new examination after two weeks of therapy revealed its complete resolution.

The patient is under clinical surveillance, was advised to stop contraceptive therapy and a hematologic workup was done after one year of completion Coumadin therapy has not revealed any thrombotic disorder.

Percutaneous closure of ASD is the standard therapy in many cardiac centers. However, complications may occur. Despite rare, late thrombosis can be a potentially catastrophic event. It can be related to incomplete endothelialization of the device, and the predictors for this condition are poorly understood. Candidates for device implantation should be carefully screened for potential thrombotic and allergic conditions prior to choosing the ideal therapy. Close follow-up shall be mandatory in these patients.

Key Words

Atrial septal defect • Septal Closure device • Interventional Cardiology

Case Presentation

Percutaneous occlusion of secundum atrial septal defects (ASD) has emerged as the first choice of treatment in many cardiac centers, because of less post-operative morbidity and shorter hospital stay when compared to surgery [1, 2]. King and Mills performed the first series of cases in 1976 [3]. However, only after the appearance of the Amplatzer Septal Occluder

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Figure 1. The Occlutech® ASD Ocludder.

(ASO) [4, 5], the method has gained wider acceptance. Nevertheless, complications have been described. More common are device embolization, cardiac erosion, atrioventricular block, atrial arrhythmias, inflammatory and allergic reactions to components of the devices (mainly nickel) and device thrombosis [6-11]. The last is commonly related to device implantation and should decline after its endothelialization (up to 6 months). In general, adult patients are treated with dual antiplatelet therapy (Aspirin plus Clopidogrel), starting with a loading dose of 300mg of Clopidogrel and 300mg of ASA two to four days before the procedure, and continuously for six months after treatment, using data from coronary angioplasty protocols [12], since there are no trials to date that have investigated the best antiplatelet therapy in this specific setting. Preoperative management may vary from different centers, but generally involve collecting general hematologic tests (complete blood count, coagulation profile), Thorax X-Ray and echocardiogram. During the procedure, patients receive intravenous heparin to maintain the Activated Clotting Time (ACT) between 200-250 seconds, antibiotic prophylaxis, and in post-procedure an echocardiogram is generally made in the first 24 hours to check device position, presence of residual shunts, evidence of new pericardial effusion and valve function. In the long term evolution, TTE is performed in one and six months, and a TOE is performed after one year of treatment.

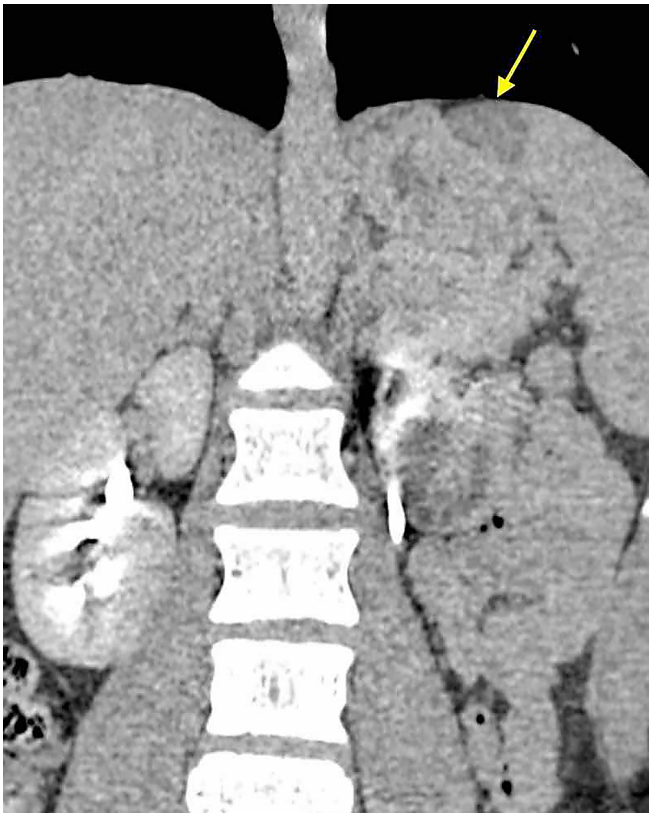


Figure 2. CT Scan showing apical splenic infarction (arrow), 6 years after ASD closure.

Pedra et al. [13] reported mid-term outcomes of secundum ASD closure with the Figulla® Occlutech® device in an observational, single-arm study that included 200 consecutive patients treated in two Brazilian referral centers. For children, the antiplatelet protocol included Aspirin in a dose of 3-5 mg/Kg (max: 200mg/day), started a couple of days before the procedure. Heparin was given (100-150 IU/Kg) during the device implantation to maintain the ACT greater than 200 seconds. Anmar and Hegazy [14] published the results of the closure of 17 ASDs in patients with less than two years of age, using the Occlutech® Figulla® Flex occluder. For this subsetting (small children), antiplatelet protocol included Aspirin in a dose of 5mg/Kg before the index procedure and for six months after the implant.

Nevertheless, there is scarce data on very late complications, mainly because of the lack of trials to investigate very long term treatment evolution.

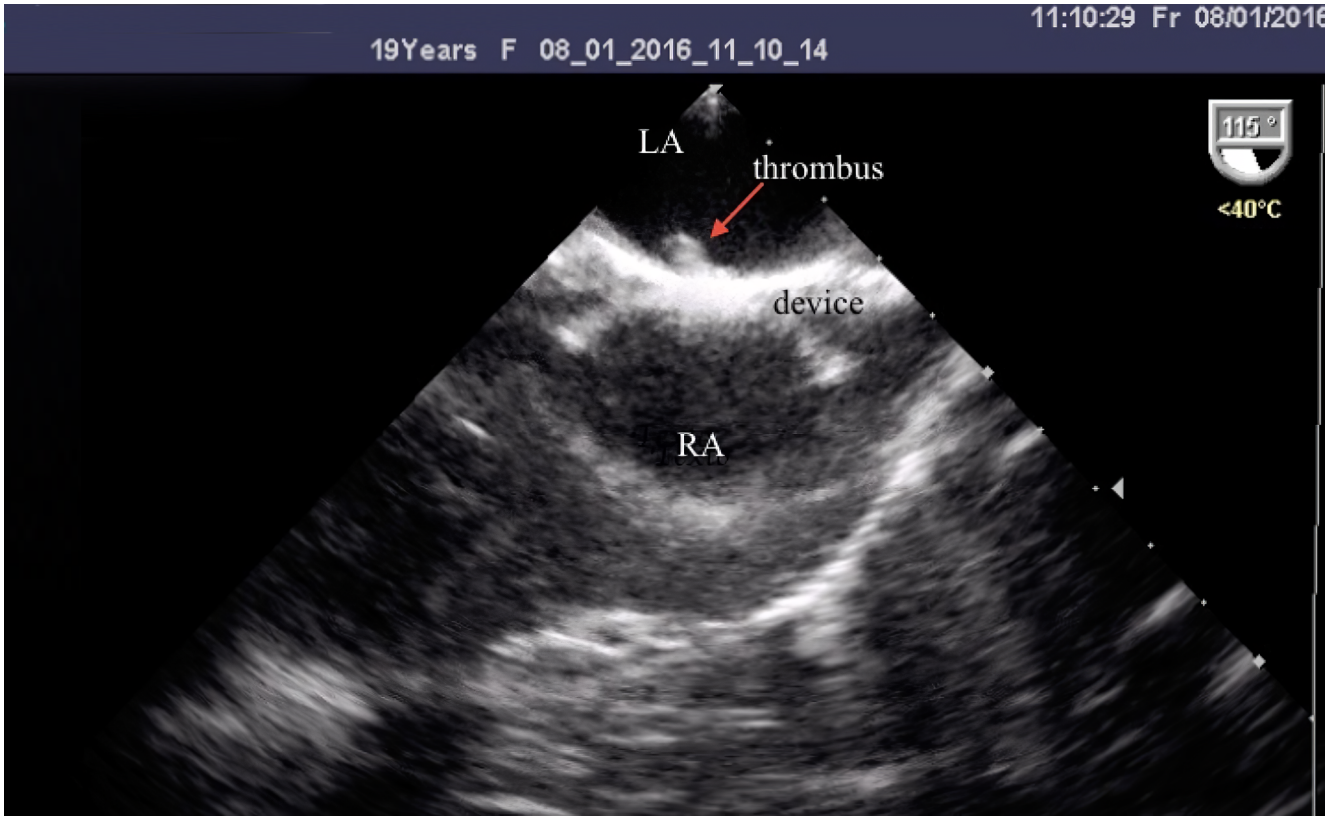


Figure 3. TOE showing mobile thrombus attached to the occluder's left atrial disk.

We present a case of a 19-year-old female who presented with a very late systemic thrombotic complication after percutaneous treatment of a large size ASD.

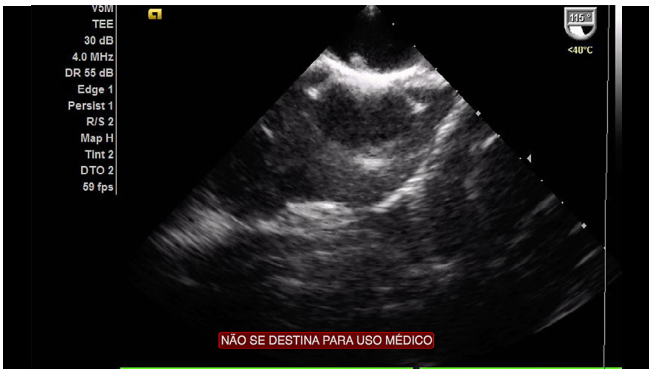
The patient had been treated six years before, with implantation of a 33mm Occlutech® Figulla® ASD occluder (Figure 1). The implant was guided by the 2-D transoesophageal TOE. There were no complications during the procedure or in the postoperative period. The patient was advised to take DAPT (ASA plus Clopidogrel) for 6 months after the procedure, but she decided personally not to take any medication, and even so, she had not any immediate and late thromboembolic complications.

Transthoracic echocardiograms (TTE) performed at one and six months, as well as a transoesophageal echocardiogram (TOE) at twelve months after the procedure showed a well-implanted device, no residual shunts and no signs of thrombus.

Six years after the procedure, the patient was taking only contraceptive therapy and never smoked. The initial symptom was acute abdominal pain. An abdominal ultrasound showed low arterial spleen flow. An AngioCT was performed, revealing a large splenic apical infarction, and multiple small ischemic areas in the spleen (Figure 2). Anticoagulation was initiated, first with Low Molecular Weight Heparin (LMWH) and after with Coumadin for one year, keeping the INR target between 2,5 to 3,5.

There were no additional complications. The first TOE showed one mobile thrombus attached to the left disc of the device (Figure 3 & Video 1), and a new examination after two weeks of therapy revealed the complete resolution of the thrombus.

After one year of anticoagulation, the patient had a complete hematologic workup, including Factor V Leiden, Prothrombin G20210A mutation, Protein C and S, Antithrombin III, Antiphospholipid antibodies (Anticardiolipin and Lupus anticoagulant) and Homocysteine, that have not shown any disorder. After that, she was prescribed ASA and Clopidogrel indefinitely, although the patient refused to take the medications.



Video 1. Shows the mobile thrombus on the occluder's left atrial disk. View supplemental video at https://doi.org/10.12945/j.jshd.2019.005.19.vid.01.

Discussion

Krumsdorf et al. [15] have investigated the incidence and clinical course of thrombus formation on atrial septal defect (n=407) and patent foramen ovale (n=593) closure devices in 1,000 consecutive patients, between august 1992 and January 2003. The mean age was 48 ± 15 years and nine different devices were used, Amplatzer (ASD and PFO devices) being the most used in this series (41% of all devices). During a follow-up period of 1 to 108 months (mean 36 ± 17 months), a thrombus formation was detected in 20 of 1,000 (2%) patients. The TOE had been performed four weeks and six months after closure in 71% of the patients. Of the 20 patients with documented thrombus formation, 17 had good outcomes with the disappearance of the thrombus following anticoagulation therapy with heparin (n=1), warfarin (n=12), or both (n=4). In three patients the thrombus was removed surgically. Coagulation disorders such as protein C and protein S deficiency and activated protein C resistance were not identified in the thrombus cases, and hyperactivity of factor VIII and thrombocytosis was found in two patients. A wire device frame fracture was also observed in 3 of the 20 (15%) thrombus patients. The authors related atrial septal aneurysm (n=4) and post-procedural paroxysmal atrial fibrillation (n=4) as significant predictors for thrombus formation.

Other hypotheses for this late complication could be incomplete endothelialization of the device. Nguyen et al. [16] described one case of very late endocarditis after twelve years of an ASD closure. The surgical findings showed incomplete endothelialization of approximately one quarter of the Amplatzer Septal Occluder, and vegetations on both sides of the device. The authors commented that although in preliminary animal studies of transcatheter ASD closure investigators have reported complete endothelialization within weeks after implantation and a 100% closure rate at 3 months, in humans investigators have observed varying degrees of endothelialization with or without late sequelae. For this setting, investigators have been analyzing surface modifications and coatings on NiTi alloys at the molecular level to enhance device healing and endothelialization [17, 18].

Conclusions

Transcatheter ASD closure is a common and widespread procedure. However, very late complications may occur. Despite very rare, late thrombosis can be a potentially catastrophic event. Candidates for device implantation should be carefully screened for potential thrombotic and allergic conditions prior to choosing the ideal therapy. Close follow-up shall be mandatory in these patients.

Conflict of Interest

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

Comment on this Article or Ask a Question

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Endovascular Treatment of Hypoplastic Gothic Aortic Arch in Combination With Congenital Absence of the Left Common Carotid Artery

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Abstract

A rare clinical case of endovascular treatment of a hypoplastic Gothic aortic arch (AA) with congenital absence of the left common carotid artery (CCA) in combination with ventricular septal defect (VSD) is presented. In early childhood, the patient underwent VSD closure with an occluder and balloon dilatation of the AA and the aortic isthmus (AI). Currently, at the age of 10, large-diameter stent implantation in the hypoplastic AA and AI was performed. Thus, a radical correction of complex congenital heart disease was performed by three-stage endovascular treatment.

Key Words

Aortic arch hypoplasia • Kinking • Left common carotid artery absence • Endovascular treatment

Introduction

Coarctation of the aorta is often associated with the hypoplasia of the aortic arch (AA), which may also occur along with other congenital heart defects. The AA is considered hypoplastic when the diameter of its proximal, distal and isthmic segments is less than 60%, 50%, and 40% of the ascending aorta diameter, respectively [1].

The hypoplastic segment of the AA leads to the appearance of a systolic pressure gradient (SPG) between the ascending and descending aorta, which is the cause of the development of hypertension [2]. Long-Term prognosis in these patients is considered unfavorable since it is a common cause of death after the fourth decade of life [3, 4]. The elimination or reduction of the SPG in the presence of narrowing/hypoplasia of the AA and aortic isthmus (AI) improves long-term results and survival.

In newborns and infants, the standard treatment for hypoplastic AA is open surgery [3]. In elder children, surgical correction of the hypoplastic AA often requires the use of extracorporeal circulation with selective antegrade cerebral perfusion, circulatory arrest, and hypothermia. These factors are associated with an increased risk of intra- and postoperative complications, as well as mortality.

Endovascular treatment options for AA coarctation and re-coarctation have been successfully used for many years. However, endovascular interventions on the AA remain technically challenging and, therefore, are rarely performed. In a number of studies [5-8] and case reports [4, 9], there are good immediate results of the AA stenting.

The absence of the left common carotid artery (CCA) is an extremely rare congenital anomaly, which

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is mostly asymptomatic unless another comorbidity is present. In the literature, there are isolated case reports on the absence of the left CCA in combination with other various anomalies of the AA [10-14]. However, there is no case reported in combination with hypoplastic Gothic AA and VSD.

We present the first, to the best of our knowledge, case of staged endovascular treatment for ventricular septal defect (VSD) in combination with AA anomaly, represented by an anatomically complex and rare variant of hypoplasia and kinking of the AA (Gothic, elongated above the sternoclavicular joint) along with congenital absence of the left CCA, looping of the right subclavian artery and anomalous origin of the left subclavian artery from the descending thoracic aorta.

Case presentation

A 10-year-old boy was admitted with complaints of headache, high blood pressure, and fatigue. The patient had a history of congenital heart defect – a VSD and patent ductus arteriosus were diagnosed at birth. At 10 months, he was first diagnosed with the AA anomaly (elongation, hypoplasia, and stenosis due to kinking with SPG of 50 mm Hg), absence of the left CCA, looping of the right subclavian artery in combination with perimembranous VSD of 7.5 mm (Figure 1). At the age of 1 year and 1.5 months, transcatheter VSD closure was done using an 8mm Amplatzer Perimembranous Ventricular septal occluder (Figure 2). Four months later (at the age of 1.5 years), transluminal balloon angioplasty for the AA and AI stenosis was performed using a Tyshak II balloon catheter (NuMED Inc., Hopkinton, NY) with a diameter of 8 mm, the SPG decreased from 53 to 35 mm Hg. Subsequently, the child was observed on an outpatient basis. According to the mother, first complaints on high blood pressure appeared in February 2018, and anti-hypertensive therapy was prescribed.

In October 2018, at the age of 10 years, the child was admitted for examination and further treatment approach determination. His blood pressure in right arm was 125/56 mm Hg and in the right leg – 70/45 mmHg. The pulse in the lower extremities was weak. The liver was 2 cm below the costal margin.

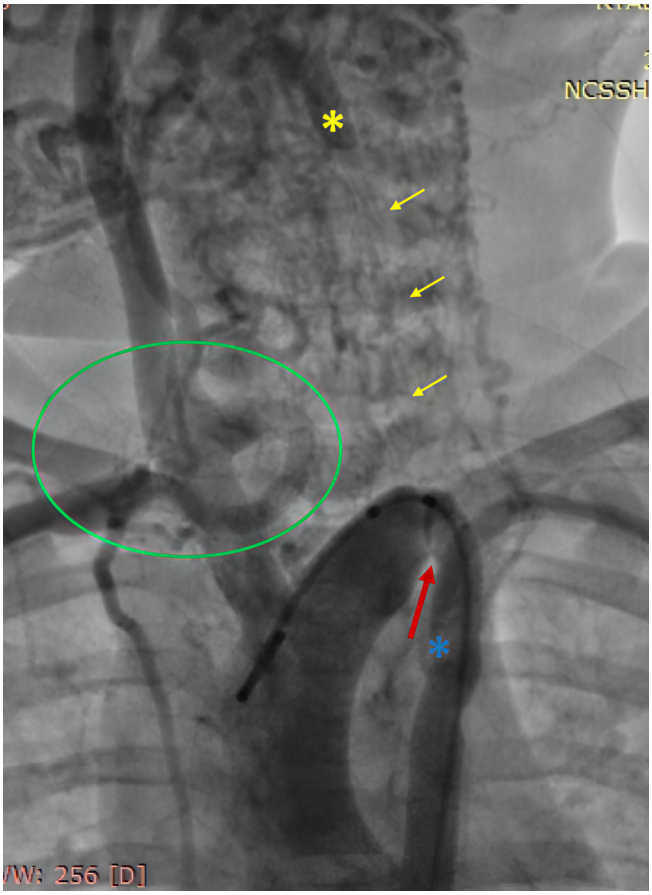

Figure 1. Aortography in the anteroposterior projection showing congenital pathology of the aortic arch: hypoplasia and kinking of the aortic arch *(red arrow)*; absence of the left common carotid artery *(yellow arrows)*; its distal part is formed by multiple collaterals and subsequently is divided into the external and internal carotid arteries *(yellow asterisk)*; coiling of the right subclavian artery *(oval)*; the left subclavian artery takes origin from the descending thoracic aorta *(blue asterisk)*.

On ECG and Holter monitoring sinus arrhythmia and signs of left ventricular hypertrophy were identified. 24-hour blood pressure monitoring during antihypertensive treatment revealed systolic hypertension at night with blood pressure up to 137/80 mmHg.

Transthoracic echocardiography showed AA gradient of 85 mmHg. Collateral blood flow in the abdominal aorta was revealed. No shunt across VSD occluder registered. Left ventricular hypertrophy was noted, ejection fraction was 78%.

Carotid and transcranial doppler ultrasound showed no changes in BCA, normal flow in the right

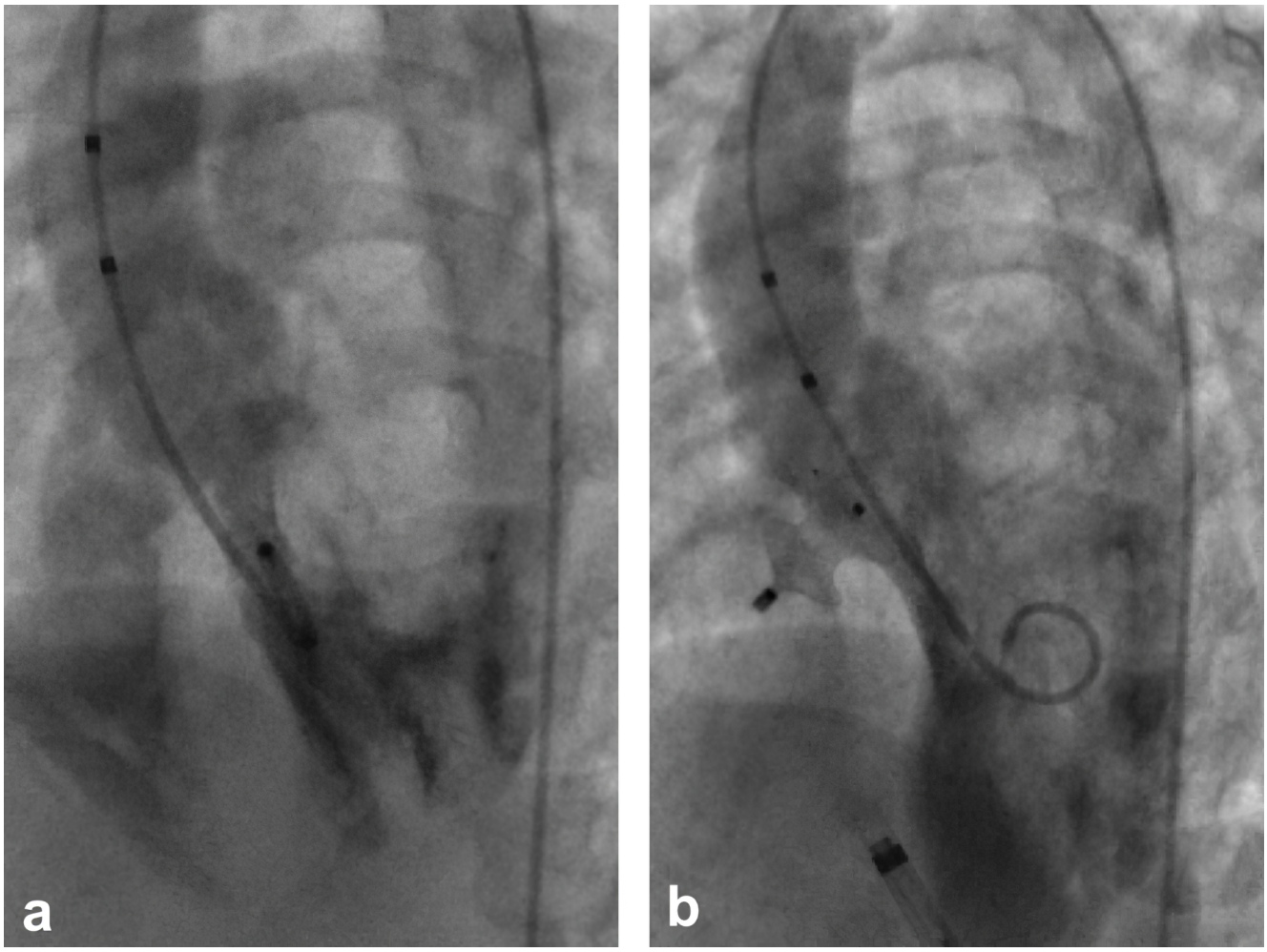

Figure 2. Endovascular closure of perimembranous VSD: ***Panel a.*** Left ventriculography showing a large shunt into the right ventricle through the VSD; ***Panel b.*** After VSD closure no shunt registered though the occluder VSD – ventricular septal defect.

CCA, the left CCA was not visualized, collateral blood flow in its distal part was registered. The vertebral arteries showed normal blood flow with multiple collateral vessels. The blood flow velocity in the intracranial parts of the internal carotid and vertebral arteries was not changed. No disturbance of venous outflow from the brain was revealed.

CT-angiography showed left-sided hypoplastic kinked AA, with stenosis up to 6.1 mm, a post-stenotic diameter of 7.9 mm, and 11.2 mm at the level of the origin of the left subclavian artery (Figure 3). The diameter of the ascending aorta was 25 mm. The BCA (8.7 mm) was divided into the right CCA (7.5 mm) and proximally coiled right subclavian artery (9 mm), with the vertebral artery taking origin from it. The right ICA of 3.4 mm, formed an S-shaped loop after bifurcation. The left CCA was not detected, in its distal part, numerous collaterals formed a short thin trunk of 3.2 mm, which subsequently was divided into the external and internal carotid arteries. The left subclavian artery (8.5 mm) took origin from the descending thoracic aorta. The circle of Willis was complete.

Considering the hemodynamically significant obstruction at the level of the AA and left CCA absence, we decided to perform stenting of the hypoplastic AA and AI.

Technique

The catheterization of the right internal jugular vein under endotracheal anesthesia was performed, a 5Fr introducer sheath was introduced and an int-

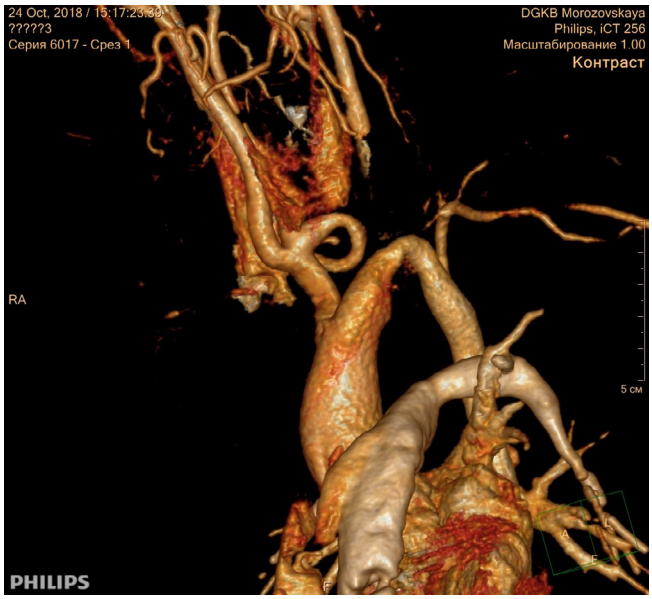

Figure 3. 3D reconstruction (VRT) of CT angiography, demonstrating pathology of the aortic arch.

racardiac electrode placed in the right ventricle for pacing. Next, retrograde catheterization of the aorta through the left femoral artery with the installation of a 9Fr introducer sheath was performed. Unfractionated heparin (100 units per kg) was injected intravenously. Aortography in the anteroposterior and left anterior oblique (LAO 45º) projections confirmed the congenital anomaly of the Gothic AA with an absence of the left CCA (Figure 1). The length of the AA hypoplasia was 34 mm with a minimal luminal diameter of 5 mm, while the diameter of the AA proximal to the BCA origin was 11.5 mm, distal to the AI – 9.6 mm. The SPG between the ascending and descending aorta was 59 mm Hg.

An exchange length, Amplatz super-stiff guidewire (Boston Scientific-City, MA) was placed in the aortic root. Over this guidewire, 9Fr Mullins sheath (Cook) was advanced to the AA. Then, a Z-med balloon dilatation catheter (NuMED, Inc., Hopkinton, NY) 12x40 mm and was advanced and placed at the aortic hypoplasia zone. Under right ventricular pacing at 200 beats/minute, balloon dilatation was performed in order to determine the localization of its "waist" and to predict stent deployment. At a pressure of 7 atm. the "waist" in the inflated balloon disappeared, and its walls were firmly attached to the walls of the aorta. Subsequently, AA stenting was performed.

A 36 mm long stent "Intrastent LD Mega" (Medtronic, Fridley, MN) was manually mounted on the same balloon catheter Z-med (12x40 mm). Then, the entire assembly (balloon with the stent mounted on it) was advanced to the area of stenosis. The correct stent position in the AA obstruction area was monitored by contrast injection via the side port of the sheath. When the proper stent position was confirmed, the balloon was manually inflated during rapid right ventricular pacing at 200 beats/minute. At a pressure of 10 atm. complete deployment of the stent was achieved with normalization of the AA geometry. Repeat aortogram showed good result, the stent was fully opened in the AA, with no signs of complications (vessel wall injury) (Figure 4). Repeat pressure gradient revealed the presence of only 6 mmHg across the area. The sheath was removed and hemostasis was achieved by direct pressure. After the operation, the anticoagulant therapy was continued, including intravenous administration of heparin (100 units per kg) twice every 6 hours, followed by oral aspirin at 4 mg/kg per day for 6 months. For the prevention of infectious complications, a broad-spectrum antibiotic was administered intraoperatively.

The postoperative period was uneventful. A day after the surgery, the arterial pulse in the lower extremities was distinct, the difference in systolic blood pressure between the right hand and leg did not exceed 10 mmHg. Doppler ultrasound after stenting showed restoration of normal blood flow in the abdominal aorta, the SPG across the stent was of 20 mmHg. The child was discharged on the 5th day after the procedure. A comprehensive examination with a chest computed tomography was planned at 6 months follow up.

Discussion

Stenting of the AA obstruction is still one of the most challenging endovascular interventions in children. In this type of congenital heart defect, balloon dilatation is often unsuccessful, and stent implantation is required [15]. Percutaneous interventions for AA hypoplasia are somewhat different from those in coarctation of the aorta [4, 5]. Managing the stenting of the AA and coarctation of the aorta, we have given up performing pre-dilatation because of the risk of aortic wall injury. However, considering the absence

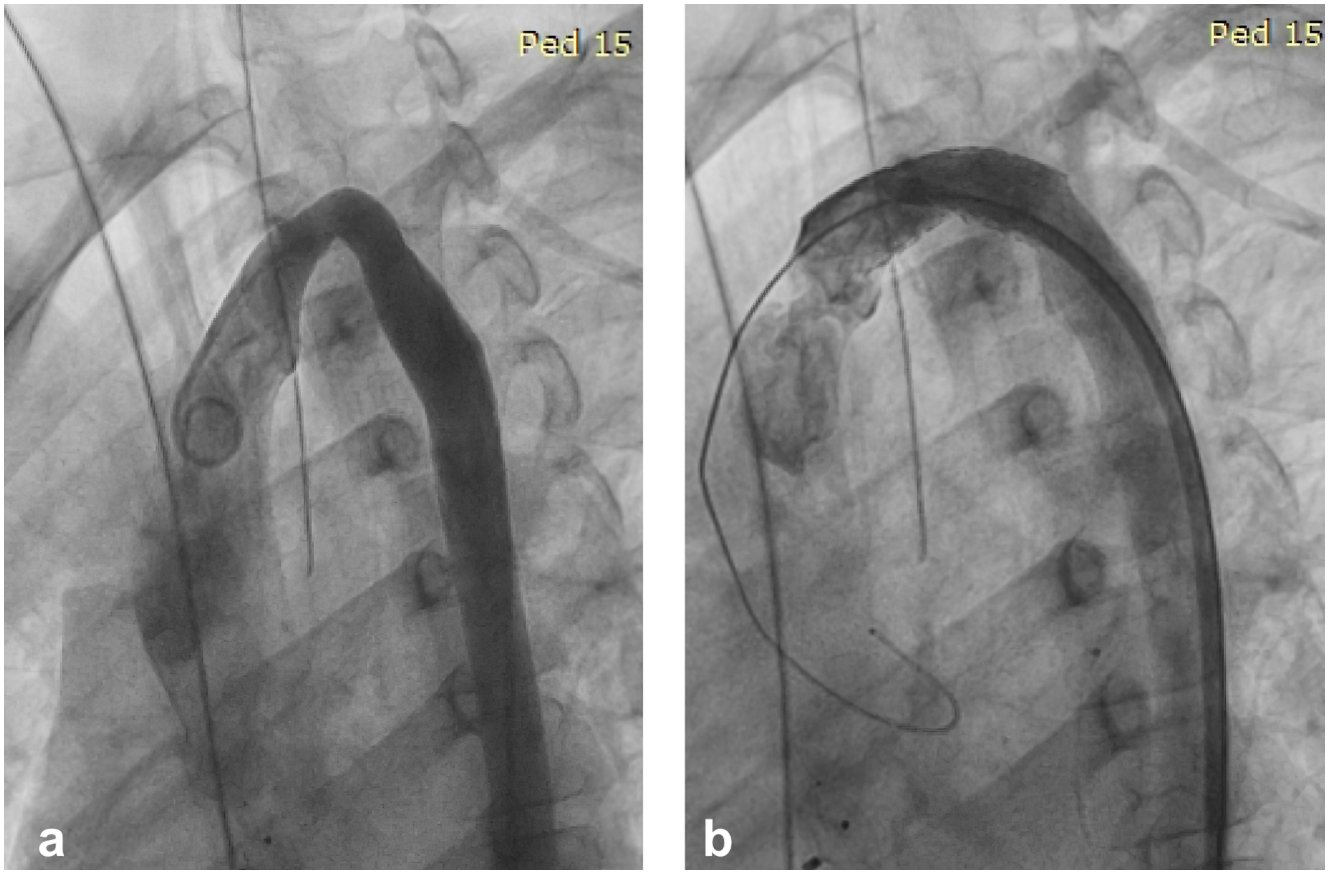

Figure 4. Aortography before ***Panel a*** and after ***Panel b*** stenting of the aortic arch and its isthmus: ***Panel a.*** Hypoplasia and kinking of the aortic arch; ***Panel b.*** After stent implantation, there's no obstruction nor kinking.

of experience in transcatheter management of a sharp-angled (Gothic) AA, it was crucial for us to evaluate the vessel wall extensibility, as well as to detect the balloon "waist" in the area of the intended stent placement. In this case, performing pre-dilatation confirmed that the chosen strategy was right. The prevention of the possible dislodgement or dislocation of the stent during AA stenting is very important. That's why it's crucial to perform the rapid right ventricular pacing during stent deployment which allows avoiding stent dislocation due to a sharp decrease in the cardiac output [8]. Once the stent is implanted in the AA, the reinforcement of the origin of the left CCA should be avoided, since this can theoretically lead to thromboembolism, as well as stenosis or occlusion of its origin. In our case, the congenital absence of the left CCA facilitated this task and allowed to implant the stent successfully with much less concern about salvaging the LCA origin.

When choosing an appropriate endoprosthesis we opted for the "Intrastent", considering that this stent has open cells and, therefore, greater flexibility which allowed the device to adapt better to the shape of the AA.

Despite the absence of the left CCA, there were no changes in cerebral blood flow, due to well-developed collaterals, as well as the complete circle of Willis. The selected strategy of the endovascular treatment turned out to be correct for this patient: the first stage was to close the VSD using the occluder during infancy, followed by the transluminal balloon angioplasty of the AA, followed treatment of hemangiomas of the face and neck, and lastly percutaneous stenting of the arch at the age of 10 years.

Follow up assessment of the stent is required. In the late postoperative period, in addition to the somatic growth of the child, endoprosthesis restenosis due to neointimal hyperplasia or stent fracture is pos-

sible [8]. If necessary, repeated endovascular intervention should be performed.

Conclusion

We present the first case of successful staged endovascular treatment of complex congenital heart disease – AA anomaly in combination with the absence of the left CCA and VSD. In a number of complex AA anomalies, such as the Gothic arch, stenting is still possible.

Conflict of Interest

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

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