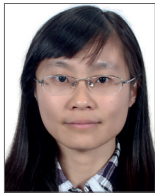# Incidence and predictors of asymptomatic pericardial effusion after transcatheter closure of atrial septal defect

Jingjin Wang[1], PhD; Mehul Patel[2], MD; Minghu Xiao[1], MD; Zhongying Xu[3], MD; Shiliang Jiang[3], MD; Xin Sun[1], MD; Liang Xu[3], MD; Hao Wang[1]*, MD, PhD

1. Department of Echocardiography, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; 2. Adult Congenital Heart Disease, Baylor College of Medicine, Houston, TX, USA; 3. Department of Radiology, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

KEYWORDS

- congenital heart disease
- risk factors
- transcatheter closure

Abstract

Aims: Pericardial effusion (PE) without obvious periprocedural complications (e.g., cardiac perforation, device erosion) may occur after transcatheter closure of secundum atrial septal defects (ASD). The aim of the study was to investigate the incidence and predictors of PE unrelated to procedural complications.

Methods and results: We included all patients who had undergone successful percutaneous ASD closure from June 2009 to April 2014 (n=2,652) with no pre-existing PE or cardiac perforation or erosion. Transthoracic echocardiography (TTE) was performed during the procedure and one, three, and six months postoperatively. After device implantation, fifty patients (1.9%) developed new-onset PE (37 immediately, 13 during follow-up). These patients were asymptomatic, stable haemodynamically, and had no new arrhythmias. PE appeared mild (5.1±1.9 mm) and homogeneously echolucent by TTE. PE diminished spontaneously. Compared with 2,602 patients without PE, factors independently predicting asymptomatic PE were the device touching the atrial free wall, device size, patient age, and total defect size. Areas under the receiver operating characteristic curves were 0.78 (p<0.001), 0.66 (p<0.001) and 0.77 (p<0.001) for device size, patient age, and total defect size, respectively.

Conclusions: This is the first systematic report of a new type of PE. Our data provide new insights into new-onset PE after percutaneous ASD closure.

*Corresponding author: Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, 167 Beilishi Road, Beijing, 100037, China. E-mail: fwwanghao@gmail.com

Abbreviations

ASD   atrial septal defect
AUC   area under curve
CI   confidence interval
PE   pericardial effusion
ROC   receiver operating characteristic
TEE   transoesophageal echocardiography
TTE   transthoracic echocardiography

Introduction

Pericardial effusion (PE) is a rare complication of transcatheter closure of a secundum atrial septal defect (ASD), with a reported incidence of 0.5-1.5%[1-3]. The reported aetiology ranges from wire perforation to catastrophic device erosion[4]. However, PE related to transcatheter closure of ASD without an obvious cause has only been described in case reports, and has not been the subject of systematic study[1,5,6]. The incidence and predictors of such PE unrelated to cardiac perforation or erosion are unknown. We sought to investigate the incidence and predictors of PE following percutaneous ASD closure. This study aimed to provide interventional cardiologists with a novel way to approach the diagnosis and differential diagnosis of new-onset PE after ASD closure.

Methods

PATIENT POPULATION

This is a retrospective study of 2,692 ASD patients who underwent transcatheter closure of secundum ASD at Fuwai Hospital, Beijing, China between June 2009 and April 2014. Eligible patients included those who had a haemodynamically significant secundum ASD. Patients with successful implantation of a device without significant complications during the procedure or follow-up were included. The significant complications were defined as device malposition, cardiac perforation or tamponade, device erosion, embolisation, and moderate to severe residual shunt. Patients who had other cardiac lesions or structural abnormalities as well as those in whom ASD closure was combined with other interventional operations were excluded[7-9].

A total of 2,692 patients underwent percutaneous ASD closure (we excluded 40 patients who had pre-existing PE from this study). The remaining patients (n=2,652) – including 50 patients with new-onset PE that appeared during the procedure or the follow-up (PE+ group) and 2,602 patients without PE during the procedure or the follow-up (PE- group) – were studied retrospectively. Patients with procedural or follow-up PE (PE+ group) were reviewed in detail, including their clinical and echocardiographic features and their outcomes. They were compared with those free from PE (PE- group).

The local institutional review board approved the study. Written informed consent was obtained from all subjects.

PROCEDURE

The fluoroscopy-guided implant procedure was carried out under local anaesthesia. Transthoracic echocardiography (TTE) was used for assessment and guidance of ASD closure. The entire procedure

was assessed by TTE instead of using the "stop flow" balloon or transoesophageal echocardiography (TEE) sizing algorithm. Defect size and number, location of the device, and the presence of PE were determined by TTE. A series of TTE scans was performed before, during, and one day after device implantation. TEE was used for diagnosis only when the patient had a suboptimal acoustic window **(Appendix Table 1)**. The interventional procedure was comparable to the international protocol except for the TTE algorithm[10,11].

QUANTITATIVE ASSESSMENT OF THE DEFECT AND DEVICE

Criteria for the device size were as follows: for adults, device size=defect size +6-8 mm, and for children (<18 years) device size=defect size +3-4 mm[12,13]. The maximum defect size was used, as measured by TTE. When multiple defects were present, the size of each defect was calculated and added together and the total defect size was used.

Four devices were used, namely the AMPLATZER® Septal Occluder (AGA Medical Corporation, Plymouth, MN, USA), Cardi-O-Fix Septal Occluder (Starway Medical Technology, Beijing, China), HeartR™ Septal Occluder (Lifetech, Shenzhen, China), and Shanghai Shape Memory Alloy Septal Occluder (Shanghai Shape Memory Alloy Co., Ltd., Shanghai, China). The last three devices were manufactured in China and are described in the Results and Discussion sections. In some cases, a device was not suitable, in which case it was retrieved and at least one other device was tried before final device placement using catheter techniques.

The device discs and their relationships with the neighbouring structures were carefully studied, including the device straddling the aorta and touching the atrial free wall. The latter was defined as either the left or right disc touching the atrial free wall in any direction according to TTE views. Multiple views of the atrial free wall were captured, including: 1) the parasternal short-axis view (posterior and inferior), 2) the four-chamber view or atypical four-chamber view (posterior and superior), and 3) the subcostal view (superior and inferior).

ASSESSMENT OF PERICARDIAL EFFUSION BY TTE

PE was quantified using the multiple views obtained with TTE: (1) position: localised or circumferential; (2) quantification: trivial (appeared only during the systolic cycle and was <5 mm), mild (during the diastolic cycle and was <10 mm), moderate (10-20 mm and was usually circumferential), large (>20 mm)[14]; (3) acoustical density: echolucent or fibrinous strands were present[15].

FOLLOW-UP

All the patients were required to be hospitalised at the time of PE identification. The patients were discharged if they were in stable condition (mild PE with no increment, no new-onset arrhythmia, being stable haemodynamically, and device position being correct). The median time of hospital stay was four days. All patients were required to appear for one, three, and six-month outpatient follow-up evaluations. Additional follow-up was not required unless there was a specific problem or complaint.

STATISTICAL ANALYSIS

Continuous variables were described as the mean±SD and categorical variables as the number (percentage). For comparisons of continuous variables, the independent samples t-test was used. The χ^2 test was used with two-tailed p-values for comparing categorical variables. Univariate and multivariate logistic regression were used to evaluate factors associated with the risk of new-onset PE. To avoid collinearity, separate models were constructed for device size and total defect size in multivariate analysis, to which we added patient age, device touching the atrial free wall, female sex, mean pulmonary artery pressure, right ventricular diameter. The odds ratio (OR) and its 95% confidence interval (CI) were calculated. Receiver operating characteristic (ROC) curves were generated for independent indices to obtain areas under the curve (AUC) and cut-offs. Analyses were performed with SPSS software, Version 20.0 (IBM Corp., Armonk, NY, USA). A value of p<0.05 was considered to indicate statistical significance.

Results

STUDY POPULATION

Of the remaining 2,652 patients (without pre-existing PE or cardiac perforation or erosion), 2,439 (92%) completed the one-month evaluation, and 2,294 (86.5%) and 2,119 (79.9%) patients completed the three and six-month evaluations, respectively. Finally, there were 50 patients with new-onset PE that appeared during the procedure or follow-up (PE+ group) and 2,602 patients without PE during the procedure or follow-up (PE- group).

THE OTHER RESULTS

A patient who was diagnosed with wire perforation (right atrium) was excluded. The patient exhibited moderate PE four hours after transcatheter closure of ASD. He suffered chest pain, fever (four days), atrial fibrillation, and hypotension. He underwent pericardiocentesis, and pericardial tamponade was alleviated after drainage of 445 ml of venous blood.

Forty patients were diagnosed with pre-existing PE (eight had moderate and 32 mild PE). There was a 1.5% incidence of pre-existing PE in the present study. No patient had hypoalbuminaemia, autoimmune disease, or renal abnormalities. Compared with 2,602 patients without PE, the strongest factor independently predicting pre-existing PE was atrial fibrillation. Compared with the PE+ group, the pre-existing PE patients were more likely to have atrial fibrillation, to be older, and to have a higher mean pulmonary artery pressure, even with smaller defect and device size **(Appendix Table 2-Appendix Table 4)**. Moreover, fewer devices tended to touch the atrial free wall in the pre-existing PE group. Therefore, the 40 pre-existing PEs were excluded as there was no new-onset PE after ASD closure.

INCIDENCE AND OUTCOME OF PE

There was a 1.9% incidence (n=50) of new-onset PE that appeared during the procedure or follow-up. The incidence of PE with each

device was 0.9%, 0.41%, 0.38%, 0.19% for the AMPLATZER Septal Occluder, HeartR Septal Occluder, Cardi-O-Fix Septal Occluder and Shanghai Shape Memory Alloy Septal Occluder (SHSMA), respectively. In all, 37 patients developed new-onset PE immediately after implantation of the device, 12 within one month, and one within three months. All cases of PE (n=50) diminished spontaneously (43 completely resolved, seven remained trivial and stable). The median time to relief (resolved or trivial) was 15 days. **Figure 1** shows a patient who developed new-onset PE during the procedure which resolved spontaneously.
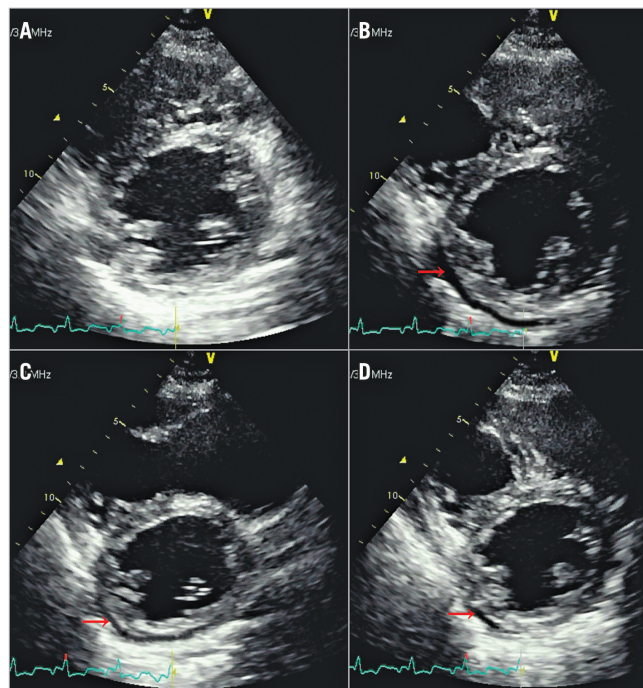
Figure 1. *Transthoracic echocardiographic view of pericardial effusion (PE, red arrow) before, during, and after the procedure. A) Before procedure. B) During release of the occluder, PE was mild (5 mm). C) One hour later, the PE had decreased to 3 mm spontaneously. D) The next day, the PE was trivial.*

ECHOCARDIOGRAPHIC CHARACTERISTICS OF PE

All cases of PE (n=50) evaluated by TTE were mild (5.1±1.9 mm) and homogeneously echolucent. There were 42 cases in the pericardial cavity of the posterior left ventricle or atrioventricular groove. Eight cases were in the pericardial cavity of the right atrium.

CLINICAL AND LABORATORY FEATURES OF THE PE+ GROUP

The patients with PE (n=50) were asymptomatic, haemodynamically stable, and experienced no new-onset arrhythmias during the procedure or the follow-up. None had autoimmune disease, allergies, or renal or hepatic abnormalities. The patients with PE had normal serum albumin (42.1±3.3 g/L) and serum creatinine (72.9±15.6 μmol/L). The white blood count (7.7±3.4×10⁹/L) with normal neutrophil and eosinophil percentages was normal in 49 patients. In the other patient, the eosinophil count was 8.6% (laboratory normal range 0.4-8.0%). All data were acquired at the time of PE identification.

CLINICAL AND PROCEDURAL COMPARISON BETWEEN THE PE- AND PE+ GROUPS

Of the total number of patients (n=2,652), 706 (26.6%) were less than 18 years of age, 1,779 (67.1%) ranged from 18 to 60 years of age, and 167 (6.3%) were more than 60 years of age. Clinical characteristics are compared between the PE+ group (n=50) and the PE- group (n=2,602) in **Table 1**. Compared with the PE- group, the PE+ patients were older, more likely to be female, and had a larger body surface area. Other clinical characteristics were similar between the two groups.

During the procedure, the PE+ group was found to have a larger defect size, device size, right ventricular diameter, and mean pulmonary artery pressure compared with the PE- group. In particular, more devices tended to touch the atrial free wall in the PE+ group but showed no significance as regards straddling the aorta. The type of device had no significant effect **(Table 2)**.

INDEPENDENT PREDICTORS OF ASYMPTOMATIC PE

Logistic regression was employed to determine the factors that predict asymptomatic PE. Univariate analysis showed that the device touching the atrial free wall, total defect size, device size, mean pulmonary artery pressure, right ventricular diameter, patient age, and female sex were significant factors **(Table 3)**. The significant factors were therefore entered into the multivariate analysis using the enter method **(Table 4)**. To avoid collinearity, separate models were constructed for device size and total defect size (R^2=0.22 in model 1, R^2=0.21 in model 2). After analysis, the device touching the atrial free wall, device size, patient age, and total defect size remained independent predictors. ROC curves were constructed to define AUC and optimal cut-offs for asymptomatic PE. Areas under the curve were 0.78 (p<0.001), 0.66 (p<0.001) and 0.77 (p<0.001) for device size, patient age, and total defect size, respectively.

Table 1. Patients' clinical characteristics.

Variable	PE- group (n=2,602)	PE+ group (n=50)	p-value
Age (years)	31.44±18.33	41.7±13.85	<0.001
Female, n (%)	1,769 (68.0)	42 (84.0)	0.016
Body surface area (m²)	1.49±0.39	1.59±0.14	<0.001
SBP (mmHg)	109.84±11.73	115.02±17.03	0.074
DBP (mmHg)	72.30±7.45	75.52±10.32	0.071
NYHA Class, n (%)			0.094
I	1,823 (70.0)	30 (60.0)	
II	650 (25.0)	19 (38.0)	
III/IV	129 (5.0)	1 (2.0)	
Comorbidities, n (%)			
Atrial fibrillation	71 (2.7)	2 (4.0)	0.914
Hypertension	202 (7.8)	6 (12.0)	0.403
Diabetes mellitus	60 (2.3)	3 (6.0)	0.219

Results are given as the number (percentage) or the mean±SD.
DBP: diastolic blood pressure; NYHA: New York Heart Association; SBP: systolic blood pressure

Table 2. Patients' procedural characteristics.

Variable	PE- group (n=2,602)	PE+ group (n=50)	p-value
Echocardiography			
Isolated defect, n (%)	2,465 (94.7)	46 (92)	0.592
Isolated defect size (mm)	16.98±6.11	23.59±5.73	<0.001
Total defect size (mm)	17.28±6.32	23.42±5.54	<0.001
Right ventricular diameter (mm)	28.04±4.09	31.54±4.19	<0.001
Left ventricular ejection fraction (%)	64.90±5.35	64.33±5.93	0.377
Procedural parameters			
Device size (mm)	24.42±7.24	31.72±6.08	<0.001
Two devices, n (%)	21 (0.8)	1 (2)	0.343
Type of device			0.987
ASO	1,287 (49.5)	24 (48.0)	
HSO	535 (20.6)	11 (22.0)	
CSO	551 (21.2)	10 (20.0)	
SHSMA	229 (8.8)	5 (10.0)	
mPAP (mmHg)	19.82±6.27	22.24±6.84	0.007
Retrieval of device, n (%)	222 (8.5)	7 (14.0)	0.267
Device touching the atrial free wall, n (%)	341 (13.1)	32 (64.0)	<0.001
Device straddling the aorta, n (%)	1,564 (60.1)	33 (66.0)	0.399
Mild residual shunt, n (%)	26 (1.0)	2 (4.0)	0.097

Results are given as the number (percentage) or the mean±SD.
ASO: AMPLATZER Septal Occluder; CSO: Cardi-O-Fix Septal Occluder; HSO: HeartR Septal Occluder; mPAP: mean pulmonary artery pressure; SHSMA: Shanghai Shape Memory Alloy Septal Occluder

The cut-off value for the device size was >27 mm, which offered 82% sensitivity and 63% specificity. The cut-off value for patient age was >39.5 years, which showed 54% sensitivity and 63% specificity. The cut-off value for total defect size was >18.5 mm, which offered 80% sensitivity and 61% specificity **(Figure 2)**.

Discussion

Clinically significant PE related to transcatheter closure of an ASD has been extensively described in previous studies, with the aetiology ranging from cardiac perforation to device erosion[4,16]. Few data, however, are available regarding asymptomatic PE unrelated to cardiac perforation or erosion. To the best of our knowledge, the present study is the first to report the incidence, natural history, clinical features, and predictors of asymptomatic PE.

This new type of PE is not due to cardiac perforation, device erosion, or other causes of pericarditis (bacterial, uraemic, or autoimmune). It occurs slowly, is of mild volume, is asymptomatic, and diminishes spontaneously. It may be described as reactive PE.

There were substantial differences between pre-existing and reactive PE involving aetiology and outcome. With pre-existing PE, the patients were more likely to have atrial fibrillation compared with control. Alternatively, there was an obvious effect of percutaneous
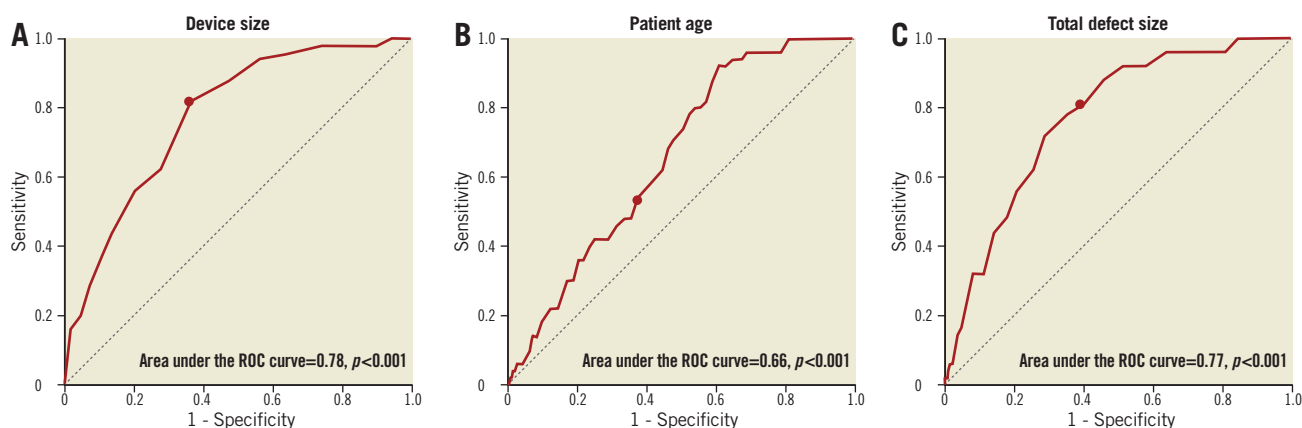
Figure 2. *Receiver operating characteristic (ROC) curve of the ability of device size, age and total defect size to predict asymptomatic pericardial effusion. Areas under the curve were 0.78 (p<0.001), 0.66 (p<0.001), and 0.77 (p<0.001) for device size (A), patient age (B), and total defect size (C), respectively (cut-offs, dark dot). A device size >27 mm offered 82% sensitivity and 63% specificity; patient age >39.5 years showed 54% sensitivity and 63% specificity; total defect size >18.5 mm offered 80% sensitivity and 61% specificity.*

Table 3. Univariate logistic regression analysis for the prediction of asymptomatic pericardial effusion.

Variable		Univariate analysis	
		OR (95% CI)	*p*-value
Age		1.03 (1.02-1.05)	<0.001
Device touching the atrial free wall		11.78 (6.54-21.23)	<0.001
Device size		1.16 (1.11-1.22)	<0.001
Type of device	ASO	1.00	
	HSO	1.06 (0.52-2.18)	0.878
	CSO	0.93 (0.44-1.97)	0.857
	SHSMA	1.12 (0.42-2.98)	0.815
Female		2.47 (1.16 -5.29)	0.020
Body surface area		2.13 (0.96-4.74)	0.063
mPAP		1.05 (1.01-1.09)	0.007
Right ventricular diameter		1.17 (1.11-1.23)	<0.001
Total defect size		1.15 (1.10-1.20)	<0.001
NYHA Class, n (%)	I	1.00	
	II	1.78 (0.99-3.18)	0.053
	III/IV	0.47 (0.06-3.48)	0.461

ASO: AMPLATZER Septal Occluder; CI: confidence interval; CSO: Cardi-O-Fix Septal Occluder; HSO: HeartR Septal Occluder; mPAP: mean pulmonary artery pressure; NYHA: New York Heart Association; OR: odds ratio; SHSMA Shanghai Shape Memory Alloy Septal Occluder

Table 4. Multivariate logistic regression analysis for the prediction of asymptomatic pericardial effusion.

Variable	Multivariate analysis	
	OR (95% CI)	*p*-value
Model 1: device size		
Age	1.02 (1.00-1.04)	0.018
Device touching the atrial free wall	7.69 (4.10-14.43)	<0.001
Female	2.10 (0.96-4.60)	0.063
mPAP	1.00 (0.96-1.05)	0.847
Right ventricular diameter	0.95 (0.86-1.06)	0.363
Device size	1.13 (1.05-1.22)	0.002
Model 2: total defect size		
Age	1.02 (1.00-1.04)	0.025
Device touching the atrial free wall	7.75 (4.11-14.61)	<0.001
Female	2.00 (0.92-4.36)	0.081
mPAP	1.01 (0.97-1.05)	0.688
Right ventricular diameter	0.88 (0.73-1.06)	0.178
Total defect size	1.18 (1.02-1.36)	0.023

CI: confidence interval; mPAP: mean pulmonary artery pressure; OR: odds ratio

ASD closure on patients with reactive PE: 74% (37/50) of patients developed new-onset PE on the day of the procedure. This was as opposed to pre-existing PE, in which no patient had an increment of PE after ASD closure. In particular, more devices tended to touch the atrial free wall in the reactive PE group, which could be a sign of procedural effect. Last but not least, the outcome of reactive PE was benign with spontaneous relief in all patients. However, with mild to moderate pre-existing PE, Reddy et al[17] speculated that, if septal defects were left untreated, the effusions may accumulate over time because of chronic volume overload, which may lead to more PEs.

Our interventional procedure is comparable to the international protocol except for the TTE algorithm. In the determination of defect measurements, defect sizes by TTE were smaller than those of TEE or three-dimensional TEE measurements[18], similar to our results included in the supplementary data. The selection of device size tended to be 6-8 mm above the defect size in our study. There was no procedure-related death, and the rate of major complications was 0.59% (14/2,392) with the strategy[19], which was not higher than that of previous algorithms[20]. The incidence of reactive PE showed no significance between the present and previous study (1.9% versus 1.6%, p=0.973)[6]. The type of algorithm had no significant effect.

The AMPLATZER Septal Occluder is the most common dedicated device for percutaneous ASD closure. However, the

Cardi-O-Fix Septal Occluder, HeartR Septal Occluder, and SHSMA Septal Occluder have been verified to be as safe and effective as the AMPLATZER Septal Occluder[21-23]. The last three devices appear to be widely used in China because of their relatively low cost. Our study demonstrated that the type of device did not have any effect in either the PE+ or the PE- group.

We postulated that the device touching the atrial free wall, device size, total defect size, and patient age might all play a role in the pathogenesis of asymptomatic PE. The device touching the atrial free wall is the strongest independent predictor. Previous findings suggested that local tissue inflammation appeared a few days after device implantation, with the response inducing entry of an exudate into the pericardial space[24]. The device straddling the aorta is not a significant factor, possibly because there is no pericardial tissue encompassing the root of the aorta. One study showed that the right ventricular size decreased over time[25], enlarging the area between the device and the atrium, possibly inducing reactive PE during follow-up. Furthermore, a previous study showed that segmental systolic left ventricular function was normal in patients with small or medium-size devices. Conversely, left ventricular function was significantly impaired in patients who underwent implantation of a large device[26]. Also, in middle-aged adults with pre-existing decreased left ventricular compliance, the acute increase in preload associated with defect closure could lead to worsening left ventricular function[27].

CLINICAL IMPLICATIONS

We undertook quantitative TTE in patients with percutaneous ASD closure. This adds to our understanding of new-onset PE related to percutaneous ASD closure. When PE is a complication of an intracardiac procedure, it is usually considered to be the result of cardiac perforation. The diagnosis and differential diagnosis of PE depend on several factors: (1) the symptoms and haemodynamic status of patients[4,28]; (2) the cardiac rhythm (blood and blood products are quite irritating, and the sinoatrial node is an epicardial structure so PE with blood may give rise to some arrhythmias[29]); (3) the echocardiographic and radiological assessment. The speed of accumulation, level, and echo density may be different for cardiac perforation and reactive PE. Reactive PE is mild, homogeneously echolucent, and diminishes spontaneously. Detection of fibrin strands implies the presence of haemorrhagic PE[15].

We demonstrated that age >39.5 years, device size >27 mm, total defect size >18.5 mm or the device touching the atrial free wall are risk factors for reactive PE.

The aetiology of PE during intracardiac procedures should be identified. Reactive PE should be considered in patients with an unexplained cause, adding to our understanding of the aetiology of new-onset PE. Pericardiocentesis can be life-saving with cardiac tamponade but may be unnecessary with reactive PE. It leads to different therapeutic strategies. Our new finding gives us a more comprehensive understanding of the diagnosis and differential diagnosis of new-onset PE. It also expands our understanding of the relationship between device selection and cardiac anatomy.

Limitations

This was a retrospective study, which is less comparable to a prospective study. Our study, limited by the TTE algorithm, albeit demonstrating a new type of PE with percutaneous ASD closure, was not validated with a TEE or balloon algorithm. Longitudinal studies may be able to clarify this further using international protocol. Although the device touching the atrial free wall was the most independent predictor, the mechanism was not validated with sufficient evidence.

Conclusions

The incidence of asymptomatic PE unrelated to cardiac perforation or erosion was low, and the natural history was self-limited. However, we identified early or delayed onset, mild volume, homogeneous echolucency, and being asymptomatic as important features of this benign condition. Our study demonstrated for the first time the characteristics of asymptomatic PE determined by TTE. The factor of the device touching the atrial free wall may be important in the pathogenesis of asymptomatic PE.

Impact on daily practice

Pericardial effusion without obvious periprocedural complications (e.g., cardiac perforation, device erosion) may occur after transcatheter closure of secundum atrial septal defects. The pericardial effusion was benign and self-limited. Early or delayed onset, mild volume, homogeneous echolucency, and being asymptomatic constitute the important features of this benign condition.

Acknowledgements

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Spence MS, Qureshi SA. Complications of transcatheter closure of atrial septal defects. *Heart.* 2005;91:1512-4.

2. Yared K, Baggish AL, Solis J, Durst R, Passeri JJ, Palacios IF, Picard MH. Echocardiographic assessment of percutaneous patent foramen ovale and atrial septal defect closure complications. *Circ Cardiovasc Imaging.* 2009;2:141-9.

3. Spies C, Timmermanns I, Schräder R. Transcatheter closure of secundum atrial septal defects in adults with the Amplatzer septal occluder: intermediate and long-term results. *Clin Res Cardiol.* 2007;96:340-6.

4. Holmes DJ, Nishimura R, Fountain R, Turi ZG. Iatrogenic pericardial effusion and tamponade in the percutaneous intracardiac intervention era. *JACC Cardiovasc Interv.* 2009;2:705-17.

5. Chessa M, Carminati M, Butera G, Bini RM, Drago M, Rosti L, Giamberti A, Pome G, Bossone E, Frigiola A. Early and

late complications associated with transcatheter occlusion of secundum atrial septal defect. *J Am Coll Cardiol.* 2002;39:1061-5.

6. Wang JK, Tsai SK, Wu MH, Lin MT, Lue HC. Short- and intermediate-term results of transcatheter closure of atrial septal defect with the Amplatzer Septal Occluder. *Am Heart J.* 2004;148:511-7.

7. Du ZD, Hijazi ZM, Kleinman CS, Silverman NH, Larntz K; Amplatzer Investigators. Comparison between transcatheter and surgical closure of secundum atrial septal defect in children and adults: results of a multicenter nonrandomized trial. *J Am Coll Cardiol.* 2002;39:1836-44.

8. Butera G, Carminati M, Chessa M, Youssef R, Drago M, Giamberti A, Pomè G, Bossone E, Frigiola A. Percutaneous versus surgical closure of secundum atrial septal defect: comparison of early results and complications. *Am Heart J.* 2006;151:228-34.

9. Cao Q, Radtke W, Berger F, Zhu W, Hijazi ZM. Transcatheter closure of multiple atrial septal defects. Initial results and value of two- and three-dimensional transoesophageal echocardiography. *Eur Heart J.* 2000;21:941-7.

10. Luermans JG, Post MC, ten Berg JM, Plokker HW, Suttorp MJ. Long-term outcome of percutaneous closure of secundum-type atrial septal defects in adults. *EuroIntervention.* 2010;6:604-10.

11. Butera G, Biondi-Zoccai G, Sangiorgi G, Abella R, Giamberti A, Bussadori C, Sheiban I, Saliba Z, Santoro T, Pelissero G, Carminati M, Frigiola A. Percutaneous versus surgical closure of secundum atrial septal defects: a systematic review and meta-analysis of currently available clinical evidence. *EuroIntervention.* 2011;7:377-85.

12. Editorial Boards of Chinese Journal of Pediatrics; Editorial Boards of Chinese Medical Journal. [Guideline of catheter interventional therapy for congenital heart diseases]. *Zhonghua Er Ke Za Zhi.* 2004;42:234-9.

13. Li GS, Kong GM, Wang YL, Jin YP, Ji QS, Li JF, You BA, Zhang Y. Safety and efficacy of transcatheter closure of atrial septal defects guided by transthoracic echocardiography: a prospective study from two Chinese Medical Centers. *Ultrasound Med Biol.* 2009;35:58-64.

14. Imazio M, Mayosi BM, Brucato A, Adler Y. Pericardial effusion triage. *Int J Cardiol.* 2010;145:403-4.

15. George S, Salama AL, Uthaman B, Cherian G. Echocardiography in differentiating tuberculous from chronic idiopathic pericardial effusion. *Heart.* 2004;90:1338-9.

16. Levy PY, Habib G, Collart F, Lepidi H, Raoult D. Etiological diagnosis of pericardial effusion. *Future Microbiol.* 2006;1:229-39.

17. Reddy SR, Thomas RL, Ross RD. Prevalence of pericardial effusions in children with large atrial or ventricular septal defect. *Am J Cardiol.* 2009;103:271-2.

18. Hascoet S, Hadeed K, Marchal P, Dulac Y, Alacoque X, Heitz F, Acar P. The relation between atrial septal defect shape, diameter, and area using three-dimensional transoesophageal echocardiography and balloon sizing during percutaneous closure in children. *Eur Heart J Cardiovasc Imaging.* 2015;16:747-55.

19. Jiang SL, Xu ZY, Zhao SH, Ling J, Zheng H, Zhang GJ, Zhang Y, Jin JL, Lu B, Dai RP, Liu YQ, Wang Y. Analysis of complications during and post interventional therapy of congenital heart disease. *Zhonghua Xin Xue Guan Bing Za Zhi.* 2009;37:976-80.

20. Geva T, Martins JD, Wald RM. Atrial septal defects. *Lancet.* 2014;383:1921-32.

21. Saritas T, Kaya MG, Lam YY, Erdem A, Akdeniz C, Demir F, Erol N, Demir H, Celebi A. A comparative study of Cardi-O-Fix septal occluder versus Amplatzer septal occluder in percutaneous closure of secundum atrial septal defects. *Catheter Cardiovasc Interv.* 2013;82:116-21.

22. Gupta SK, Sivasankaran S, Bijulal S, Tharakan JM, Harikrishnan S, Ajit K. Trans-catheter closure of atrial septal defect: Balloon sizing or no Balloon sizing - single centre experience. *Ann Pediatr Cardiol.* 2011;4:28-33.

23. Sun WF, Dong ZF, Gong K, Zhang GP, Cui T, Xia YD, Dong J, Shen Y. Transcatheter closure with use of the SHSMA occluder in 180 patients with congenital heart defects: preliminary results. *Tex Heart Inst J.* 2010;37:531-7.

24. Foth R, Quentin T, Michel-Behnke I, Vogt M, Kriebel T, Kreischer A, Ruschewski W, Paul T, Sigler M. Immunohistochemical characterization of neotissues and tissue reactions to septal defect-occlusion devices. *Circ Cardiovasc Interv.* 2009;2:90-6.

25. Du ZD, Cao QL, Koenig P, Heitschmidt M, Hijazi ZM. Speed of normalization of right ventricular volume overload after transcatheter closure of atrial septal defect in children and adults. *Am J Cardiol.* 2001;88:1450-3.

26. Castaldi B, Santoro G, Di Salvo G, Gaio G, Palladino MT, D'Aiello F, Iacono C, Pacileo G, Calabro R, Russo MG. Impact of the Amplatzer atrial septal occluder device on left ventricular function in pediatric patients. *Pediatr Cardiol.* 2013;34:1645-51.

27. Masutani S, Taketazu M, Ishido H, Iwamoto Y, Yoshiba S, Matsunaga T, Kobayashi T, Senzaki H. Effects of age on hemodynamic changes after transcatheter closure of atrial septal defect: importance of ventricular diastolic function. *Heart Vessels.* 2012;27:71-8.

28. Imazio M, Cecchi E, Demichelis B, Ierna S, Demarie D, Ghisio A, Pomari F, Coda L, Belli R, Trinchero R. Indicators of poor prognosis of acute pericarditis. *Circulation.* 2007;115:2739-44.

29. Kaygin MA, Dag O, Gunes M, Senocak M, Limandal HK, Aslan U, Erkut B. Posterior pericardiotomy reduces the incidence of atrial fibrillation, pericardial effusion, and length of stay in hospital after coronary artery bypasses surgery. *Tohoku J Exp Med.* 2011;225:103-8.

Supplementary data

Appendix Table 1. Comparison between TTE and TEE measurements.

Appendix Table 2. Comparison between pre-existing PE group and PE- group.

Appendix Table 3. Predictors for pre-existing pericardial effusion by logistic regression analysis.

Appendix Table 4. Comparison between pre-existing PE group and PE+ group.

Supplementary data

Appendix Table 1. Comparison between TTE and TEE measurements.

Variable	TTE (n=344)	TEE (n=344)	*p*-value
Defect size	20.18±5.78	21.19±5.97	<0.001
Defect numbers, n (%)			<0.001
1	314 (91.3)	314 (91.3)	
2	26 (7.6)	24 (7.0)	
3	4 (1.1)	6 (1.7)	

Results are given as the number (percentage) or the mean±SD.

Appendix Table 2. Comparison between pre-existing PE group and PE- group.

Variable	Pre-existing PE group (n=40)	PE- group (n=2,602)	*p*-value
Age (years)	50.48±17.41	31.44±18.33	<0.001
Female, n (%)	36 (90)	1,769 (68.0)	0.002
Body surface area (m²)	1.60±0.33	1.49±0.39	0.052
SBP (mmHg)	116.54±12.36	109.84±11.73	0.010
DBP (mmHg)	74.23±8.92	72.30±7.45	0.262
NYHA Class, n (%)			0.038
I	21 (52.5)	1,823 (70.0)	
II	16 (40)	650 (25.0)	
III/IV	3 (7.5)	129 (5.0)	
Comorbidities, n (%)			
Atrial fibrillation	11 (27.5)	71 (2.7)	<0.001
Hypertension	7 (17.5)	202 (7.8)	0.035
Diabetes mellitus	2 (5)	60 (2.3)	0.241
Isolated defect, n (%)	37 (92.5)	2,465 (94.7)	0.568
Total defect size (mm)	20.83±5.86	17.28±6.32	0.005
Right ventricular diameter (mm)	30.73±4.57	28.04±4.09	<0.001
Left ventricular ejection fraction (%)	63.7±5.31	64.90±5.35	0.427
mPAP (mmHg)	27.05±7.00	19.82±6.27	<0.001

Results are given as the number (percentage) or the mean±SD. DBP: diastolic blood pressure; mPAP: mean pulmonary artery pressure; NYHA: New York Heart Association; SBP: systolic blood pressure

Appendix Table 4. Comparison between pre-existing PE group and PE+ group.

Variable		Pre-existing PE group (n=40)	PE+ group (n=50)	*p*-value
Age (years)		50.48±17.41	41.7±13.85	0.009
Female, n (%)		36 (90)	42 (84.0)	0.537
Body surface area (m²)		1.60±0.33	1.59±0.14	0.939
SBP (mmHg)		116.54±12.36	115.02±17.03	0.641
DBP (mmHg)		74.23±8.92	75.52±10.32	0.627
NYHA Class, n (%)				0.433
I		21 (52.5)	30 (60.0)	
II		16 (40)	19 (38.0)	
III/IV		3 (7.5)	1 (2.0)	
Comorbidities, n (%)	Atrial fibrillation	11 (27.5)	2 (4.0)	0.008
	Hypertension	7 (17.5)	6 (12.0)	0.552
	Diabetes mellitus	2 (5)	3 (6.0)	0.836
Echocardiography				
Isolated defect, n (%)		37 (92.5)	46 (92)	0.624
Total defect size (mm)		20.83±5.86	23.42±5.54	0.035
Right ventricular diameter (mm)		30.73±4.57	31.54±4.19	0.381
Left ventricular ejection fraction (%)		63.7±5.31	64.33±5.93	0.637
Procedural parameters				
Device size (mm)		27.33±6.27	31.72±6.08	0.001
Two devices, n (%)		1 (2.5)	1 (2)	0.694
Type of device				0.824
ASO		19 (47.5)	24 (48.0)	
HSO		11 (27.5)	11 (22.0)	
CSO		8 (20)	10 (20.0)	
SHSMA		2 (5)	5 (10.0)	
mPAP (mmHg)		27.05±7.00	22.24±6.84	0.002
Retrieval of device, n (%)		4 (10)	7 (14.0)	0.749
Device touching the atrial free wall, n (%)		11 (27.5)	32 (64.0)	0.001
Device straddling the aorta, n (%)		27 (67.5)	33 (66.0)	0.531
Mild residual shunt, n (%)		0 (0)	2 (4.0)	0.501

Results are given as the number (percentage) or the mean±SD. ASO: AMPLATZER Septal Occluder; CSO: Cardi-O-Fix Septal Occluder; DBP: diastolic blood pressure; HSO: HeartR Septal Occluder; mPAP: mean pulmonary artery pressure; NYHA: New York Heart Association; SBP: systolic blood pressure; SHSMA: Shanghai Shape Memory Alloy Septal Occluder

Appendix Table 3. Predictors for pre-existing pericardial effusion by logistic regression analysis.

Variable		Univariate analysis		Multivariate analysis	
		OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age		1.07 (1.05-1.09)	<0.001	1.04 (1.02-1.06)	0.001
Female		4.24 (1.50-11.95)	0.006	3.70 (1.28-10.68)	0.015
NYHA Class	I	1.00		1.00	
	II	2.14 (1.11-4.12)	0.023	1.79 (0.89-3.61)	0.103
	III/IV	2.02 (0.59-6.86)	0.260	2.38 (0.642-8.82)	0.195
Atrial fibrillation		13.52 (6.50-28.14)	<0.001	3.79 (1.54-9.33)	0.004
Hypertension		2.52 (1.10-5.76)	0.029	0.88 (0.35-2.20)	0.779
Total defect size		1.07 (1.02-1.12)	0.006	0.93 (0.85-1.00)	0.063
mPAP		1.10 (1.07-1.14)	<0.001	1.07 (1.03-1.12)	0.001
Right ventricular diameter		1.13 (1.07-1.21)	<0.001	1.13 (1.01-1.26)	0.031

Statistical analysis: univariate and multivariate logistic regression were used to evaluate factors associated with the risk of pre-existing PE. All factors (patient age, gender, NYHA class, atrial fibrillation, hypertension, total defect size, mPAP, and right ventricular diameter) on univariate analysis were entered into multivariate models. The enter method was performed with the models. A value of p<0.05 was considered to indicate statistical significance. CI: confidence interval; mPAP: mean pulmonary artery pressure; NYHA: New York Heart Association; OR: odds ratio