INTERMEDIATE-TERM FOLLOW-UP RESULTS OF TRANSCATHETER CLOSURE OF VENTRICULAR SEPTAL DEFECT USING AMPLATZER® DEVICE VERSUS NIT-OCCLUD® LÊ VSD COIL SYSTEM

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Abstract. Transcatheter ventricular septal defect (VSD) is an alternative method of VSD closure, especially in perimembranous (PmVSD) type and doubly committed subarterial (DCSA) type VSD. The aim of this retrospective study was to review and report intermediate-term (up to 5-years) results of transcatheter closure of VSD in patients who received Amplatzer® device (device) or Nit-Occlud® Lê VSD Coil System (coil). Of 247 patients who underwent transcatheter closure during the 2003 to 2015 study period, there were 240 (97.1%) successful procedures (187 device, 53 coil). Of the 240 included patients, 115 were male and 125 were female, and the median (range) age and weight were 12 years (range: 1-67) and 40.3 kg (range: 10-97), respectively. Median VSD size in the device group was larger than that of the coil group. [7 mm (range: 3-18) *vs* 5 mm (range: 2.5-9.3); $p<0.001$]. Complete closure was comparable between groups. Sixty-nine (26%) of all patients had DCSA VSD. Twenty-six patients (49.1%) had DCSA VSD in the coil group, while only 43 patients (23%) had DCSA VSD in the device group. Although pre-closure aortic regurgitation (AR) was comparable between groups (22.9% *vs* 32%; $p=0.448$), AR was significantly higher in the coil group than in device group ($p<0.001$). When comparing VSD types, post-procedure AR was higher in DCSA VSD than in PmVSD ($p=0.001$). At the end of the 5-year follow-up, 98.6% of DCSA VSD had less than mild AR. Closure rates were comparable between closure methods for both PmVSD and DCSA VSD. The progression of AR was higher in DCSA VSD patients, but a majority of those patients had less than mild AR at end of 5 years.

Key words: Ventricular Septal Defect, VSD, Amplatzer® Device, Nit-Occlud® Lê VSD Spiral Coil System

INTRODUCTION

Ventricular septal defect (VSD) is one of the most common congenital heart defects that is treated by surgical closure in Thailand (Sakornpant and Kojaranjit, 2011; Ratanasit *et al*, 2015). Several long-term complications of isolated VSD, including endocarditis and aortic regurgitation (AR), are well-recognized (Jortveit *et al*, 2016;

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Karonis *et al*, 2016). Transcatheter VSD closures have been performed at Siriraj Hospital since 2003 (Durongpisitkul *et al*, 2003). In 2011, we reported the initial success of transcatheter closure of VSD in 109 patients. Seventy-six patients were in the Amplatzer® group (62 patients received the Amplatzer® membranous device and 14 patients received the Amplatzer® muscular device) and 33 patients were in the Nit-Occlud® Lê VSD Coil group (Pfm coil), with a median follow-up duration of 8 months (6-76) (Chungsomprasong *et al*, 2011). However, longer-term follow-up evaluation of the extent of post-AR closure for both perimembranous VSD (PmVSD) and doubly committed subarterial (DCSA) VSD is an ongoing topic of interest among those who perform and study transcatheter closure of VSD (Tomita *et al*, 2004; Tomita *et al*, 2005; Chen *et al*, 2015b; Sanoussi *et al*, 2015; Amano *et al*, 2016). Accordingly, the aim of this retrospective study was to review and report intermediate-term (up to 5-years) results of transcatheter closure of VSD in patients who received Amplatzer® device (device) or Nit-Occlud® Lê VSD Coil System (coil).

MATERIALS AND METHODS

This retrospective study reviewed the medical charts of 240 patients that underwent transcatheter closure with either Amplatzer® device or Nit-Occlud® Lê VSD Coil System at Siriraj Hospital during the 2003 to 2015 study period. The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (approval no. 584/2013).

Indications for transcatheter closure of VSD included one or more of the following: (1) hemodynamic data indicative of left to right shunt

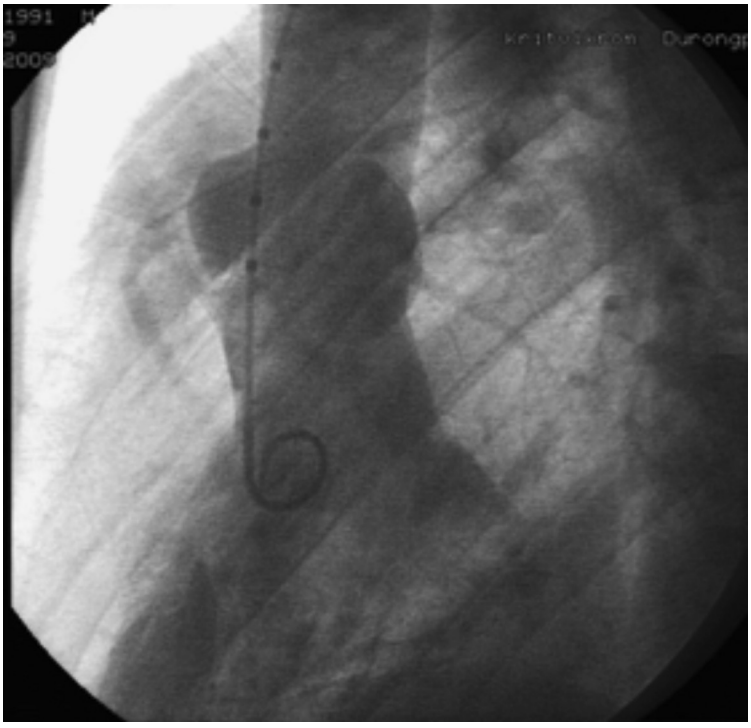

Fig 1– Left ventriculography in steep left anterior oblique view (up to 90 degrees) shows delineation of VSD border of DCSA VSD.

by echocardiography or cardiac catheterization (Qp:Qs >1.5); (2) clinical signs and symptoms of heart failure; (3) evidence of left side chamber enlargement by echocardiography; (4) prolapsed coronary cusp with trivial to mild AR (Figs 1-2); (5) risk of prolapsed coronary cusp with right coronary cusp deformity index >0.3 or right coronary cusp imbalance index >1.3 (Tomita *et al*, 2004), or prolapse of non-coronary cusp (Tomita *et al*, 2005); and/or, (6) the size of the defect is not larger than the size of the available devices.

Procedure

A complete description of the procedure along with device selection was previously reported in detail (Durongpisitkul *et al*, 2003; Chungsomprasong *et al*, 2011). Briefly, all procedures were performed under general anesthesia with prophylactic antibiotics. All aortic valve prolapses and pre-closure AR were documented using transesophageal echocardiography (TEE). Complete right and left cardiac catheterization was performed. Left ventricular angiogram was performed to define the location and size of the defect. In cases of DCSA VSD, a steep LAO view (up to 90 degrees) was preferred due to delineation of the VSD border (Fig 1). Judkins Right catheter, LIMA, or Benston catheter were used for VSD engagement. In some cases the catheter curve was reshaped to facilitate passage into VSD tunnel. A complete arteriovenous loop of glide wire was performed. The delivery sheath (TorqueVue™; St. Jude Medical, St. Paul, MN) was inserted through the femoral vein and advanced along the wire to the Judkins Right catheter using the kissing technique into the right atrium, the right ventricle, and then through the VSD until the sheath reached the

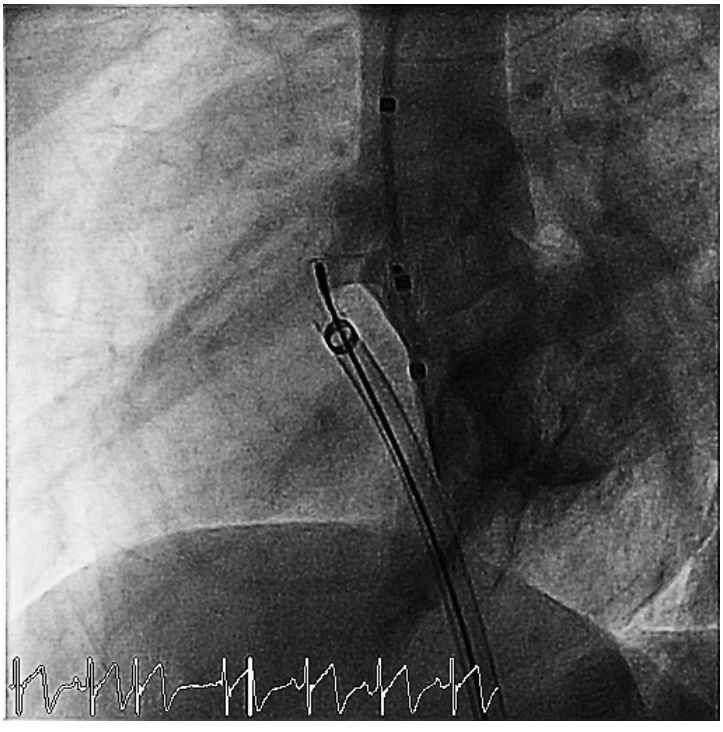

Fig 2– Left ventriculogram in steep left anterior oblique view shows Amplatzer® Muscular VSD device (undersized by 1-2 mm) deployed with left ventricular disc open and at a position just below the prolapsed aortic cusp to avoid injury.

ascending aorta. The opposing Judkins Right catheter was advanced to push the tip of the sheath into the left ventricle apex. In some cases (particularly DCSA VSD cases), if access to the left ventricle apex could not be obtained, then the device or coil would be deployed via the ascending aorta. All Pfm coils were deployed via the ascending aorta. We selected the device size using measurements from both echocardiographic and angiographic methods. The original recommendation for selection of Amplatzer® membranous VSD device size was to calculate the size from the square root of the longest diameter multiplied by the shortest diameter. However and given that the Amplatzer® muscular VSD device is a symmetrical disc device, we generally choose a device size that is 1 mm less than or equal to the largest defect diameter. In DCSA VSD cases, we found that the superior border of the defect could not be well-delineated in some cases. In these cases, we intentionally started with an undersized Amplatzer® muscular device to avoid injuring the aortic cusp, with the left ventricular disc positioned below the prolapsed aortic cusp (Fig 2). In 2006, the Nit-Occlud® Lê VSD Spiral Coil System was introduced at our center. This system was used in patients that had PmVSD with aneurysm and an opening less than 6-8 mm. After 2008, the Nit-Occlud® Lê VSD Coil was also adopted for use in patients with DSCA VSD (Fig 3). Patients were observed for catheter-related complications during the post-catheterization period. Infective endocarditis prophylaxis and antiplatelet dosage of aspirin were given for at least 6 months after successful procedure or until the defect was completely occluded.

Statistical analysis

Data analysis was performed using SPSS Sta-

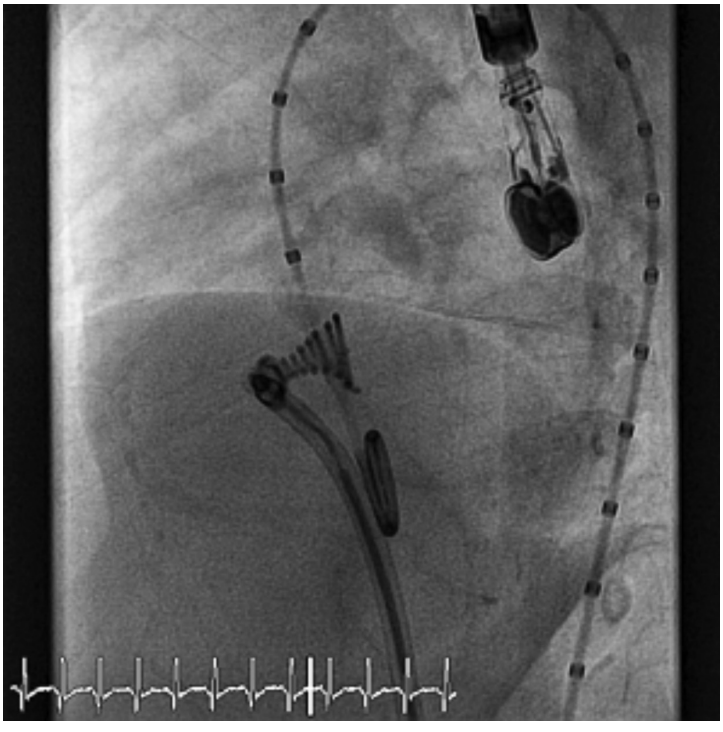

Fig 3– Steep left anterior oblique projection shows Nit-Occlud® Lê VSD Coil System positioned in a doubly committed subaortic ventricular septal defect. Part of the left ventricular loop coil is open in the left ventricle, and the reversed loop coil is open in the right ventricle.

tistics version 20 (IBM, Armonk, NY). Chi-square test, independent *t*-test, or Mann-Whitney *U* test were used to compare the Amplatzer® device group and the Pfm coil group. Nominal variables are reported as frequency or percentage, and continuous variables are presented as mean ± standard deviation if normally distributed and as median and range of non-normally distributed. Categorical data are reported as percentage (%). For all analyses, a *p*-value <0.05 was regarded as being statistically significant.

RESULTS

Transcatheter VSD closure was successfully performed in 240 of 247 patients (97.1%) dur-

Table 1
Comparison of demographic, clinical, and hemodynamic characteristics between the Amplatzer® device group and the Nit-Occlud® Lê VSD Coil (Pfm coil) group.

	Amplatzer® device (*n*=187)	Pfm coil (*n*=53)	*p*-value
Age (yrs), median (range)	14 (1-67)	1 (1-29)	<0.001
Weight (kg), median (range)	44 (10.1-97)	26.6 (10.1-93.5)	<0.001
Height (cm), median (range)	151 (80-186)	129 (81-180)	0.001
Gender (M:F)	88:99	27:26	0.617
VSD size (mm), median (range)	7 (3-18)	5 (2.5-9.3)	<0.001
VSD type, %			
Pm	57.8%	39.6%	0.004
Pm with inlet extension/aneurysm	10.7%	11.3%	
DCSA	23.0%	49.1%	
Muscular	4.8%	0%	
Post-surgical repair	3.7%	0%	
Hemodynamic data, mean±SD			
Mean AO pressure (mmHg)	82±15	75±16	0.008
Mean PA pressure (mmHg)	22±7	20±6	0.134
Qp:Qs	1.75±0.6	1.7±0.7	0.290
Pulmonary arteriolar resistance (units m^2)	1.6±1.6	1.4±1.2	0.608
Flu time (min), mean±SD	22.4±10.7	22.7±11.5	0.807
Procedure time (min), mean±SD	81.8±31.3	84.9±28.9	0.526
LOS (days), mean±SD	1.7±1.1	2.1±1.7	0.121

A *p*-value<0.05 indicates statistical significance. VSD, ventricular septal defect; Pm, perimembranous; DCSA, doubly committed subarterial; AO, aortic pressure; PA, pulmonary arterial pressure; Qp:Qs, pulmonary blood flow : systemic blood flow; LOS, length of stay; SD, standard deviation.

ing the 2003 to 2015 study period. The procedure was unsuccessful in seven patients due to transient atrioventricular block during crossing of VSD in 2 patients, inability to engage VSD in 1 patient, and worsening of AR after deployment of device/coil in 4 patients. There were 215 isolated VSD patients. Twenty-five patients (10.4%) had comorbidity that required an additional procedure, such as device closure for atrial septal defect or PDA, or balloon valvuloplasty of pulmonary valve stenosis. Of 240 patients who had complete closure, there were 129 PmVSD, 25 Pm with extension to inlet or aneurysm, 69 DCSA (outlet) VSD, 9 muscular VSD, 1 inlet VSD, and 7 patch leakage VSD (5 from tetralogy of Fallot and 2 from complete atrioventricular septal defect). The average follow-up period was 49.5±42.9 months (median: 39.7). Residual shunt and AR were reported at intervals of 24 hours, one month, six months, one year, and five years. More than 70% of patients were followed-up for at least 5 years.

Of 240 patients, 187 were in the Amplatzer® device group (114 Amplatzer® Muscular VSD device, 67 Amplatzer® Membranous VSD device, 6 Amplatzer® Duct Occluder, and 2 Amplatzer® Duct Occluder II) (device group) and 53 were in the Nit-Occlud® Lê VSD Coil group (coil group).

Demographic, clinical, hemodynamic, and immediate procedural data are presented in Table 1. Patients in the device group were significantly older than patients in the coil group [median: 14 years (range: 1-67) *vs* 1 year (1-29); (p<0.001)]. Device group patients weighed more than coil group patients [median: 44 kg (10.1-97) *vs* 26.6 kg (10.1-93.5); p<0.001]. The median diameter of VSD was larger in the device group than in coil group [7 mm (3-18) *vs* 5 mm (2.5-9.3); p<0.001]. There were no statistically significant differences in hemodynamic data during cardiac catheterization between groups, with the exception of high mean aortic blood pressure in the device group. Regarding VSD type, 57.8% of device group patients and 39.6% of coil group patients had PmVSD, whereas 23.0% of device group patients and 49.1% of coil group patients had DCSA VSD (p=004).

Immediate procedure-related complications (Table 2)

Of 240 patients who had successful procedure, VSD device or coil embolization were found in five patients in device group three patients in coil group. All devices were successfully retrieved and a larger sized device was deployed. Two of three cases in the coil group were replaced with an Amplatzer® device, and the other was replaced with a larger Nit-Occlud® Lê VSD Coil. Other immediate

Table 2
Comparison of complications between the Amplatzer® device group and the Nit-Occlud® Lê VSD Coil (Pfm coil) group.

Complications, *n*	Amplatzer® device (*n*=187)	Pfm coil (*n*=53)	*p*-value
Embolization	5	3	0.226
Hemolysis	1	2	0.065
Blood transfusion	2	2	0.175
Arterial occlusion	1	0	0.594
Death	1	0	0.594

A p-value<0.05 indicates statistical significance.

procedure-related complications are shown in Table 2. One patient who had Amplatzer® perimembranous VSD device with residual shunt after closure developed hemolysis that required surgical removal of the device on day 5 post-catheterization. All other complications were resolved within a few days after the procedure. The one patient who died in this study had residual shunt from repair of tetralogy of Fallot and complete atrioventricular septal defect. The patient had severe pulmonary hypertension and residual VSD after surgical closure. The patient underwent transcatheter closure of the residual VSD and later developed severe pulmonary hypertension and hemorrhage within 48 hours, and died at 14 days after admission.

Residual shunt

Residual shunt was classified at trivial, small, or larger than moderate. At the 24-hour follow-up time point, patients in the device group had 19.8% trivial shunt, 0.5% small shunt, and 1.1% larger than moderate shunt, as compared to 20.8% trivial shunt, 0.0% small shunt, and

Table 3
Comparison of residual shunt between the Amplatzer® device group and the Nit-Occlud® Lê VSD Coil (Pfm coil) group.

	Amplatzer® device (*n*=187)	Pfm coil (*n*=53)	*p*-value
Residual shunt at first day post-procedure, %			
Trivial	19.8	20.8	0.832
Small	0.5	0.0	
Larger than moderate	1.1	0.0	
Residual shunt at 1-month post-procedure, %			
Trivial	12.3	15.1	0.842
Small	0.5	0.0	
Larger than moderate	0.5	0.0	
Residual shunt at 6-months post-procedure, %			
Trivial	10.2	17.0	0.536
Small	2.7	1.9	
Larger than moderate	0.5	0.0	
Residual shunt at 1-year post-procedure, %			
Trivial	10.7	17.0	0.607
Small	1.1	1.9	
Larger than moderate	0.5	0.0	
Residual shunt at 5-years post-procedure, %			
Trivial	11.6	14.6	0.802
Small	0.8	0.0	
Larger than moderate	0.8	0.0	

A *p*-value <0.05 indicates statistical significance.

0.0% larger than moderate shunt in the coil group (p=0.832) (Table 3). Degree of residual shunt was not significantly different between groups at any follow-up time point. We found one patient in the device group (inlet with large multiple opening of VSD aneurysm) that improved from larger than moderate shunt to trivial shunt. One patient with DCSA VSD in the coil group had shunt progression that required a second procedure using an Amplatzer® Muscular VSD device.

Effect on bundle branch, atrioventricular block, and pacemaker implantation (Table 4)

Pre- and post-procedure electrocardiogram (ECG) results were collected from both groups. We found that 12.2% of patients in the device group had right bundle branch block (RBBB), as compared to no patients in the coil group. Moreover, all RBBB appeared only in PmVSD patients. Post-procedure ECG showed new RBBB in 10 patients in the device group, as compared to 2 patients in the coil group (p=0.014). Five patients developed complete atrioventricular block (CAVB) within two weeks post-procedure (3 Amplatzer® Membranous VSD device, 1 Amplatzer® Muscular VSD device, and 1 Nit-Occlud® Lê VSD Coil). One patient who received an Amplatzer® Membranous VSD device (patient number 95; device year 2009) developed CAVB at one month. No CAVB was reported after the one-month time point. Three of five CAVB patients received hydrocortisone treatment, and CAVB was resolved in 2 of those 3 patients (one Amplatzer® Membranous VSD device and one Nit-Occlud® Lê VSD Coil). In total, four patients received permanent pace maker implantation (3 Amplatzer® Membranous VSD device and 1 Amplatzer® Muscular VSD device).

Aortic regurgitation (AR)

The severities of aortic regurgitation were classified as none, mild, moderate and severe according to European Association of Echocardiography (Lancellotti *et al*, 2010) as shown in Fig 4. Aortic valve prolapse (AVP) was found to be significantly lower in the device group than in the coil group (32.6% *vs* 50.9%; p=0.015), the

Table 4
Comparison of ECG finding between the Amplatzer® device group and the Nit-Occlud® Lê VSD Coil (Pfm coil) group (N=214).

	Amplatzer® device (n=164)	Pfm coil (n=50)	p-value
RBBB, n (%)			
Pre-closure RBBB	20 (12.2)	0 (0)	0.01
Post-closure RBBB	30 (18.2)	1 (2)	0.004
New-onset RBBB, n (%)	10 (6.1)	1 (2)	0.251
Rhythm after closure, n (%)			
Normal sinus rhythm	170 (90.9)	52 (98.1)	0.7999
1st degree AVB	10 (5.3)	0 (0)	
2nd degree AVB	2 (1.1)	0 (0)	
3rd degree AVB	5 (2.6)	1 (2)	
Permanent pacemaker, n (%)	4 (2.1)	0 (0)	0.001

A p-value<0.05 indicates statistical significance. RBBB, right bundle branch block; AVB, atrioventricular block.

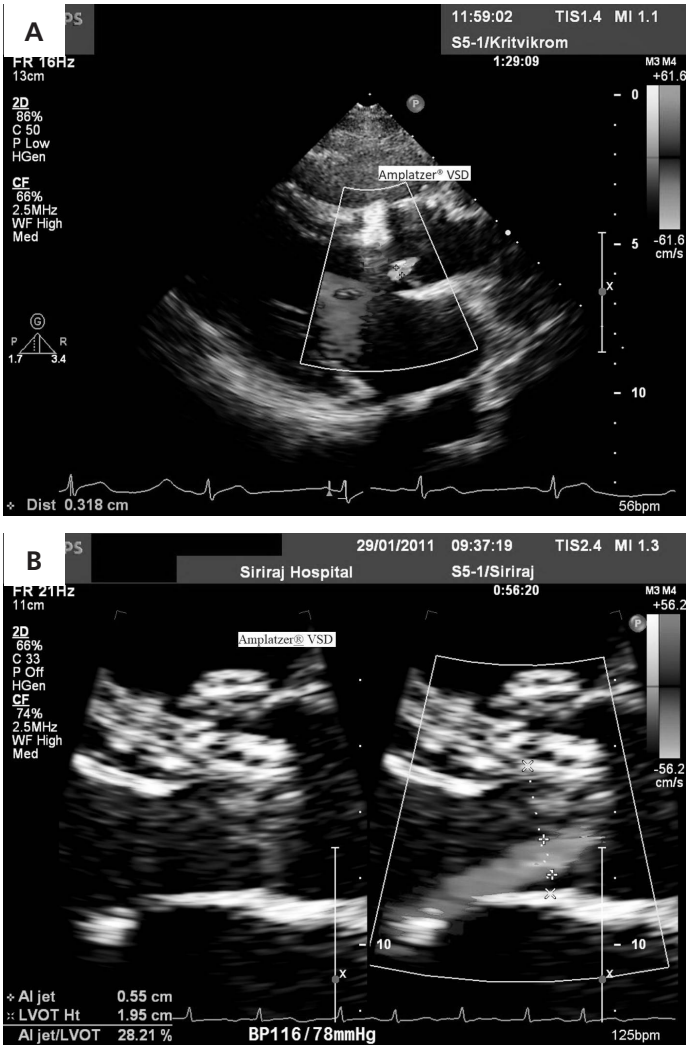

Fig 4– Post-Amplatzer® VSD device closure, echocardiography demonstrate mild and moderate aortic regurgitation (Fig A and B, respectively).

frequency of pre-procedure AR was comparable between the device group and the coil group for both trivial to mild (17% *vs* 24.5%) and moderate to severe (5.9% *vs* 7.5 %) (*p*=0.448). Regarding post-procedure degree of AR, progressive AR was significantly higher in the coil group than in the device group at every follow-up time point (Table 5). Worsening of AR, defined as change in degree of AR to the next level of severity, was found in 7 of 187 (3.7%) device group patients and in 11 of 53 (20.7%) coil group patients (*p*=0.191).

Comparison between perimembranous VSD (PmVSD) and doubly committed subarterial VSD (DCSA VSD) groups (Tables 6, 7)

Given the ongoing interest in the effectiveness of transcatheter closure between perimembranous VSD (PmVSD) and doubly committed subarterial (DCSA) VSD among those who perform and study transcatheter closure of VSD, we divided patients into the PmVSD group (including PmVSD with some extension into the muscle, and PmVSD with or without aneurysm or mus-

Table 5
Comparison of aortic regurgitation (AR) between the Amplatzer® device group and the Nit-Occlud® Lê VSD Coil (Pfm coil) group relative to pre-closure aortic valve prolapse, pre-closure AR, and post-closure.

	Amplatzer® device (*n*=187)	Pfm coil (*n*=53)	*p*=value
Pre-aortic valve prolapse, %	32.6	50.9	0.015
Pre-closure AR, %			
None	76.5	67.9	0.448
Trivial to mild	17.0	24.5	
Moderate to severe	5.9	7.5	
Post-procedure AR at 24 hours, %			
None	75.9	60.4	0.025
Trivial to mild	24.1	39.6	
Moderate to severe	0.0	0.0	
Post-procedure AR at 1 month, %			
None	77.5	59.6	0.029
Trivial to mild	21.9	38.5	
Moderate to severe	0.5	1.9	
Post-procedure AR at 6 months, %			
None	76.9	60.4	0.048
Trivial to mild	22.6	37.7	
Moderate to severe	0.5	1.9	
Post-procedure AR at 1 year, %			
None	77.5	58.5	0.019
Trivial to mild	22.5	39.6	
Moderate to severe	0.5	1.9	
Post-procedure AR at 5 years, %			
None	74.4	58.3	0.024
Trivial to mild	24.8	41.7	
Moderate to severe	0.8	0.0	
Worsening AR, *n* (%)	7 (3.7)	11 (20.7)	0.191

A *p*-value<0.05 indicates statistical significance.

cular defect) and DCSA VSD (outlet) type VSD group. After exclusion of 7 patch leakage VSD patients in our study, there were 233 patients, with 164 in the PmVSD group and 69 in the DCSA VSD group. The hemodynamic characteristics of both groups were comparable (Table 6). We found the mean defect size to be larger in the PmVSD group than in the DCSA VSD group (7.1±2.6 mm *vs* 5.6±1.8 mm; *p*=0.001).

The devices used in each group were different (Table 6). Among patients with PmVSD, a larger number of Amplatzer® devices was used than Nit-Occlud® Lê VSD Coils (137 *vs* 27); however, more coils were used than devices in patients with DCSA VSD (43 *vs* 26; *p*=0.001). Degree of residual shunt was classified as trivial, small, or moderate. Residual shunt classification results at each time point between the PmVSD and

Table 6
Comparison of demographic, clinical, and hemodynamic characteristics between perimembranous ventricular septal defect (PmVSD) group and doubly committed subaortic ventricular septal defect (DCSA VSD) group.

Characteristics	PmVSD (*n*=164)	DCSA VSD (*n*=69)	*p*-value
Demographic			
Age (yrs), median (range)	12.5 (1-67)	12 (1-54)	0.549
Weight (kg), median (range)	40.4 (10.1-97)	37 (10.1-93.5)	0.328
Height (cm), median (range)	146.8 (80-186)	147 (85-182)	0.619
Gender (M:F)	88:99	27:26	0.617
VSD size (mm), median (range)	8 (2-20)	8 (4-16)	<0.001
VSD device, *n* (%)			
Amplatzer® device	137 (83.5)	43 (62.3)	0.001
Pfm coil	27 (16.5)	26 (37.7)	
Hemodynamic data, mean±SD			
Mean AO (mmHg)	81±15	80±18	0.579
Mean PA (mmHg)	21±7	20±5	0.288
Qp:Qs	1.8±1.5	1.1±0.8	0.016
Pulmonary arteriolar resistance (units m^2)	1.6±1.5	1.1±0.9	0.003
Flu time (min), mean±SD	21.8±10.1	23.1±11.4	0.477
Procedure time (min), mean±SD	81.2±31.5	84.1±21.7	0.526
LOS (days) , mean±SD	1.8±1.3	1.6±0.6	0.187

A *p*-value<0.05 indicates statistical significance. Pfm coil, Nit-Occlud® Lê VSD Coil System; VSD, ventricular septal defect; Pm, perimembranous; DCSA, doubly committed subarterial; AO, aortic pressure; PA, pulmonary arterial pressure; Qp:Qs, pulmonary blood flow:systemic blood flow; LOS, length of stay; SD, standard deviation.

Table 7
Comparison of degree of aortic regurgitation (AR) between perimembranous ventricular septal defect (PmVSD) group and doubly committed subaortic ventricular septal defect (DCSA VSD) group.

	PmVSD (*n*=163)	DCSA VSD (*n*=69)	*p*-value
Pre-aortic valve prolapse, %	21.5	73.9	<0.001
Pre-closure AR, %			
None	85.9	49.3	<0.001
Trivial to mild	11.0	36.2	
Moderate to severe	3.1	14.5	
Post-procedure AR at 24 hrs, %			
None	85.3	44.9	<0.001
Trivial to mild	14.7	55.1	
Moderate to severe	0.0	0.0	
Post-procedure AR at 1 month, %			
None	84.0	52.2	<0.001
Trivial to mild	15.3	46.4	
Moderate to severe	0.6	1.4	
Post-procedure AR at 6 months, %			
None	82.7	53.6	<0.001
Trivial to mild	16.6	44.9	
Moderate to severe	0.6	1.4	
Post-procedure AR at 1 year, %			
None	83.4	50.7	<0.001
Trivial to mild	15.9	47.8	
Moderate to severe	0.6	1.4	
Post-procedure AR at 5 years, %			
None	80.2	50.9	<0.001
Trivial to mild	15.9	47.8	
Moderate to severe	0.6	1.4	
Worsening AR, *n* (%)	15/124 (9.1)	8/69 (11.6)	<0.001

A *p*-value<0.05 indicates statistical significance.

DCSA groups were, as follows: 24 hours (19.0%, 0%, 0.6% *vs* 17.4%, 0%, 1.4%; *p*=0.792); 1 month (11.0%, 0%, 0% *vs* 15.9%, 0%, 1.4%; *p*=0.172); 6 months (11.0%, 0%, 0.6% *vs* 10.1%, 4.3%, 1.4%; *p*=0.198); 1 year (11.7%, 0%, 0% *vs* 11.6%, 0.9%, 2.9%; *p*=0.08); and, 5 years (12.9%, 0%, 0% *vs* 10.5%, 1.8%, 1.8%; *p*=0.235). Residual shunt findings were comparable between VSD types. Predictably, the degree of post-closure AR was significantly higher in the DCSA VSD group than in the PmVSD at any duration of follow-up (*p*<0.001). We observed a trend towards less progression of AR in the PmVSD group than in the DCSA VSD group at the 1-year follow-up time point (%AR trivial to mild 15.9% and 0.6% moderate to severe in the PmVSD group *vs* %AR 47.8% trivial to mild and 1.4% moderate to severe in the DCSA VSD group). Progression of AR was observed in 15 of 164 (9.1%) PmVSD patients and in 8 of 69 (11.6%) DCSA VSD patients (*p*<0.001) (Table 7).

DISCUSSION

We reported the intermediate-term follow-up results of transcatheter closure of VSD in 240 patients, with a success rate of 97.1%. Patients were divided into the Amplatzer® device group (device group) and the Nit-Occlud® Lê VSD Coil group (coil group). Mean VSD size in the device group was larger than in the coil group. One hundred thirty-seven devices and 27 coils were used to treat patients with PmVSD, and 43 devices and 26 coils were used to repair defects in patients with DCSA VSD (*p*=0.001). The one patient who died in this study had residual shunt from repair of tetralogy of Fallot with complete atrioventricular defect and died from complications of pulmonary hemorrhage two weeks after closure. Progressive post-procedure AR was higher in DCSA VSD than in PmVSD.

In 2014, a systemic review entitled "A systematic review on the efficacy and safety of transcatheter device closure of ventricular septal defects (VSD)" reported that, from 37 publications and 4,406 patients, the pooled success rate of transcatheter closure in VSD was 96.6% (Yang *et al*, 2014), which was comparable to the 97.1% success rate found in our study. Regarding immediate residual shunt at 24 hours post-procedure, residual shunt rates were 19.8% trivial, 0.5% small, and 1.1% moderate for the device and 20.8% trivial, 0.0% small, and 0.0% moderate for the coil. Our rates were lower than the 25.5% (95% CI: 18.9-32.1) pooled rate from the aforementioned meta-analysis group (Yang *et al*, 2014). At the 5-year follow-up time point, percentages of residual shunt were lower in both groups, as follows: 11.6% trivial, 0.8% small, and 0.8% moderate in the device group and 14.6% trivial, 0.0% small, and 0.0% moderate in the coil group. The percentage of residual shunt was comparable between the PmVSD and DCSA VSD groups.

When transcatheter closure of VSD was first performed, CAVB could develop up to several years after the procedure was performed (Yip *et al*, 2005; Sullivan, 2007; Song *et al*, 2009). PmVSD defects were occluded using the Amplatzer® Membranous VSD Occluder with good results during the early period (Hijazi *et al*, 2002; Durongpisitkul *et al*, 2003; Fu *et al*, 2006). However, we stopped using the Amplatzer® Membranous VSD Occluder in 2008 after reports of CAVB started being published. One of the suspected causes of CAVB when using the Amplatzer® Membranous VSD Occluder centered on its narrow 2 mm waist and an attempt to oversize the device in order to achieve a stable straddle position (Liu *et al*, 2004; Yip *et al*, 2005 Sullivan, 2007; Song *et al*, 2009; Kloecker *et al*, 2010; Erdem *et al*, 2012). We found the Amplatzer® Muscular VSD device with a symmetrical disc and longer waist to be associated with less chance of oversizing and it allowed us to avoid force injuring the conducting system along the VSD anatomy. This allowed us to use undersize device by 1-2 mm when compare to largest defect diameter. Our initial results showed that only 4

of 116 patients (3.4%) received a permanent pacemaker as a result of CAVB – 3 from Amplatzer® Membranous VSD device and 1 from oversizing of Amplatzer® Muscular VSD device during the early years after the procedure was adopted. No patients have developed CAVB at our center since 2009.

In the meta-analysis study by Yang, *et al* (2014), 85.3% of PmVSD type cases were closed, as compared to 53.4% in our study, and Amplatzer® device or Nit-Occlud® Lê VSD Coil were used in both studies. Forty-two percent of our patients (69 patients) were DCSA VSD, which was much higher than the proportion in most of the studies in the meta-analysis.

Progressive AR in DCSA, even after surgical VSD closure, is a well-known long-term potential complication (Layangool *et al*, 2008; Menting *et al*, 2015; Sanoussi *et al*, 2015; Amano *et al*, 2016; Jortveit *et al*, 2016). Incidence of late AR progression among patients after repair of subpulmonic infundibular VSD was unexpectedly high at 7.7% (Amano *et al*, 2016; Rahmath *et al*, 2016). One study reported no difference in degree of AR after closure (Egbe *et al*, 2015). Our study found pre-closure AR to be comparable between the device and the coil (22.9% *vs* 32%; p=0.448). After closure, we found AR to be lower in the device than in the coil at 24 hours (24.1% *vs* 39.6%; p=0.025), 1 month (22.4% *vs* 40.4%; p=0.029), 6 months (23.1% *vs* 39.6%; p=0.048), 1 year (22.4% *vs* 41.5%; p=0.019), and at 5 years (23% *vs* 41.5%; p=0.024). In addition, there were 11 patients in the coil group and 7 patients in the device group (p=0.191) that had progressive AR after 5 years of follow-up.

Patients with PmVSD had a lower proportion of pre-closure AR than patients with DCSA VSD (14.1% *vs* 50.7%; p<0.001). This trend was observed at each of the follow-up time points, as follows: 24 hours (14.7% *vs* 55.1%; p<0.01), 1 month (15.9% *vs* 47.8%; p<0.001, 6 months (16.5% *vs* 53.3%; p<0.001), 1 year (16.5% *vs* 47.8%; p=0.019), and 5 years (16.5% *vs* 49.2%; p<0.001). Our study found a higher proportion of AR than the pooled rate reported in the systemic review by Yang *et al* (2014). of 2.0% (95% CI: 1.0-2.9). This difference between studies may have been due to a higher proportion of DCSA VSD or perhaps for double disc device design of VSD device. However, longer term follow-up may be needed to reveal the progression of aortic regurgitation.

The Nit-Occlud® Lê VSD coil was introduced in 2006. This system can be considered for closure in selected cases of DCSA VSD with less than mild AR. In this study, we encountered several instances in which the coil became trapped in the aortic valve while pulling from the aorta to the left ventricular outflow tract (LVOT) in patients with DCSA VSD. Over time and after developing a better understanding of patient anatomy in certain cases of DCSA VSD with only trivial AR and prolapsed AV with right coronary cusp deformity index close to 0.3 (Tomita *et al*, 2004) (protrudes less than 3 mm into the LVOT), we elected to use an Amplatzer® Muscular VSD device that was slightly smaller (1-2 mm) than the defect in order to avoid injuring the AV. In contrast to the previous believe that a device may always cause injury to the aortic valve, we believed that a undersize device size (1-2 mm smaller than the defect size) of symmetrical disc Amplatzer® Muscular VSD Occluder may safely deployed while avoiding injury to aortic valve similar to other devices that are used for DCSA VSD (Fu *et al*, 2006; Qin *et al*, 2008; Lertsapcharoen *et al*, 2013; Chen *et al*, 2015a; Chen *et al*, 2015b; Ghaderian *et al*, 2015; Tutar *et al*, 2015). Our study found that 98.6% of DCSA VSD patients had either no AR or trivial to mild AR at the 5-year follow-up. We found only 1 moderate AR DCSA VSD patient. That patient was in the Amplatzer® device group and had progressed from mild to moderate AR. Based on these findings, we believe that both PmVSD and DCSA VSD with only trivial AR can be closed

using transcatheter method.

In conclusion, transcatheter closure of VSD in both PmVSD and DCSA VSD can be achieved by using either the Amplatzer® Device or the Nit-Occlud® Lê VSD Spiral Coil System, with comparable closure rates between systems. The progression of AR was higher in DCSA VSD patients, but a majority of those patients had less than mild AR at end of 5 years.

CONFLICTS OF INTEREST

The authors hereby declare no personal or professional conflicts of interest regarding any aspect of this study.

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