Am J Cardiovasc Dis 2012;2(1):68-74
www.AJCD.us /ISSN:2160-200X/AJCD1111003

Original Article

Long-term results of the amplatzer cribriform occluder for patent foramen ovale with associated atrial septal aneurysm: impact on occlusion rate and left atrial functional remodelling

Gianluca Rigatelli[1], Fabio Dell'Avvocata[1], Paolo Cardaioli[1], Gabriele Braggion[1], Massimo Giordan[1], Alberto Mazza[2], Chiara Fraccaro[1], Mauro Chinaglia[3], Jack P Chen[4]

[1]Section of Adult Congenital and Adult Heart Disease, Cardiovascular Diagnosis and Endoluminal Interventions, Rovigo General Hospital, Rovigo, Italy; [2]Division of Internal medicine, Rovigo General Hospital, Rovigo, Italy; [3]Neurosciences department, Rovigo General Hospital, Rovigo, Italy; [4]Saint Joseph's Heart and Vascular Institute, Atlanta, GA, USA

Received November 18, 2011; accepted November 29, 2011; Epub December 15, 2011; Published January 1, 2012

Abstract: Background: Treatment of patients with concomitant patent foramen ovale (PFO) and atrial septal aneurysm (ASA) poses a number of challenges; while some authors have suggested the off-label use of the Amplatzer Cribriform Occluder in such anatomy, the long-term outcomes of this strategy is unknown. Our study aimed to assess the long-term impact on closure rate, left atrial functional remodelling, and clinical outcomes of off-label implantation of Amplatzer ASD Cribriform Occluder in patients with PFO and ASA. Methods: We prospectively enrolled 160 consecutive patients with previous stroke (mean age 36 ± 9.5 years, 109 females), significant PFO and ASA. All patients were treated with Amplatzer Cribriform Occluder to ensure the most complete possible coverage of the ASA. Residual shunt and LA passive and active emptying, LA conduit function, and LA ejection fraction were computed before and after 6 months from the procedure and then yearly. All patients underwent successful transcatheter closure (mean ratio device/diameter of interatrial septum = 0.74). Results: Incomplete ASA coverage during intraprocedural intracardiac echocardiography was observed in 71 patients. During mean follow-up of 3.6 ± 1.8 years, when compared to patients with complete coverage, there were no differences in LA functional parameters and complete occlusion achieved in 150/160 patients (93.7%). No new cerebral ischemic events, aortic erosions or device thrombosis were recorded during the follow-up. Conclusions: The use of the Amplatzer ASD Cribriform to treat PFO and associated ASA seems safe and effective: relatively small Occluder devices are probably effective enough to promote left atrial functional remodelling.

Keywords: Patent foramen ovale, stroke, embolism, cardiac anatomy, echocardiography

Introduction

Coexistent atrial septum aneurysm (ASA) has been reported in past studies as an important risk factor or contributor for recurrent stroke in patients with patent foramen ovale [1-4]; thus its stabilization during percutaneous closure of patent foramen ovale (PFO) remains one of the goals of the closure procedure. Many "ad hoc" devices and strategies have been proposed to treat PFOs associated with moderate or large ASAs. These include the use of large devices to cover the entire ASA [5], transseptal puncture to deploy the device as centrally as possible with respect to the fossa ovalis [6], the implantation of multiple devices [7], and finally medical therapy alone; nonetheless, none have proven ideal. Currently available devices are not designed specifically for ASA: this anatomical condition mandates a relatively stiff device with equal diameter portions on both atrial sides to stabilize and reconfigure the aneurysmal interatrial septum. The only device with such characteristics, the Amplatzer Cribriform Occluder, has been designed for multiperforated interatrial septum and its use in moderate or large ASA

Table 1. Demographic, clinical, and echocardiographic features of enrolled patients

	Healthy Controls n°40	Enrolled patients n°160	p
Age	37.4±11. 1	36±9.5	ns
Male/Female	16/24	51/109	ns
Heart rate	73.3±12. 7	76.8±10. 2	ns
Body surface	1.78±0.2	1.69±0.2	ns
iTDV (ml/m2)	73.1±13.5	70.4±17.0	ns
Suga index	6.36±2.1	6.1±2.3	ns
Systolic pulmonary pressure (mmHg)	14.6±2.4	14.8±1.9	ns
TC-D shower pattern	0	62/160 (38.7%)	<0.01
TC-D curtain pattern	0	98/160 (61.2%)	<0.01
Basal shunt on TEE without Valsalva	0	112/160 (70%)	<0.01
R-L shunt on TEE:			
-moderate	0	58/160 (36.2%)	<0.01
-large	0	102/160 (63.7%)	<0.01
ASA (TEE):	0	160/160 (100%)	<0.01
≥3 RL or LR ASA	0	99/160 (61.8%)	<0.01

ASA: atrial septal aneurysm; iTDV: indexed telediastolic LV volume; PFO: patent foramen ovale; TC-D: transcranial Doppler; TEE: transesophageal echocardiography.

has been only suggested [8-9]: its long-term safety and efficacy in this setting has never been reported. Our study aimed to assess the long-term impact on closure rate, left atrial functional remodelling, and clinical outcomes of off-label implantation of Amplatzer ASD Cribriform Occluder in patients with concomitant PFO and ASA.

Materials and methods

From December 2005 to December 2009, We prospectively enrolled 160 consecutive patients with previous stroke (mean age 36 ± 9.5 years, 109 females), significant PFO, and moderate to large ASA on echocardiography (at least 3 RL to 5 RL following the Olivares classification [10]) referred to our centre for catheter-based PFO closure according to standard indications [11]. All patients were treated with Amplatzer Cribriform Occluder to ensure the most complete possible coverage of the ASA in compliance with a maximal device/ interatrial septum length ratio of 0.80. Written informed consent was obtained from all patients enrolled in the study. Residual shunt and LA passive and active emptying, LA conduit function, and LA ejection fraction were computed before and after 6 months from the procedure and subsequently yearly by transcranial Doppler (TDC) and transthoracic echocardiography (TTE); and compared with a control group formed by 40 voluntary healthy subjects investigated with TTE at study initiation.

Echocardiographic protocols and definitions

Transthoracic and transesophageal echocardiography (TEE) was conducted using a GE Vivid 7 (General Electric Corp., Nowrfolk, VI, USA) one month before the procedure and repeated at six months post-closure: LA volumes and function, as well as shunt degree as assessed by contrast injection and Valsalva maneuver under local anaesthesia, were recorded [12].

LA passive and active emptying, LA conduit function, and LA ejection fraction were evaluated by TTE before and 1 month after PFO closure. Assessed parameters included: LA volumes as determined at the mitral valve opening (maximal, Vmax) at the onset of atrial systole (P wave of the electrocardiogram, Vp) and at mitral valve closure (minimal, Vmin), from the apical two- and four-chamber views by means of the biplane area-length method via software within the system. The following formula was used to calculate LA volume [13-14]: Volume= 8· 4· Ach (A2ch/3П) · common length (where A4ch and A4ch = LA area in 4- and 2-chamber views, respectively). LA functional parameters were calculated as described in **Table 1**. LA ejection

fraction served as a measure of LA systolic performance; and acceleration (SAT) and deceleration (SDT) times of systolic phase of pulmonary venous flow (PVF) corresponded to LA relaxation and compliance, respectively. The pre- and post -operative echocardiographic findings were evaluated by two blinded physicians. ASA were classified following Olivares et al [10]. Residual shunt was assessed by contrast TEE and TCD [12-15].

Intracardiac echocardiography protocol

Enrolled patients underwent intra-procedural intracardiac echocardiographic (ICE) assessment using the mechanical 9F 9MHz UltraICE catheter (EP Technologies, Boston Scientific Corporation, San Jose, CA, USA). The ICE study was conducted as previously described [16], by performing a manual pull-back from the superior vena cava to the inferior vena cava through 5 sectional planes. ICE monitoring of the implantation procedure was conducted in the 4-chamber plane. Particular attention was given to measurement of the diameter of the entire length of the interatrial septum in the aortic valve plane: our institutional policy was to implant devices of diameter not exceeding a ratio device/length of the interatrial septum of 0.8, to minimize risk of erosion and atrioventricular valves interferences.

Closure protocol

Combined antibiotic therapy (gentamicin 80 mg plus ampicillin 1 g or Vancomicin 1 g, if allergy, had been recorded on anamnesis) was administered intravenously 1 hour before the procedure. The right femoral vein was catheterized through an 8F sheath and used for pre-closure right heart catheterization; the sheath was subsequently replaced with a 10 or 12F long sheath for device implantation. The left femoral vein was catheterized with an 8F sheath and replaced with a precurved 9F long sheath for ICE study.

On the basis of ICE study and the extent of ASA, we implanted the Amplatzer ASD Cribriform Occluder (AGA Medical Corp., Plymouth, MN, USA) 25, 30, or 35 mm, a well-known device composed of two parallel nitinol wire-mesh disks. This device was selected for its rigid structural design, offering superior interatrial septal stabilization and less residual shunt, as compared to other devices [17]. Eventual multifenestrated ASA was approached with previously described multi-wire technique [18].

Follow-up protocol

All patients were administered aspirin 100 mg/day for 6 months after the procedure. Follow-up evaluations consisted of TEE at 1 month, with mandatory repeat study at 6 months if even minimal shunt was detected. Post-procedural assessment further included TTE at 1, 6, and 12 months; TCD at 1 month; Holter monitoring at 1 month; and combined cardiologic and neurological visit at 1, 6, 12 months.

Statistical analysis

Subject pre-procedural TTE and TEE values were compared to those obtained in the control group and at 6-month and at last follow-up echocardiographic examination. All values were corrected for R-R interval and body surface area. Chi-square, ANOVA, and paired T-student tests were used to compare frequencies and continuous variables between groups. Statistical analysis was performed using a statistical software package (SAS for Windows, version 8.2; SAS Institute; Cary, NC). A probability value of < 0.05 was considered to be statistically significant.

Results

When compared with healthy subjects, the enrolled patients at baseline demonstrated greater reservoir function and passive and active emptying, but lower conduit function and LA ejection fraction (**Table 2**). Mean LAA peak flow velocity was 45.3 ± 16.7 cm/s, not significantly different from the control group.

All patients underwent successful transcatheter closure (25 mm device in 141 patients, 30 mm device in 20 patients, and 35 mm in 9 patients; mean ratio device/diameter of interatrial septum = 0.74). Incomplete ASA coverage was observed in 71 patients on both orthogonal views during intraprocedural ICE. Complete occlusion was globally achieved immediately in 134/160 patients (83.7%). **Table 2** demonstrated a non-significant difference in complete occlusion rate at 12 months follow-up between complete and incomplete coverage patients, with predominance of small shunts in incomplete coverage

Table 2. Comparison of complete occlusion rates between complete and incomplete coverage groups over the first 12 months after the closure procedure.

	3 months	6 months	12 months
Complete coverage group (89 patients)	89.8% (7 trivial, 2 small shunt)	93.2% (5 trivial, 1 small shunt)	94.3% (4 trivial shunt, 1 small)
Incomplete coverage group (71 patients)	76.0% (9 trivial, 8 small shunts)	88.7% (4 trivial, 4 small shunt)	92.9% (2 trivial, 3 small shunts)

Table 3. Echocardiographic data of healthy subjects and study group before and after closure (not adjusted for type I error risk).

	Healthy Subjects n°40	Patients before closure n°160	Incomplete coverage after closure n°71	Complete coverage after closure n°89	p
Systolic Acceleration Time	202.1±42.1	182.5±52.0	199.9±42.9	201.2±40.3	0.03
Systolic Deceleration Time	211.3±50.1	252.1±63.0	214.2±52.0	213.3±54.0	0.02
Reservoir function (ml/mq*sec$^{-0.5}$)	33.18±13.53	38.55±10.92	34.1±11.51	32.6±10.7	0.04
LA passive emptying (ml/mq*sec$^{-0.5}$)	25.2±11.30	31.35±10.05	26.2±9.8	26.1±10.20	0.04
LA conduit function (ml/mq*sec$^{-0.5}$)	29.9±12.1	27.95±10.54	29.0±11.0	30.07±12.0	0.04
LA active emptying (ml/mq*sec$^{-0.5}$)	14.2±10.5	16.75±4.90	14.8±3.20	15.0±6.70	0.02
LA passive emptying fraction (%)	0.31 ±0.27	0.22±0.07	0.31±0.45	0.32±0.65	0.02
LA conduit fraction (%)	1.08±0.77	0.84±0.55	1.08±0.53	1.10±0.95	0.04
LA active emptying fraction (%)	0.41±0.18	0.34±0.10	0.37±0.19	0.38±0.20	0.01
LA ejection fraction (%)	0.60±0.12	0.50±0.6	0.61±0.6	0.63±0.86	0.03

LA: left atrial atrium

group and trivial shunts in complete coverage group (global complete occlusion at 12 months 93.7%). At last follow-up echocardiographic control, after a mean of 3.6 ± 1.8 years (range 1 to 5 years), active and passive emptying, as well as conduit function and LA ejection fraction, tended to normalize in both complete and incomplete coverage groups (**Table 3**) to levels of healthy subjects, reflecting shrinkage of the uncovered ASA portion.

Aside from four patients in the incomplete coverage group with episodes of AF lasting up to 48 hours, no other peri-operative or long-term complications, including ictus or transient ischemic attack recurrence, were observed in the enrolled patients. Interestingly, no device-related thrombosis or aortic erosions were observed on follow-up echocardiography, which also confirmed shrinkage of the uncovered ASA portion in the incomplete coverage group with diminution of the maximum atrial septal excursion from 21.3 ± 2.4 to 7.1 ± 2.5 mm ($p<0.01$). This value compared well with the maximum excursion of the complete coverage group (from 16.8 ± 1.6 to 5.5 ± 1.5 mm, $p<0.01$).

Discussion

Our study suggests that treatment of PFO and associated ASA with the Amplatzer Cribriform Occluder device is safe and effective, resulting in low rate of residual shunt even in presence of incomplete ASA coverage. In particular, our data demonstrated that the strategy of maintaining a ratio of device diameter/ interatrial septum diameter < 0.8 is sufficient to promote the fibrotic healing process even in the uncovered portion of the ASA, resulting in positive effect on left atrial functional remodelling. Beneficial shrinkage of the uncovered portion of ASA during the fibrotic healing process with stabilization of the interatrial septum was suggested by the normalization of LA parameters of active and passive emptying, as well ejection fraction, which, as previously investigated [19-20], are clearly altered in PFO patients with ASA.

The presence of ASA likely contributes to the pathophysiology of paradoxical embolism, and it remains a challenge for PFO treatment. Presence of ASA or hypermobility of the atrial septum have been implicated as independent pre-

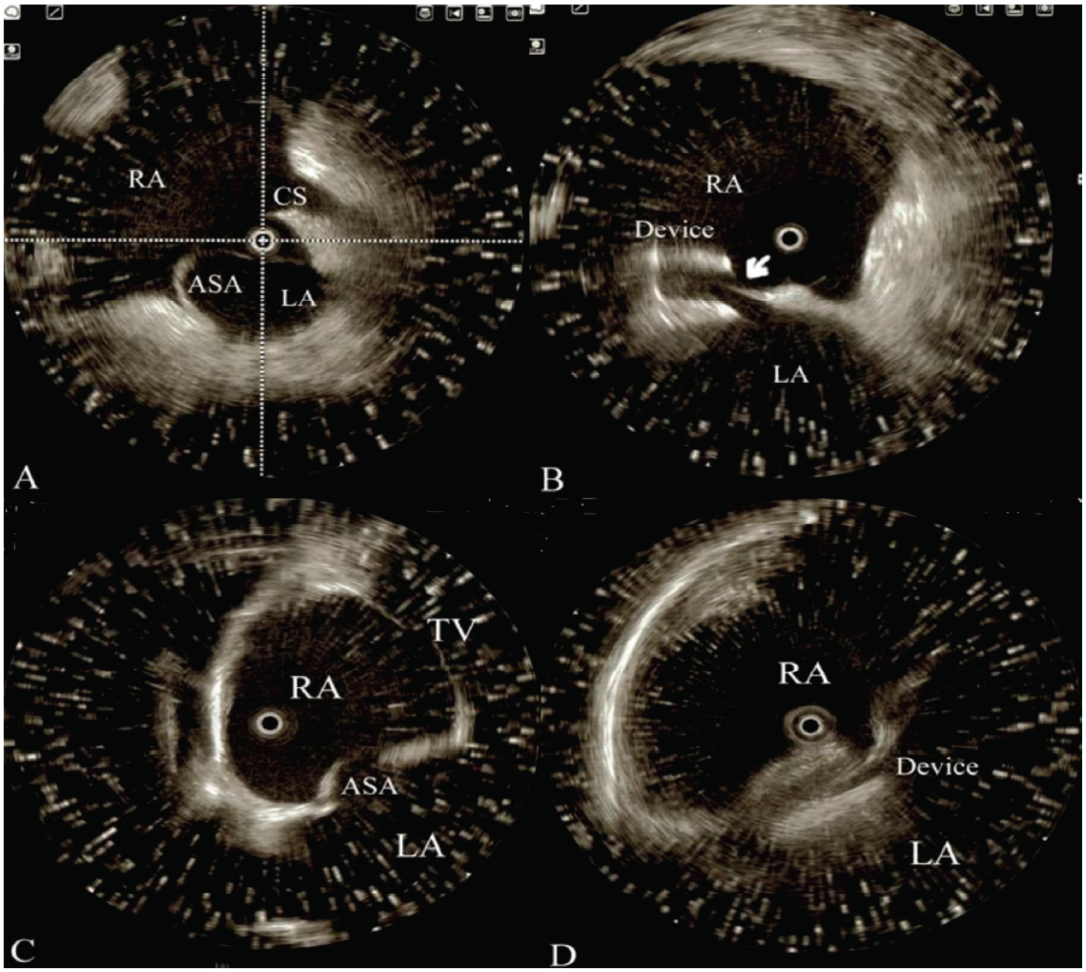

Figure 1. Incomplete coverage and complete coverage of ASA associated to PFO: PFO and associated huge ASA (5 RL) as visualized during ICE monitoring before (A) and after (B) 30 mm Amplatzer ASD Cribriform Occluder implantation. Note the uncovered ASA portion after device release (arrow). PFO and moderate ASA (3 LR) before (C) and after (D) implantation of a 25 mm Amplatzer ASD Cribriform Occluder with complete coverage of the ASA.

dictors of stroke recurrence, with a hazard ratio of 6.04 [21-22], as well as affect closure rate in large series [23-23]. Moreover, in previous studies, the concomitant presence of PFO and ASA has been correlated with increase in white matter lesions in ischemic stroke patients [25] and also with impaired left atrial and left atrial auricular function [26-27].

The coexistence of ASA poses obvious technical challenges in percutaneous treatment of the symptomatic PFO. In specific, a large ASA can frequently distort the PFO opening so that it lies eccentrically with respect to the ASA and oval fossa. In such cases, complete ASA coverage is accomplished only by a large device or with one approximating the length of the interatrial septum, a strategy carrying the inherent risks associated with large sized devices (Figure 1). Indeed, the implantation of large devices of 30 mm or more, if exceeding the length of the interatrial septum, have been correlated with mid- and long-term complications including increased frequencies of arrhythmias, device thrombosis, aortic and atrial erosions [28], and residual shunt [29]. While these occurrences are potentially hazardous in every patient, they are especially regrettable in young patients.

The uses of other techniques, such as transseptal puncture, have similar potential drawbacks, including pericardial effusion, tamponade, and aortic puncture [6]. In the case of multiperforated ASA, the multiple-device technique of

crossing all the eventual fenestrations, with multiple device implantation, while feasible [30], does not prevent device/interatrial septal misalignment or aortic impingement.

The use of the Amplatzer ASD cribriform Occluder, a device specifically designed for cribrosus secundum ASD, in patients with PFO and associated ASA was initially described firstly in 2008 by Silvestry et al [8] and in 2009 by Musto and colleagues [9]. Both series reported excellent immediate success and good occlusion rate during short-term follow-up. Our data confirmed these findings; moreover, our data have continued to demonstrate a high occlusion rate with absence of complications during long-term follow-up.

In conclusion, limitations including the relatively small sample size, lack of randomization, as well as short-term follow-up limit the widespread applicability of our findings. Nontheless, the present study, to our knowledge, is the first to suggest long-term efficacy and safety of the Amplatzer ASD Cribriform Occluder in treatment of ASA associated with PFO in symptomatic patients. Finally, the study offers reassurance that even an incomplete coverage of the ASA using a device smaller than the ASA extension may be sufficient to promote positive remodelling of the left atrium.

Address correspondence to: Dr. Gianluca Rigatelli, Section of Adult Congenital Heart Disease, Cardiovascular Diagnosis and Endoluminal Interventions, Rovigo General Hospital, Rovigo, Italy, Via WA Mozart, 9, 37040 Legnago, Verona, Italy. Tel: +3903471912016; Fax: +39044220164; E-mail: jackyheart@libero.it

References

[1] Homma S, Sacco RL, Di Tullio MR, Sciacca RR, Mohr JP. Atrial anatomy in non-cardioembolic stroke patients: effect of medical therapy. J Am Coll Cardiol 2003; 42: 1066-1072.

[2] Mas JL, Zuber M. Recurrent cerebrovascular events in patients with patent foramen ovale, atrial septal aneurysm, or both and cryptogenic stroke or transient ischemic attack. French Study Group on Patent Foramen Ovale and Atrial Septal Aneurysm. Am Heart J 1995; 130: 1083-1088.

[3] Arquizan C, Touze E, Moulin T, Woimant F, Ducrocq X, Mas JL. Patent Foramen Ovale and Atrial Septal Aneurysm Study Group. Blood Pressure, smoking and oral contraceptive control after cryptogenic stroke in young adults in the PFO-ASA Study. Cerebrovasc Dis 2005; 20: 41-45.

[4] Mugge A, Daniel WG, Angermann C, Spes C, Khandheria BK, Kronzon I, Freedberg RS, Keren A, Denning K, Engberding R. Atrial septal aneurysm in adult patients. A multicenter study using transthoracic and transesophageal echocardiography. Circulation 1995; 91: 2785-2792.

[5] Rigatelli G, Cardaioli P, Braggion G, Aggio S, Giordan M, Magro B, Nascimben A, Favaro A, Roncon L. Transesophageal echocardiography and intracardiac echocardiography differently predict potential technical challenges or failures of interatrial shunts catheter-based closure. J Interv Cardiol 2007; 20: 77-81.

[6] Tande AJ, Knickelbine T, Chavez I, Mooney MR, Poulose A, Harris KM. Transseptal technique of percutaneous closure results in persistent interatrial shunting. Cathet Cardiovasc Interv 2005; 65: 295-300.

[7] Schwerzmann M, Windecker S, Wahl A, Nedeltchev K, Mattle HP, Seiler C, Meier B. Implantation of a second closure device in patients with residual shunt after percutaneous closure of patent foramen ovale. Cathet Cardiovasc Interv 2004; 63: 490-495.

[8] Silvestry FE, Naseer N, Wiegers SE, Hirshfield JW Jr, Herrmann HC. Percutaneous transcathter closure of patent foramen ovale with the Amplatzer Cribriform septal Occluder. Catheter Cardiovasc Interv 2008; 71: 383-387.

[9] Musto C, Cifarelli A, Pandolfi C, De Felice F, Fiorilli R, Caferri G, Violini R. Transcatheter closure of patent foramen ovale associated with atrial septal aneurysm with Amplatzer Cribriform Septal Occluder. J Invasive Cardiol 2009; 21: 290-293.

[10] Olivares-Reyes A, Chan S, Lazar EJ, Bandlamudi K, Narla V, Ong K. Atrial septal aneurysm: a new classification in two hundred five adults. J Am Soc Echocardiogr 1997; 10: 644-656.

[11] SPREAD – Stroke Prevention and Educational Awareness Diffusion: Stroke Italian Guidelines. IV Edition. 2005. www.spread.it.

[12] Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise J, Solomon S, Spencer KT, St John Sutton M, Stewart W; American Society of Echocardiography's Nomenclature and Standards Committee; Task Force on Chamber Quantification; American College of Cardiology Echocardiography Committee; American Heart Association; European Association of Echocardiography, European Society of Cardiology. Recommendations for chamber quantification. Eur J Echocardiogr 2006; 7: 79-108.

[13] Sloan MA, Alexandrov AV, Tegeler CH; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: transcranial Doppler ultrasonogra-

phy: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2004; 62: 1468-1481.
[14] Rigatelli G, Hijazi ZM. Intracardiac echocardiography in cardiovascular catheter-based interventions: different devices for different purposes.J Invasive Cardiol 2006; 18: 225-233.
[15] Boudoulas H, Triposkiadis F, Barrington W, Wooley CF. Left atrial volumes and function in patients with mitral stenosis in sinus rhythm. Acta cardiol 1991; 46: 147-152.
[16] Stefanidis C, Dernellis J, Lambrou S, Toutouzas P. Left atrial energy in normal subjects, in patients with symptomatic mitral stenosis and in patients with advanced heart failure. Am J Cardiol 1998; 82: 1220-1223.
[17] Rigatelli G, Dell'Avvocata F, Ronco F, Giordan M, Cardaioli P. Patento val foramen transcatheter closure: result of a strategy based on tailoring the device to specific patients's anatomy. Cardiol young 2010; 20: 144-149.
[18] Zanchetta M, Rigatelli G, Pedon L, Zennaro M, Carrozza A, Onorato E. Catheter closure of perforated secundum atrial septal defect under intracardiac echocardiographic guidance using a single amplatzer device: feasibility of a new method. J Invasive Cardiol 2005; 17: 262-265.
[19] Goch A, Banach M, Piotrowski G, Szadkowska I, Goch JH. Echocardiographic evaluation of the left atrium and left atrial appendage function in patients with atrial septum aneurysm: implications for thromboembolic complications. Thorac Cardiovasc Surg 2007; 55: 365-370.
[20] Rigatelli G, Aggio S, Cardaioli P, Braggion G, Giordan M, Dell'avvocata F, Chinaglia M, Rigatelli G, Roncon L, Chen JP. Left atrial dysfunction in patients with patent foramen ovale and atrial septal aneurysm: an alternative concurrent mechanism for arterial embolism? JACC Cardiovasc Interv 2009; 2: 655-662.
[21] Lee JY, Song JK, Song JM, Kang DH, Yun SC, Kang DW, Kwon SU, Kim JS. Association between anatomic features of atrial septal abnormalities obtained by omni-plane transesophageal echocardiography and stroke recurrence in cryptogenic stroke patients with patent foramen ovale. Am J Cardiol 2010; 106: 129-134.
[22] Goel SS, Tuzcu EM, Shishehbor MH, de Oliveira EI, Borek PP, Krasuski RRA, Rodriguez LL, Kapadia SR. Morphology of the patent foramen ovale in asymptomatic versus symptomatic (stroke or transient ischemic attack) patients. Am J Cardiol 2009; 103: 124-129.
[23] Ford MA, Reeder GS, Lennon RJ, Brown RD, Petty GW, Cabalka AK, Cetta F, Hagler DJ. Percutaneous device closure of patent foramen ovale in patients with presumed cryptogenic stroke or transient ischemic attack: the Majo Clinic experience. JACC Cardiovasc Interv 2009; 2: 404-411.
[24] Von Bardeleben RS, Richter C, Otto J, Himmrich L, Schnabel R, Kampmann C, Rupprecht HJ, marx J, Hommel G, Munzel T, Horstick G. Long term follow up after percutaneous closure of PFO in 357 patients with paradoxical embolism: difference in occlusion system and influence of atrial septal aneurysm. Int J Cardiol 2009; 134: 33-41.
[25] Ueno Y, Shimada Y, tanaka R, Miyamoto N, Tanaka Y, Hattori N, Urabe T. Patent foramen ovale with atrial septal aneurysm may contribute to white matter lesions in stroke patients. Cerebrovasc Dis 2010; 30: 15-22.
[26] Na Jo, Shin SY, Lim He, Choi CU, Kim SH, Kim JW, Kim EJ, Lee EM, Rha SW, Park CG, Seo HS, Oh DJ, Kim YH. Impaired transport function of the left atrium and left atrial appendage in cryptogenic stroke patients with atrial septal aneurysm and without patent foramen ovale. Eur J Echocardiogr 2011; 12: 140-147.
[27] Rigatelli G, Ronco F, Cardaioli P, Dell'Avvocata F, Braggion G, Giordan M, Aggio S. Incomplete aneurysm coverage after patent foramen ovale closure in patients with huge atrial septal anuerysm: effects on left atrial functional remodelling. J Interv Cardiol 2010; 23: 362-367.
[28] Schoen SP, Wiedeman S, Block M et al. Interatrial septal closure devices and aortic perforation: a note of caution. J Invasive Cardiol 2009; 21: E39-41.
[29] Greutmann M, Greutmann-Yantiri M, Kretschmar O, Senn O, Roffi M, Jenni R, Luescher TF, Eberli FR. Percutaneous PFO closure with Amplatzer PFO: Predictors of residual shunt at 6 months follow-up. Congenit Heart Dis 2009; 4: 252-257.
[30] Ewert P, Berger F, Kretcschmar O, Abdul-Khaliq H, Stiller B, Lange PE. Feasibility of transcatheter closure of multiple effects within the oval fossa. Cardiol young 2001; 11: 314-319.