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Immediate and short term outcome post VSD closure using nitocclud PFM coil, a single center experience

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A B S T R A C T

Objectives: We sought to study the immediate and short term outcome post VSD closure using nitocclud PFM coil to document the safety and efficacy of the procedure.

Patients and Methods: The study included 16 patients with perimembranous subaortic VSD who were scheduled for elective trans catheter VSD closure using nitocclud PFM coil in the period from May 2014 to July 2016. All patients underwent full clinical examination, ECG and full echocardiographic study immediately before trans catheter closure as well as 24 h, 1 month and every 6 months after the procedure. Any intra or post procedural complications and their respective management were recorded.

Results: The mean age of the study subjects was 7.4 years. The distance between the defect and the aortic valve was an average of 5.4 ± 1.8 mm, and the left ventricular opening averaged 10.6 ± 3.7 mm. immediate closure of the VSD was achieved in 25% of the cases. This percentage increased to 75% after 1 month. Intravascular hemolysis developed 3 days after the procedure in one patient with a residual shunt and was successfully managed by a PDA Amplatzer occluder device implanted in the residual defect. Three children had transient self-limiting bradycardia and junctional rhythm during the procedure.

Conclusion: VSD closure using nitocclud PFM coil is safe and effective in selected patients. However, we report hemolysis in one patient with residual shunt which needs careful follow up and prompt management.

1. Introduction

Ventricular septal defect (VSD) is the most common congenital heart disease, accounting for 40% of all congenital heart diseases (CHD). It has an overall prevalence of 3.94 per 1000 patients [1]. A notable marked increase in incidence rates is observed from 1.56 to 53.2 per 1000 live births, this can be attributed to the advancement in imaging and screening programs. This increase in prevalence and incidence requires proper management plan and follow up of these patients as this will have a high impact on the wellbeing of the community [2].

The Clinical presentation of VSD is variable, depending on several factors, such as size, location, direction, shunt fraction and other associated cardiac defects. It may be present as isolated form, or in complex combinations which in accordance needs careful assessment and the use of different diagnostic modalities for accurate diagnosis of such patients [1].

A perimembranous Ventricular septal defect (PmVSD) is situated in the membranous portion of the septum. It is located immediately below the aortic valve and the outflow tract of the left ventricle. PmVSD is the most common type of VSD accounting for 75% of all VSDs after infancy. Fibrous continuity between leaflets, tricuspid and aortic valve is a diagnostic feature [3]. Fig. 1.

Although surgical closure is the gold standard in management of VSD, percutaneous closure for VSD is considered an effective management, with no statistical difference in success rate and fewer complications: as better cosmetic results, shorter hospital stay, no need for exploratory thoracotomy and blood transfusion. Patient selection is crucial for high success rate [4].

In 1987 ***Lock* et al.** described the first percutaneous VSD closure for six patients using Rashkind double umbrella device [5]. Since then percutaneous VSD closure has been used as an alternative to surgery [6]. Most commonly used devices for percutaneous closure of VSD are Amplatzer septal occluder, Amplatzer PDA occluder, Amplatzer muscular VSD occluder, concentric Amplatzer VSD occluder, and eccentric Amplatzer VSD occluder. The most significant complication observed following percutaneous closure of VSD was permanent and complete heart block. This has led to safety concerns among cardiologists. To alleviate these concerns, a newer device Nit-Occlud® Lê VSD has been manufactured [7,8].

The Nit Occlud® Lê VSD coil (PFM: Produkte für die Medizin AG, Cologne, Germany). Nit Occlud® Lê VSD coil has a specific nature,

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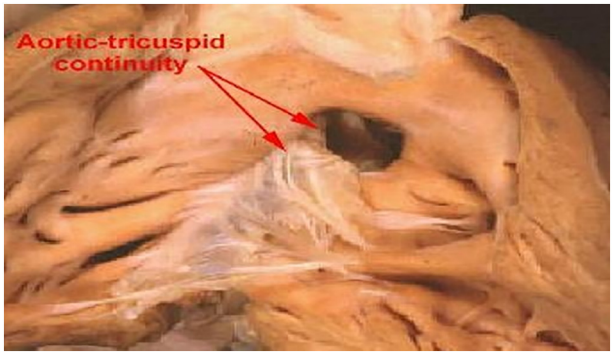

Fig. 1. Specimen of perimembranous VSD with arrow pointing to Aorto-tricuspid leaflet continuity in the postero-inferior margin.

designed and manufactured specifically for VSD closure [9].

There are few case reports and case series published about percutaneous closure of VSD with Nit Occlud® Lê VSD coil. In addition observational mid-term and long-term data are missing. Interestingly there are no cases of permanent complete heart block after percutaneous closure with Nit Occlud® Lê VSD coil in the literature [10]. In this study, we reported the immediate- and short-term results after percutaneous closure of VSD with Nit Occlud® Lê VSD coil (PFM).

2. Patients and Methods

The study included 16 patients with perimembranous VSD who underwent elective percutaneous VSD closure using Nit Occlud® Lê VSD coil in the period from May 2014 to July 2016. All patients underwent full clinical examination, Electrocardiogram and full echocardiographic study immediately before percutaneous closure as well as 24 h, 1 month and 6 months after the procedure. Any intra or post procedural complications and their respective management were recorded.

2.1. Echocardiographic Assessment Before Percutaneous Closure

VSD assessment was performed which included: Site of the VSD, size of the VSD from both sides of the defect (LV and RV side measurements were obtained), pressure gradient across the defect, relationship of the VSD to the surrounding structures, VSD proximity from the aortic valve and detection of aortic valve cusp prolapse if present, detection of aneurysmal tissue, size of the aneurysm and it's exact relation to the septal leaflet of the tricuspid valve was noted. The Flow ratio (Pulmonary flow to systemic flow) was also calculated. Assessment of aortic, ticuspid, mitral and pulmonary valve was also done in all patients [11].

2.2. Electrocardiogram

12 lead Electrocardiogram was performed for all patients before and after percutaneous closure, and during further follow up visits. Electrocardiogram was assessed regarding heart rate, rhythm, PR interval and QRS duration [11].

2.3. Procedure

Percutaneous closure of VSD was performed under general anesthesia in all patients. All percutaneous VSD closures were guided by trans-thoracic echocardiography or trans-esophageal echocardiography. All patients received intravenous heparin (100 units/kg) and antibiotics before the procedure. All patients underwent right and left heart catheterization through the percutaneous trans-femoral route. Assessment of the defect was performed in multiple views. The angiographic view that best profiled the defect was used as a reference for closure. In most cases modified left anterior oblique 60° cranial 20° and left anterior oblique 45° cranial 45° were used [12,13].

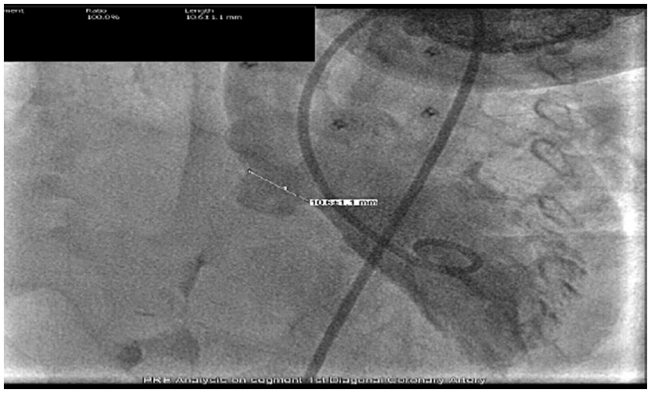

Fig. 2. Left ventriculography showing measurement of the base of aneurysm in patient number 9.

2.4. Measurements Calculated Using Angiographic and Echocardiographic Data

Measurements of the defect size from left and right ventricular sides and its distance from the aortic and tricuspid valve were confirmed using angiography and transthoracic or transesophageal echocardiography (Fig. 2).

2.5. Selection of Device Size

The size of the Nit Occlud® Lê VSD coil used was 2 mm more than angiographic measurement of the left ventricular side of the defect and double on the right ventricular side of the defect. The device comes in the following sizes 8/6, 10/6, 12/6, 12/8, 14/8, and 16/8 mm [12,13].

A 0.035 in Terumo wire was passed through the defect in a multipurpose or cut pig tail catheter according to the anatomy of the defect. And the defect was crossed from the right side and snared in either the pulmonary artery or right ventricle or inferior vena cava. It was captured with a snare to create a complete arterio-venous loop. The delivery sheath was inserted through the femoral vein and advanced to the ascending aorta through the defect. The size of delivery sheath for Nit Occlud® Lê VSD coil was chosen according to the coil size. The first loops were opened in the ascending aorta, and then the device was slowly withdrawn into the left ventricle and into the VSD pouch. Confirmation of position was performed by several hand injections. Following this, the next loops were opened in the left ventricle, and the device was slowly pulled back, the last part of the loops is opened in the defect on the right ventricular side. A left ventricular angiogram was performed to check the location of the device and the residual shunt, before the device was deployed (Fig. 3) [12,13].

2.6. Description of the Device

The Nit Occlud® Lê VSD coil (Fig. 4) is made of nitinol coils. It has a cone in cone configuration, its proximal cone is reversed. The distal coil loops are reinforced to be replaced on the left ventricular side of the defects. The proximal cone is however more flexible, and should be deployed partially on the left ventricular side of the defect. Finally the last two proximal coil loops are placed on the right ventricular side. Nomenclature of the device refers to the sizes of the largest diameter of left ventricular coil, then by the largest diameter right ventricular coil [9].

Patients were assessed immediately, one and six months after percutaneous closure:

- Electrocardiogram assessment: Regarding heart rate, rhythm, PR

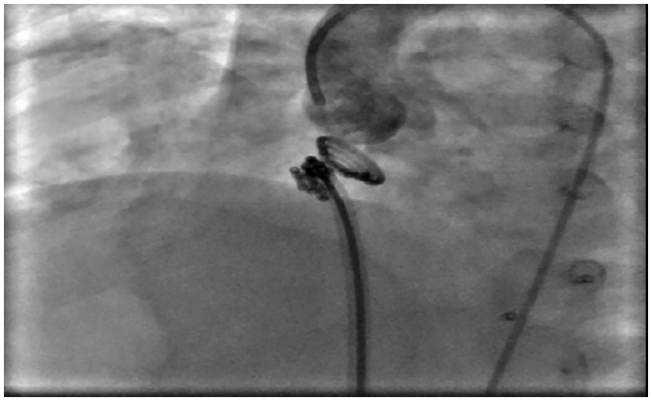

Fig. 3. Aortography during Nit Occlud® Lê VSD coil closure in patient number 9 before coil release.

Fig. 4. The Nit Occlud® Lê VSD coil.

interval and QRS duration.

- Echocardiography assessment: Presence of residual flow and pressure drop across the defect, device cooptation across the defect and the septum, relation of the device to the surrounding structures and valvular assessment regarding any valvular regurgitation.

3. Statistics

3.1. Results

The mean age of the study subjects was 7.4 years. Mean weight of patients was 27.4 kg. Mean distance between the defect and the aortic valve was 5.2 mm. Mean size of left and right ventricular openings of the defect were 10.8 and 5.7 mm respectively. Aneurysmal tissue was present in 88% of cases. Multiple VSDs (multiple holes through the aneurysm) recorded by echocardiography was present in 25%. Mean shunt fraction (Qp/Qs) was 2.3 (Table 1).

Mean angiographic defect size from left and right ventricular sides were 11 and 5.5 mm respectively. Device size ranged from 8 × 6 to16 × 10. In one patient severe intravascular hemolysis occurred 3 days after the percutaneous closure which required blood transfusion of two units of packed red blood cells. Re-intervention was successfully performed using PDA Amplatzer occluder which resulted in sudden cessation of residual flow and hemolysis subsided subsequently (Table 2). Immediate closure of the VSD was achieved in 31% of the cases, this percentage increased to 50% and 70% after 1 month and 6 months respectively (Table 3).

Three patients had transient self-limiting bradyarrhythma; all of them were asymptomatic. One case developed transient 2:1 block which resolved 3 days later with steroid therapy. One case was discovered to have asymptomatic first degree heart block. And another patient developed transient sinus bradycardia.

4. Discussion

Although diagnosis of VSD occur at young age due to the widespread use of echocardiography, affordable cost of the investigation and early referral from pediatrician. However patients mean age at percutaneous closure was 7.4 years. This may be attributed to the fact that in most cases regular follow up was preferred aiming for spontaneous closure. Indications for percutaneous closure included symptomatic left to right VSD shunt, and evidence of left ventricular overload which may possibly have developed over time [14,15].

All patients underwent percutaneous closure of PmVSD through retrograde approach using Nit Occlud® Lê VSD coil except one patient whom underwent re-intervention and was managed by PDA Amplatzer occluder device for intractable hemolysis. Percutaneous closure of VSD was categorized by Rodriguez et al. as: [49].

a. Successful: VSD Closed
b. Failed: all attempts to close VSD, or crossing the VSD with the catheter without successfully closing it (Example in case of device embolization)
c. Aborted: Percutaneous closure VSD was aborted for some reason or feature (Example in case of development of complete heart block while crossing the defect)

In our study successful closure was achieved in 100% of cases. We found our results similar to Rodrigues et al. High success rate was attributed to interventional cardiologist learning curve, clear understanding of exclusion criterion, better selection of cases with hemodynamic evaluation and experienced echocardiographic assessment. In addition success rate was attributed to presence of aneurysmal tissue, appropriate defect size and prolapse of sinus of valsalva [4]. Haas et al. reported 92% (102/111 patients) success rate for percutaneous closure of aneurysmatic PmVSD using Nit Occlud® Lê VSD coil. Failure was due to the inability to advance the delivery sheath through the defect, and one defect was too large to be closed with the devices available [10].

From our experience several technical issues were crucial to the overall success of percutaneous closure of PmVSD. Firstly, crossing the PmVSD without entangling the tricuspid valve tensor apparatus was the most crucial step toward successful closure and was especially challenging with the presence of aneurysmal tissue.

Secondly, for the aneurysmal PmVSD, placing the coil inside the aneurysmal sac at all times was an important step for minimizing heart rhythm disturbances and complications. Meanwhile, given that aneurysmal tissues were often adjacent to or even part of the tricuspid valve, caution should be taken when the operator passes the wire and catheter through the tricuspid valve to establish the arteriovenous circuit.

Thirdly, detection of new tricuspid regurgitation using echocardiography was routinely carried out before the release of the coil.in our study only one patient had moderate TR on follow up, although there was no apparent entanglement of the tricuspid valve septal leaflet within the coil we believe that the coil closeness to the valve hindered the free motion of the septal leaflet thus affecting the cooptation line of the three leaflets causing the moderate tricuspid regurgitation.

Only one patient had new mild aortic regurgitation after VSD closure, again there was no obvious encroachment on the aortic valve by the coil but we can explain this new aortic regurgitation by the proximity of the defect to the aortic valve, the large coil size used in this teenage patient and the fact that he developed sinus bradycardia and first degree heart block later during his follow up and on holter monitoring.

In addition selection of the size of the device is important for a

Table 1
Baseline characteristics before percutaneous closure.

ID	Gender	Age (year)	Weight (Kg)	AV-VSD (mm)	LV defect size (mm)	RV defect size (mm)	Aneurysm	multiple VSD jets	Qp/Qs
1	F	2.67	14	6	10	5	Yes	No	1.9
2	F	2.17	12	7	6	3	Yes	No	2.4
3	F	5.5	22	4.6	5	3.3	No	No	2.3
4	F	10.25	37	9	14	8.5	Yes	Yes	2.8
5	F	6	25	9	6	3	Yes	No	3.8
6	F	4.5	13	4	12.5	6.5	Yes	yes	4
7	M	4	13	4	13	7.5	Yes	yes	2
8	M	11	28	5	13	6	No	No	1.8
9	F	13	48	7	14	7	Yes	No	2
10	M	8	22	3	12	6	Yes	No	1.4
11	M	5	19	4.7	10	5	Yes	No	1.8
12	F	6	25	5	10	5.5	Yes	No	2
13	F	17	60	4	13	7	Yes	No	2.4
14	F	3.3	16	5	10	6	Yes	No	1.8
15	F	2.75	13	3	11	6	Yes	yes	1.9
16	M	17	72	3	14	6	Yes	No	1.9

M = male, F = female. AV–VSD distance between VSD and rim of Aortic valve.

Table 2
Procedural data.

ID	LV defect size (mm)	RV defect size (mm)	Device size (mm)	Complications
1	12	6	14 × 8	No
2	8	3	10 × 6	No
3	8	4	10 × 6	No
4	12	7	14 × 8	No
5	10	5	8 × 6	Hemolysis
6	12	6	14 × 8	No
7	12	7	14 × 8	No
8	12	6	14 × 8	No
9	14	8	16 × 10	No
10	12	6	14 × 8	No
11	10	4	12 × 6	No
12	10	5	12 × 6	No
13	12	6	14 × 8	No
14	8	5	10 × 6	No
15	10	5	12 × 6	No
16	14	5	16 × 8	No

Table 3
Echocardiographic follow up assessments.

ID	Valvular affection	RF 24 h post closure	RF 1 month post	RF 6 month post	RF 12 month post	Follow up time (month)
1	No	Yes	Yes	No	No	12
2	No	No	No	No	No	12
3	No	Yes	Yes	Yes	No	12
4	No	Yes	Yes	Yes	Yes	12
5	No	Yes	No	No	No	12
6	No	Yes	Yes	Yes	–	6
7	No	Yes	No	No	–	6
8	Mild aortic regurgitation	Yes	No	No	–	6
9	No	No	No	No	–	6
10	No	No	No	No	–	6
11	Moderate tricuspid regurgitation	Yes	Yes	–	–	6
12	No	Yes	Yes	–	–	1
13	No	Yes	Yes	–	–	1
14	No	No	No	–	–	1
15	No	Yes	Yes	–	–	1
16	No	No	No	–	–	1

RF = residual flow across ventricular defect after percutaneous closure.

successful percutaneous closure. The Nit Occlud® Lê VSD coil is recommended to be 2–4 mm larger than the opening of the VSD from the left ventricular side and double the defect size from the right ventricular side. An oversized device should be avoided to prevent possible complete atrioventricular block and valve impingement. Finally, strict adherence to the inclusion and exclusion criteria for percutaneous closure is crucial to the overall success of the intervention.

Nit Occlud® Lê VSD coil has a specific nature, it has cone in-cone configuration. The mechanism of closure in Nit Occlud® Lê VSD coil involves filling up the defect with the device without real stenting [10].Flow reduction leads to obstruction of the defect and subsequent endothelialization. Residual flow was related to the presence of aneurismal tissue that is not in continuous alignment with the septum. This aneurismal tissue was sometimes found to be in relation with the tricuspid valve. Release of Nit Occlud® Lê VSD coil is usually preferred within the aneurysmal tissue to decrease the rate of valvular affection, and rhythm disturbance. However this is possibly associated with higher rate of residual flow.

Rodriguez et al. demonstrated lower rates of residual shunt after percutaneous closure using Nit Occlud® Lê VSD coil. This difference in results was possibly explained by the fact that in our study 25% of patients had multiple VSD jets. On the other hand multiple VSD jets were only present in 11% of cases in Rodriguez study. Multiple VSD jets denoted fenestrated VSD or multiple small defects or disperse aneurysmal tissue leading to turbulent and multiple VSD jets. Multiple VSD jets were significantly related to the presence of residual flow [4].

In this study three patients had transient self-limiting bradyarrhythma; all of them were asymptomatic. Currently, it is believed that rhythm abnormalities may be related to inflammatory edema of tissues in the membranous interventricular septum. Haas et al. reported a case experienced transient complete atrioventricular block after percutaneous closure PmVSD using Nit Occlud® Lê coil. However this patient regained sinus rhythm with steroid therapy after one week. In addition, other six cases developed new-onset right bundle branch block [10].

We may conclude that perimembranous type VSD and oversizing of the device were strongly related with bradyarrhythmia. This is due to the critical anatomical location of the conduction system of the heart in relation to the rim of the defect in PmVSD. Since PmVSD lie in close proximity to the cardiac conduction tissue, given that the conduction axis penetrates through the postero-inferior margin of the defect. Bulky closure devices can exert pressure on the adjacent conducting system, resulting in bradyarrhythmia [16]. Heart block can be divided into early or acute-onset type and late-onset type. Mechanical trauma and/or compression of the conduction system by the delivery system or the device are the most common causes of the acute-onset type. For the late-onset type, inflammation and fibrosis may play a major role. If the

heart block occurs during or within several days after the procedure, device removal is the best intervention to recover sinus rhythm [17].

In this study we report a case developed significant hemolytic anemia that required blood transfusion and underwent successful re-intervention for implantation of a second device (Amplatzer PDA occluder device). And subsequently complete resolution of residual flow and hemolysis. Ventriculography during the first intervention showed proper configuration and position of the Nit Occlud® Lê VSD coil. However pre-procedural ventriculography during re-intervention revealed a more vertical orientation of the Nit Occlud® Lê VSD coil from the right ventricular side. The presence of aneurysmal tissue may have prevented migration of the device. Discrepancy between echocardiographic and angiographic measurements of the defect may have caused undersizing of the Nit Occlud® Lê VSD coil. Hemolysis after percutaneous VSD closure is caused by residual high velocity blood flow across the coil, this high shearing effect results in mechanical fragmentation of red blood cells. It is a rare complication that can cause significant sequelae. The rate of hemolysis following percutanous VSD closure ranges from 0.7-15%% [9].

Murat Saygı et al. reported development of hemolysis in 4 out of 24 patients underwent percutaneous closure using Nit Occlud® Lê VSD coil. In two cases hemolysis resolved spontaneously. One case underwent successful re-intervention using Amplatzer Duct Occluder II which showed no residual flow. However in another case hemolysis persisted after re-intervention using detachable coil due to persistence of residual shunting and hemoglobinuria. This patient underwent surgery and subsequently hemolysis stopped. Therefore it is advisable to use a device with high occluding property in patients who suffer intractable hemolysis and undergoing re-intervention after percutaneous closure with Nit Occlud® Lê VSD coil [18].

5. Conclusion

In selected cases, the Nit-Occlud® Lê VSD coil device can be used safely for percutaneous closure of perimembranous ventricular septal defects. Regular follow up should be offered to patients with residual flow across the defect after percutaneous closure and awareness of possible complications as hemolytic anemia, bradyarrhythmia, and valvular affection and proper management plans should be available.

Consent

The authors declare that written informed consent was obtained from all the patients enrolled in the study.

Conflict of Interest

All authors declare that there is no conflict of interest. This study was approved by our institutional review board and informed consent was obtained from the parents of all the children enrolled in the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

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