Interventional device closure of perimembranous ventricular septal defects: challenges, pitfalls, and advancements in device technology

Abstract

Percutaneous closure is the standard therapy for muscular Ventricular Septal Defects (VSDs) beyond infancy with a low rate of major complications. The story is somewhat different for Perimembranous Ventricular Septal Defects (PmVSDs) where surgery remains in 2021 the preferable treatment approach in some centers, due to the historical incidence of Complete Atrioventricular Block (CAVB) that has been associated with the asymmetrical Amplatzer Membranous VSD Occluder. It is certain that transcatheter closure of PmVSD is one of the most complex cardiac interventions and have stringent demands on device design due to several challenging considerations. Despite that, experienced interventionists have been continuously reporting successful experiences with PmVSD closure using a variety of device occluders in an off-label indication. Recent meta-analyses confirmed the very good outcomes of this approach and the non-inferiority compared to surgery. However, these devices represent a compromise, as they are not specifically designed to be placed in the perimembranous position. To date, no device achieved market approval in the United States. The need for a device dedicated to PmVSD transcatheter closure is mandatory to standardize the technique and we are very close to achieving this goal. The most recent KONAR-Multifunctional Occluder (MFO) has been smartly designed, combining technical features of previous devices, to tackle encountered difficulties and the outcomes of emerging clinical reports are consecutively encouraging. The MFO specifications are particular but limitations are present and need to be highlighted. This continuous advancement in device technology through continuous physician input will lead to the birth of the ideal device for this intervention.

Keywords: Congenital heart disease • Device closure • Multifunctional occluder • Perimembranous • Ventricular septal defect

Abbreviations

ADO: Amplatzer Duct Occluder; AoV: Aortic valve; CAVB: Complete Atrioventricular Block; LRD: Left Retention Disk, LV: Left Ventricle; MFO: Multifunctional Occluder, PmVSD: Perimembranous Ventricular Septal Defect; RRD: Right Retention Disk; RV: Right Ventricle; SAR: Sub-Aortic Rim; TEE: Transesophageal Echocardiography; TV: Tricuspid Valve; VSD: Ventricular Septal Defect

Introduction

Transcatheter therapy offers unbeatable advantages when compared to cardiac surgery [1-3]. Several devices have been designed and tested over the years to percutaneously close PmVSDs [4-7]. However, the Amplatzer asymmetrical device has been associated with a high risk of CAVB, prompting many to abandon this intervention and pushing other interventionists to use devices designed for other applications in an off-label basis.
Challenges of interventional device closure of PmVSD

The history of VSD interventional closure dates back to 1988 when Lock, et al. from Boston reported the first case series of successful closure of muscular VSDs using the Rashkind device [15]. Afterward, other cardiologists followed his lead and used various devices to percutaneously close VSDs but residual leaks and device embolization were not uncommon [6]. The introduction of the Amplatzer muscular VSD Occluder solved this problem as it achieved market approval in the United States and is to date the most commonly used device for percutaneous closure of muscular VSDs, with good reported results [16,17].

Experience in transcatheter closure of PmVSDs was quite different. The intervention presents three specific challenges related to the perimembranous location of the defect and carries a significant risk of complications. Besides the highly heterogeneous anatomical morphology, perimembranous defects are very close to the aortic valve and some PmVSDs can extend beneath the septal leaflet of the tricuspid valve towards the inlet septum [5]. Moreover, PmVSDs amenable to closure beyond early infancy are hemodynamically restrictive but the high-pressure nature of the left-to-right shunt increases the risk of device instability. The double-disc design with septal rims was necessary to hold the device in place, but the nearby aortic valve raised the level of the challenge. The proximity of the conducting tissue to the margins of the PmVSD made the procedure even more challenging as sometimes, a simple wire manipulation across the defect may cause conduction abnormalities [5].

In an attempt to address these challenges, the leader market Amplatzer introduced a specially designed eccentric device, called Amplatzer Membranous VSD Occluder, making the closure of PmVSDs possible, effective and standardized. The device was designed with the aortic edge of the asymmetric left ventricular disc shorter (0.5 mm) than the long apical one (5.5 mm). The lower pole of the left ventricular disc contained a platinum marker to orient device positioning. Its first use was reported by Hijazi, et al. and closure rates were excellent when pooling data from literature [8-10,12,17,18]. However, the procedure was described as challenging as the implantation required an arterio-venous circuit and there was a certain difficulty in properly orienting the occluder. Most importantly, the device never achieved pre-market approval due to the high incidence of CAVB [8-12].

Cardiovascular impact of VSD closure

Significant and chronic left-to-right shunting across the VSD leads to left-side chambers volume overload and dilatation with eventually eccentric Left Ventricle (LV) hypertrophy due to amplification of LV wall stress [29]. Moreover, the alteration in systemic hemodynamics related to non-corrected cardiac defects can influence both the systemic and pulmonary vascular performance and theoretically promote the development of endothelial dysfunction and morphological vascular wall
alterations [30,31]. Previous studies showed that timely surgical closure of VSD is associated with a positive outcome on various LV parameters [32,33]. However, the time-related reduction of these parameters is not uniform with a slower pace of LV mass regression compared to other parameters [34]. Closure of cardiac shunts can promote early and long-term amelioration in the systemic vascular endothelial function [35], speculating that left cardiac chambers remodeling can influence the systemic performances of the endothelium [36]. Previous studies demonstrated amelioration in nitric oxide production in the vascular stream after percutaneous closure of cardiac defects [37], partially explaining the complex relationship between the left chambers remodeling and endothelial function [31,38]. With this in mind, the impact of transcatheter PmVSD closure on LV remodeling and systemic hemodynamics also deserves to be fully investigated with a focus on the time course and degree of expected changes.

Discussion

Multifunctional occluder: Advantages and limitations

As a result of a long-standing effort to solve the complex challenges of transcatheter PmVSD closure, the MFO was recently released as the latest addition to the armamentarium of Lifetech (Shenzhen, China) combining the advantages of previous devices to tackle most of the aforementioned difficulties [13,14,39,40]. The device is made of new soft woven mesh with 144 threads of 0.002 inch Nitinol wires to offer high conformability to the defect with a reduction in the theoretical risk of conduction abnormalities and improvement in the profile (Figure 1). The self-expanding device is hybridly designed to combine the advantages of single and double-disc Amplatzer duct occluder devices. The two retention discs are joined by a cone-shaped 4 mm long waist. The Right Retention Disk (RRD) is connected to the central waist by a millimetric connection making it articulated, thus allowing the operator to accommodate the device to various aneurysmal anatomicies reducing interference with the Tricuspid Valve (TV). The retention rims exceed the largest waist diameter by 2 mm or 2.5 mm allowing closure of more complex PmVSDs (with deficient or absent Sub-Aortic Rim (SAR)). The availability of eight incremental sizes helps in tailoring the patch as much as possible to the size of the hole, covering a large spectrum of defects even in small patients as the delivery system is low profile (5 to 7 Fr.) and partnered with a slim cable to minimize unwanted damage. The waist of the four large models is securely sewn with a PTFE-membrane to increase occlusion capacity and the double-sided screw increased procedural flexibility with both side deliverability.

That being said, drawbacks still exist. First and foremost, there is a size limitation as the largest Left Retention Disk (LRD) diameter is 18 mm. Moreover, in defects with deficient or absent SAR and LV entry-to-Right Ventricle (RV) exist diameters ratio<2, device oversizing is needed for stability. Therefore, transvenous delivery (arterio-venous circuit) is required to control the deployment of the LRD first within the aneurysm and the possible interference with the Aortic Valve (AoV). In fact, the non-articulating LRD didn't allow to extrapolate the maneuver of pushing on the delivery cable in an attempt to re-orientate the LRD in the LV far away from the AoV. This maneuver successfully used with retrogradely delivered Amplatzer Duct Occluder (ADO) II devices would displace the MFO's central waist solidly connected to the LRD. Furthermore, the RRD is a bit too large and can easily interfere with the TV movement if not properly deployed. The delivery system remains relatively large for the retrograde approach, especially in small-sized patients. Finally and most importantly, the incidence of CAVB is not completely eliminated. Leong, et al. recently reported the early occurrence of CAVB following PmVSD closure using MFO in a 26-year-old woman with subsequent device surgical removal [41]. We believe that unintended conduction tissue damages are well controlled with the device's very soft and flexible design along with the avoidance of unreasonable oversizing [14,42,43]. However,
caution is always the best statement and only long-term follow-up will reveal the real risk [44,45].

**Recommendations for PmVSD closure with MFO**

Pre-procedural transthoracic echocardiography planning is highly advisable with a focus on 3 measurements to guide the primary selection of the device size to be later reassessed, by angiography and intra-procedural transesophageal echocardiography (TEE). The LV entry diameter is measured using 3 views (parasternal short-axis, apical 3 chambers view, and subcostal LV-Aorta). The SAR, defined as the distance between the AoV annulus and the upper margin of the color flow across the defect is measured using 4 views (parasternal long-axis view, apical 3-chambers, apical 5-chambers, and subcostal LV-Aorta). The parasternal short-axis view is also used to define the number and diameters of the RV exit(s) taking into account the largest color Doppler flow. The measurement of the depth is not reliable on transthoracic ultrasound. Single plane 55°-60° LAO/20° cranial projection with per-procedural TEE imaging is sufficient to delineate the anatomy and to precisely guide the entire intervention. SAR length and LV entry diameter are measured on angiography at the largest diastolic phase on the LV side and compared to TEE measurements to average both measurements. The RV exit diameter is evaluated on TEE especially in aneurysmal anatomy and is defined as the narrowest color Doppler diameter during diastole, while the number of exits is better assessed on angiography. Angiography is also used to precisely evaluate the defect depth.

The most common anatomical variant in PmVSDs is the presence of an aneurysm. In case of a large aneurysmal pouch and especially when SAR is deficient or absent, we preferably implant the device within the aneurysm itself to close the true anatomical hole and not to place the device at the entrance of the LV side, avoiding the insertion of an oversized device [14]. This attitude was previously reported to reduce the risk of CAVB as the device is placed far from the conduction system [5]. If the redundant tissue of the aneurysm is relatively small and the device could cover the hole along with the aneurysm it is better to close the true anatomical LV entry with the most appropriate device.

The retrograde implantation of MFO is our first choice of approach as it allows simple deliverability with a decrease in radiation exposure and proper control of valvular interferences [13,46]. However, the prograde transvenous approach offers the possibility to precisely control AoV-to-LRD interference, especially in challenging cases with deficient or absent SAR. In tall adult patients, the delivery sheath inserted transarterially is not long enough to pass across the defect and thus transvenous delivery is required.

**Future directions and improvements**

We expect in the near future to see an ideal device being marketed for PmVSD closure in children and adults with complete safety. The ideal device is foreseeable as a hybrid fusion of the most promising occluders, the ADO II and the MFO with some additional features. It should be as soft as ADO II or MFO to limit the risk of conduction abnormalities. The double disk design is a must. In fact, the single-disk design of ADO I that was supposed to be an advantage in reducing TV injury can turn out in some cases a disadvantage related to the prograde implantation process. When passing a PmVSD (with multiple exits) from the LV side, the wire might pass through the non-targeted (small) exit. Therefore, when deploying the ADO I transvenously, the secondarily deployed right side of the device might squeeze in that small exit and interfere with the TV movement, causing stenosis and or regurgitation. The retention disks should be asymmetrical with the RRD 2 to 4 mm smaller than the LRD as the main target is only to occlude the LV entry. Both retention disks should be smartly flexible to offer high anatomical conformability (i.e. ADO II) and allow the operator to position each of the retention disks independently for the waist and far away from the nearby valves. The LRD flexibility is highly needed in defects with deficient or absent SAR that are closed retrogradely. The tapered design of the connecting waist is advantageous to accommodate the PmVSD most common conical shape. However, an anatomically adaptable waist (conforming not only to the size but also to the shape, therefore, precisely filling the hole and not only covering it) is ideal. This might eliminate the common attitude of device oversizing thereby avoiding defect “stenting” as previously seen with the asymmetrical Amplatzer device, where the expansion of the device over time exerted pressure on the conducting tissue. Small 2 mm retention rims would be sufficient for device stability (no need for the 2.5 mm rims in odd-sized MFO or the 3 mm rims in ADO II). Both side deliverability is as mandatory as the low profile to allow procedural flexibility and retrograde closure in very small babies with limited risk of tissue damages. Longer delivery sheaths are needed for retrograde delivery in adults. A larger portfolio with LRD diameters up to 20 mm is necessary to cover larger defects. Regarding the delivery cable, the slimness of the MFO cable is excellent for reducing the system profile. When it comes to flexibility, a heavy cable will certainly lead to destabilizing the implanted device with an unwanted rebound effect post-release, meanwhile, a very floppy cable (i.e. Trevisio) will impede appropriate positioning especially in retrograde deliveries.

**Conclusion**

The addition of the MFO device to the armamentarium of “off-
label” devices used for percutaneous closure of complex PmVSDs is highly valuable, yet some technical limitations are present. Until we witness the birth of the ideal device, patients should benefit from the unbeatable benefits of transcatheter therapy. Albeit a high level of expertise is needed as operators should be very flexible in using a variety of devices and able to modify implantation techniques that are most suited for the anatomy. Appropriate patient selection is of paramount importance to the success of the procedure.

Conflict of Interest

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References