

Percutaneous Left Atrial Appendage Occlusion: Feasibility, Safety and Effect on Echocardiographic Parameters of Cardiac Function and Anatomy

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Resumo

Background: Percutaneous left atrial appendage (LAA) occlusion is an alternative strategy for the prevention of stroke in patients with high-risk atrial fibrillation (AF).

Objective: To assess the feasibility and safety of LAA occlusion with the Amplatzer Cardiac Plug (ACP) as well as the effect on echocardiographic parameters.

Methods: Patients with nonvalvular paroxysmal or permanent AF, with CHADS2 risk score ≥ 2 and contraindication to oral anticoagulation were included in the study. Under monitoring of transesophageal echocardiography (TEE), the ACP device was implanted in the AAE, according to appropriate echocardiographic measurements. Clinical and echocardiographic controls in the second and eighth months were performed.

Results: The group consisted of 11 patients (7 men), aged 73 ± 8 years and CHADS2 score 3 ± 1 . The procedure was successfully performed in all patients with hospital discharge after 7 ± 3 days. TEE showed no interference with adjacent structures or device embolization. There were two cardiac tamponade, treated with good clinical outcome. After follow-up, there was no clinical event, although two patients have shown minimal residual flow through the ACP, and one patient shown thrombus covering the device. There were no differences in the left ventricular dimension and ejection fraction, or the left atrial size and volume.

Conclusion: The percutaneous LAA closure with ACP is technically feasible and does not interfere with usual parameters of cardiac anatomy and function. However, serious complications can arise and their clinical safety and efficacy must be tested in randomized prospective studies.

Keywords: Atrial Appendage/pathology; Cardiac Catheterization/instrumentation; Atrial Fibrillation/complications; Echocardiography.

Introduction

Atrial Fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice, associating with significant morbidity-mortality and cost¹. AF increases the risk of cardiac thromboembolism, estimating 5% of the average annual rate of Ischemic Cerebral Vascular Accident (ICVA) in individuals with A of non-valvular origin¹. Oral anticoagulation with vitamin K antagonists, especially warfarin, reduces the incidence of ICVA, but this treatment is underused for several reasons². It is estimated that only 50% of the patients with indication are effectively treated with warfarine³. The recent introduction of new anticoagulant

agents, with action as effective as that of warfarin, increased the costs of the treatment and did not reduce the risk of bleeding⁴. Ecocardiographic and anatomical studies have shown that about 90% of cardiac thrombi in patients with non-valvular AF are formed in the Left Atrial Appendage (LAA)^{5,6}, leading to the concept that the exclusion of the LAA from the systemic circulation represents a strategy to reduce ICVA and other embolic events. From the good results with surgical ablation of the LAA § 0, we proposed a less invasive approach, via catheter, using specially designed devices for percutaneous closure of the LAA in patients with AF, as PLAATO⁸ g1 and WATCHMAN⁹. In the first place, there is still limited experience with clinical results and safety of the procedure. In addition, one does not know if the implantation of the device in the LAA might influence structural or functional aspects of the cardiac chambers. The objective of this study was to report the feasibility, safety

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and early follow-up of percutaneous occlusion of LAA with ACP, in addition to evaluating the possible impact of the intervention on the usual echocardiography parameters of analysis of cardiac structure and function.

Methods

Population

Observational non analytical study with series of implantation cases of the ACP device in LAA, covering the hospitalization period and the first months after the procedure. All patients eligible for the procedure were paroxysmal AF carriers or permanent of non-valvular origin with CHADS2 risk score > 2 and contraindications to the use of oral anticoagulant¹¹. Exclusion criteria were considered the presence of intracardiac thrombus, endocarditis or other infections, possibility of interference over other intravascular or intracardiac structures, left ventricular ejection fraction below 30%, LAA ostium less than 17 mm or greater than 32 mm and LAA depth lower than 10 mm. This study was approved by the Ethics Committee of our institution (n. 2,136) and an informed consent form was signed by all patients.

ACP device

The system consists of three parts, containing a trans-septal access sheath containing, a delivery catheter (9F to 13F), and a self-expandable device. This device consists of an expandable nitinol mesh with a polyester membrane inside,

having a proximal disc and a distal lobe, connected by flexible articulated waist (Figure 1). The size of the lobe varies from 16 to 30 (increments of 2 mm) and the disc size varies from 20 to 36 mm. The disc seals the ostium of the LAA and the lobe accommodates inside (the pacifier principle).

Echocardiogram

Transthoracic Echocardiogram (TTE) and Transesophageal Echocardiogram (TEE) prior to the procedure were performed by the same examiner (SHB) in all patients, using Philips IE33 echocardiograph (Philips Medical Systems, USA). In accordance with the recommendations of the American Society of Echocardiography (ASE), systolic and diastolic dimensions were determined of the Left Ventricle (LV), LV mass, volumes and LV ejection fraction (Simpson method), Left Atrial Dimension (LA), rated volume of the LA and rate of diastolic dysfunction¹².

Procedure

The interventions were performed under general anesthesia via the femoral vein and with continuous monitoring of bi and tri-dimensional TEE. After transeptal puncture guided by TEE, a Mullins catheter was introduced into the LA and angiography was performed using a pigtail catheter positioned in the LAA. Echocardiographic multiplanar sections (approximately 0, 45, 90 and 120 degrees) were made to estimate the size of the LAA (ostium lap and depth), taking as reference the Circumflex

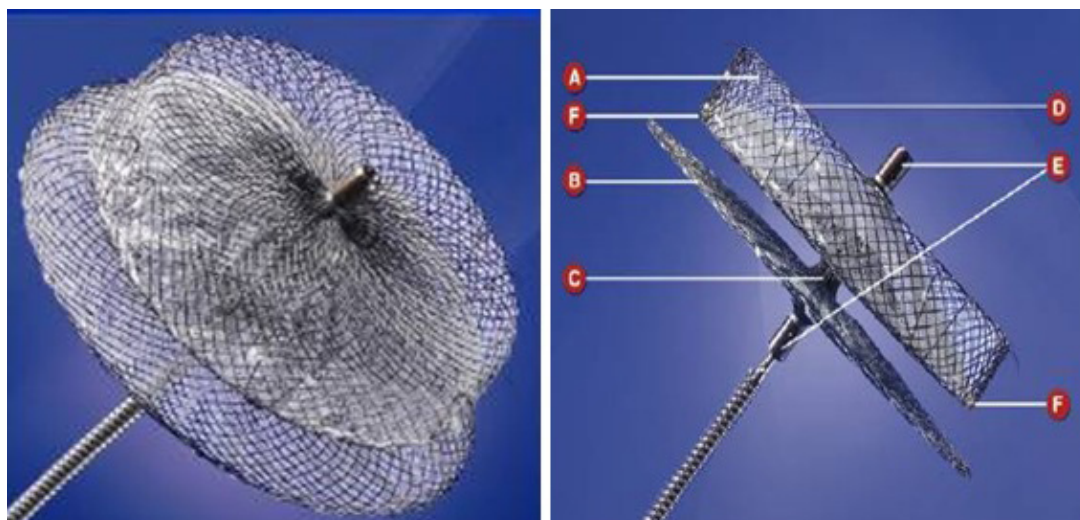


Figure 1- Image of the Amplatzer Cardiac Plug™; A) Lobe, B) Disc, C) Waist, D) Stabilization Guide, E) Radiopaque mark, and F) Radiopaque hooks.

Artery (LCX) and the Left Superior Pulmonary Vein (LSPV). The ostium was defined as the internal distance of the LAA between the projections of LCX and the edge of the LSPV (Figure 2) The lap was defined as the internal distance of the LAA between the projections of LCX and the edge of the LSPV (Figure 2) The depth was estimated from the average point of the ostium, projecting a line up to the bottom of the LAA, parallel to its inclination angle (Figure 3) Such a depth must reach at least 10 mm to enable the procedure. Then the anteroposterior radiographic and right anterior oblique projections were performed for staining of the LAA and to measure its angiographic dimensions. From the set of echocardiographic and angiographic measures, the size of the ACP device to be implanted was defined, with lobes 2-4 mm above the larger size of the lap of the LAA obtained. After release of the device, the immediate result was checked in room by TEE (Figure 4) and angiography. The desired parameters were: clear separation between lobe and disc appearance in lobe "tire", concave appearance of the disc and alignment to the anatomical trajectory of the LAA. After the procedure, control TTE was performed in the intensive care unit. Dual antiplatelet therapy

was used for 45 days after the procedure, followed by monotherapy with acetylsalicylic acid (at least 2 patients with contraindications).

Follow-up

Patients were monitored through regular consultations with a clinical assistant. TTE and TEE were performed two months after the procedure, and TTE after about eight months. Adverse events were defined as serious complications (death, ischemic stroke, systemic embolism, device embolization and cardiac tamponade) and minor complications (small pericardial effusion without hemodynamic repercussion, transient myocardial ischemia by gaseous embolism and bleeding at the site of venipuncture requiring invasive intervention or transfusion).

Statistical Analysis

The occurrence of events was expressed as absolute number. Continuous variables were presented as mean and standard deviation. Comparisons between the variables before and after the procedure were made by the paired Student t test. Significance was defined as $p \leq 0.05$.

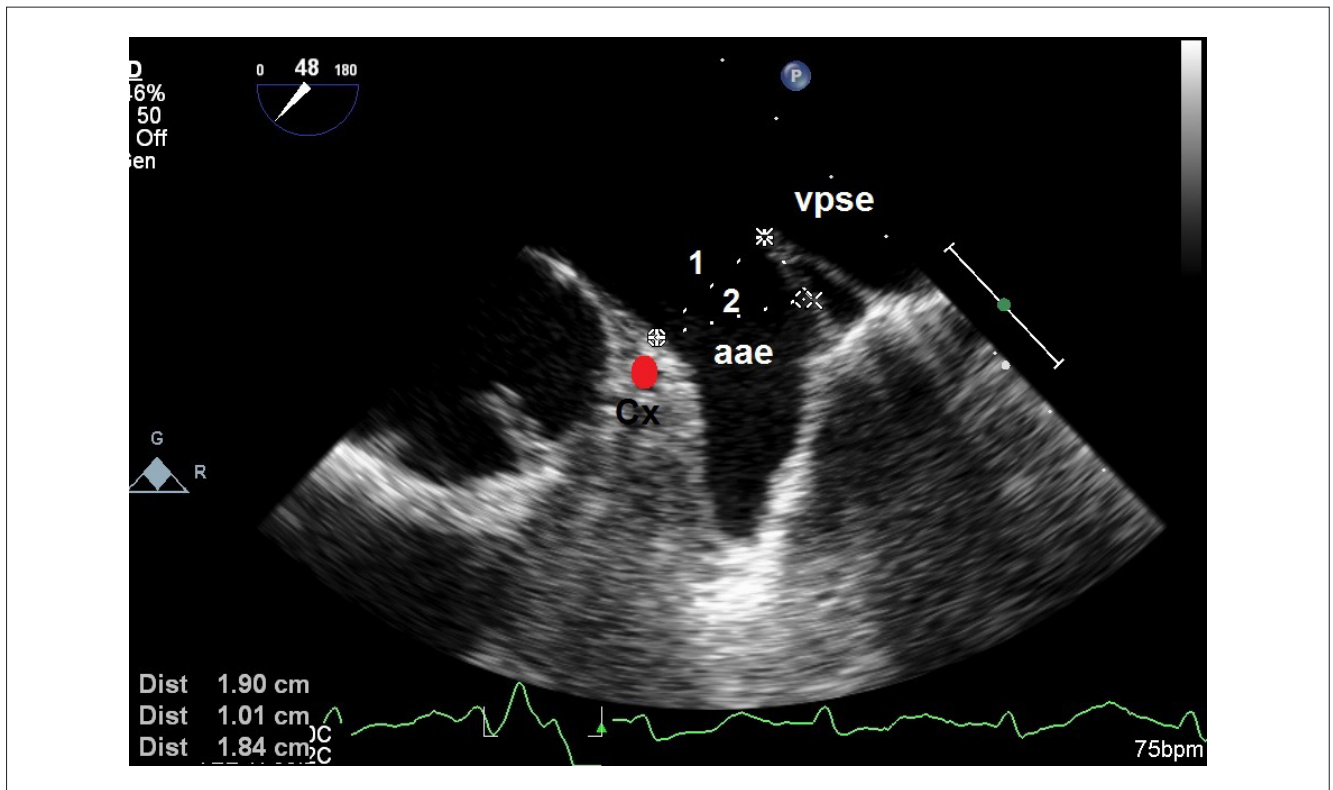


Figure 2 - Usual measures of the left atrial appendage (LAA). Size 1 (ostium), internal distance between the projections of the Circumflex Artery (LCX) and the upper edge of the left superior pulmonary vein. Size 2 (lap); internal distance between the projection of LCX and 1.0 cm below the edge of LSPV.

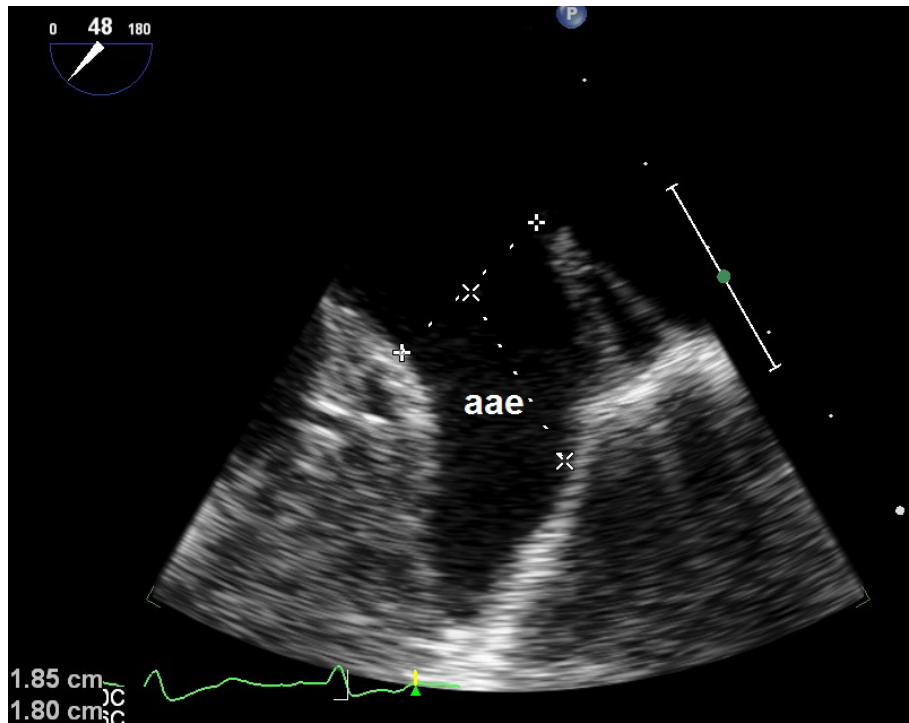


Figure 3 - Depth of the left atrial appendage (LAA). Estimated distance from the average point of the ostium, projecting a line up to the bottom of the appendage, parallel to its inclination angle.

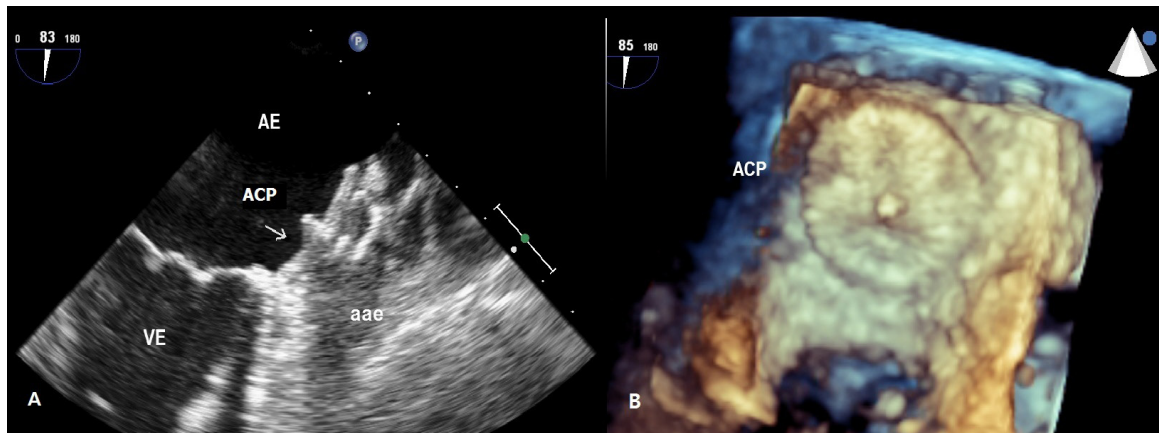


Figure 4 - Appearance of the left atrial appendage occlusion (LAA) by the Amplatzer Cardiac Plug (ACP) to bi-dimensional transesophageal echocardiogram (A: tip of the arrow indicates the disc of the prosthesis) and tri-dimensional (B: view in face of the ACP). LA, left atrium; LV, left ventricle

Results

Basal Characteristics

We evaluated 14 patients eligible for occlusion of the LAA, but excluded 3 (2 by the presence of thrombus in the LAA and 1 individual who did not agree with the procedure).

The demographic, clinical, echocardiographic and angiographic characteristics of the 11 patients included in the study are listed in Table 1. The group consisted of 7 men and 4 women, aged between 73 +/- 8 years, BMI 24 +/- 4 and average CHADS2 score 3 +/- 1. All patients were diagnosed with systemic arterial hypertension, 7 with chronic coronary disease (5 with previous

Table 1 - Demographic, clinic, echocardiographic and angiographic characteristics of the study patients

Patient/ Gender	Age (years)	SAH	DM	CHF	ICVA	Score CHADS2	Echo (mm)	Angio (mm)	Size of ACP (mm)
1 ♂	77	+	-	+	-	3	19	19	22
2 ♂	t	+	+	-	-	2	17	18	20
3 ♂	69	+	+	-	-	2	28	29	30
4 ♀	87	+	+	-	-	3	26	27	30
5 ♂	61	+	+	-	-	2	23	24	26
6 ♀	80	+	-	+	+	5	22	22	24
7 ♂	71	+	+	-	-	2	23	24	26
8 ♀	82	+	-	-	+	4	21	19	24
9 ♂	59	+	-	-	+	3	18	20	22
10 ♀	72	+	-	-	+	3	21	24	24
11 ♂	77	+	-	-	-	2	17	19	20

HAS/SAH: systemic arterial hypertension; DM: diabetes mellitus; AVC/CVA: cerebral vascular accident; AIT/TIA: transitory ischemic attack; ECO/ECHO: measure of the left atrial appendage to echocardiogram; Angio: measure of the left atrial appendage to angiography; ACP: Amplatzer cardiac plug.

angioplasty with pharmacological stent), 5 of diabetes mellitus, 4 of ICVA and 2 of congestive cardiac failure. Seven patients had paroxysmal AF and 4, permanent AF. Contraindications to oral anticoagulation were poor adherence to treatment with great lability in anticoagulation control (4 patients), high previous digestive bleeding (2 patients), repetition epistaxis, previous bleeding cerebral vascular accident, melanoma with generalized metastases, kidney disease and elderly with frequent falls. The average percentage of LV ejection fraction was $63 \pm 10\%$ and LA dimension was 43 ± 6 mm. Eight patients showed uni-lobulated LAA and 3 were bi-lobulated. The average dimensions of the lap of the LAA were 21 ± 4 mm by TEE and 22 ± 4 mm by angiography. The average size of ACP used was 24 ± 3 mm.

Feasibility and hospital complications

Occlusion was successfully performed in all patients. Transesophageal echocardiography showed no interference with adjacent structures such as the LSPV and the mitral valve. In 2 patients it was detected minimal residual flow by ACP, one in the upper edge (Figure 5B) and one on the bottom edge. There was no case of death, device embolization, systemic embolism, ischemic stroke or transient myocardial ischemia. In 2 patients it was diagnosed minimal posterior pericardial effusion, one in the catheterization laboratory after transeptal puncture, and the other in transthoracic control examination at the ICU after the procedure. In both there were no clinical or hemodynamic effects.

Even in the case diagnosed during the procedure, continuous monitoring of TEE and angiography allowed occlusion of the LAA to be successfully completed. Both did not require invasive intervention, evolving with spontaneous resolution (absence of stroke by serial echocardiograms and at 60 days). Additionally, 2 patients had cardiac tamponade. One patient was diagnosed during the procedure, after obvious contrast extravasation and significant hypotension. Pericardiocentesis was performed in the room successfully in the reversal of the condition (discharged from the hospital after seven days). The other patient had a clinical condition of cardiac tamponade two hours after the procedure, with the bedside TTE confirming the presence of an important pericardial effusion. Pericardiocentesis was performed, with resolution of the condition (discharged from the hospital after six days). Finally, there was one case of bleeding at the puncture site requiring blood transfusion. On average discharge from the hospital was granted 7 ± 3 days after the intervention.

Late complications

After two months, TEE continued to show minimum residual flow by ACP in two individuals. In another patient, there was a small thrombus overlying the surface of the ACP (Figure 5A). In two individuals there was still minimal flow by color Doppler through the interatrial septum. During follow-up of 8.6 ± 1.4 months, 2 patients died, both from causes unrelated to the procedure (one died from complications of melanoma

and another patient died from renal failure, respectively three and four months after implantation). None suffered embolic event or other medical complications.

Echocardiographic parameters

The evolution of echocardiographic parameters analyzed in 11 patients pre-intervention and after two months is exhibited in Table 2. There were no significant differences between the parameters studied during the two periods of the study. TTE performed in 9 remaining patients at the end of follow-up showed similar findings. At baseline, 4 patients had permanent AF and diastolic function was considered not assessable. In the remaining seven subjects, only one had normal diastolic function and 6 showed grade I diastolic dysfunction (abnormal relaxation). All remained unchanged after follow-up.

Discussion

Based on the current high prevalence of AF and the difficulties inherent in the chronic treatment with oral anticoagulants, such

as the occurrence of bleeding, need for continuous laboratory monitoring and frequent contraindications, new approaches for the prophylaxis of ischemic stroke have been proposed². Percutaneous occlusion of LAA evolved from the finding that this is the most frequently afflicted site by thrombus in patients with non-valvular original AF⁵. In this study, we report the early experience with the feasibility, and echocardiographic impact of the percutaneous occlusion of LAA with the most recent dedicated device, ACP.

Although the group and observation time are still relatively small, good technical results were achieved in terms of efficiency of the procedure. The ACP has been successfully implanted in all patients and, although two serious complications (cardiac tamponade) occurred, there was no death, ischemic stroke, systemic embolism or device embolization. Still in the hospital phase, three minor complications (two small pericardial strokes and one bleeding) were observed, but without the need for invasive intervention and without sequelae. In evolution, it was found a small thrombus adhered to the ACP in a patient. This

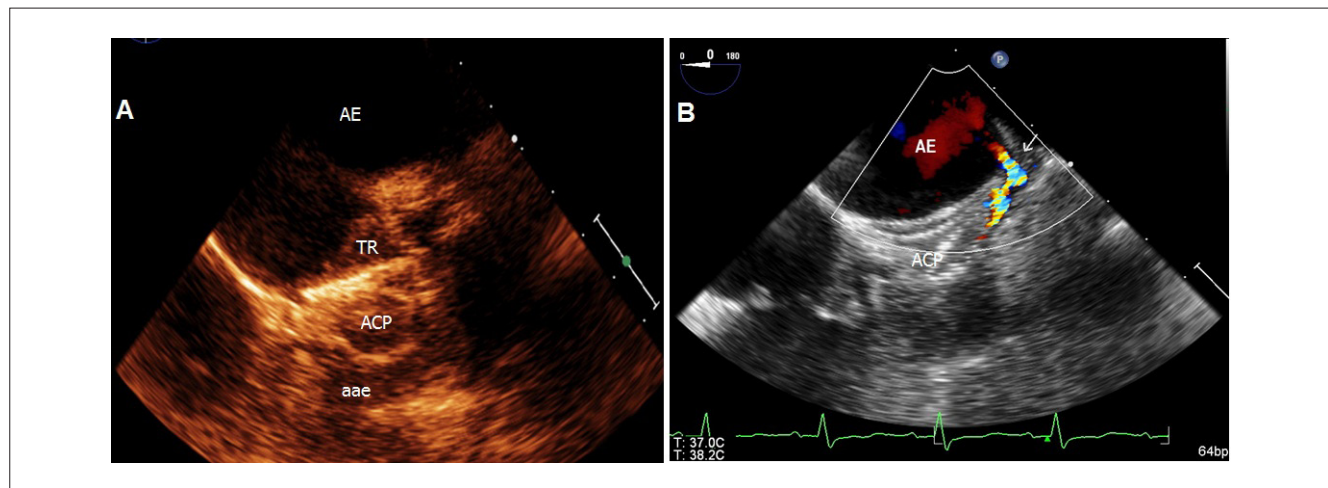


Figure 5 - Late complications of percutaneous occlusion of the left atrial appendage (LAA) with the Amplatzer Cardiac Plug (ACP). A – Thrombus covering the ACP disc (observe inadequate position of the device, with part of the appendage exposed). B – Small residual shunt through the upper edge of the ACP (tip of the arrow). LA, left atrium.

Table 2 - Echocardiographic parameters studied before (pre) and after (post) two months of percutaneous occlusion of the left atrial appendage

Echocardiography Parameter	Pre	Post	p
DDVE (mm)	50 ± 6	50 ± 6	0,80
FE (%)	63 ± 10	60 ± 10	0,14
IMVE (g/m ²)	109 ± 34	107 ± 32	0,81
AE (mm)	43 ± 6	43 ± 5	0,70
VIAE (ml/m ²)	36 ± 10	36 ± 11	0,71

DDVE: diastolic dimension of the left ventricle; FE: ejection fraction; IMVE: left ventricle mass index; AE: anterior-posterior dimension of the left atrium; VIAE: indexed volume of the left atrium.

phenomenon was probably related to poor alignment of the prosthesis in this particular case, resulting in improper position and residual exposure of small area of the LAA (Figure 5A). Although frustrating, this thrombus formation resulted in no clinical event. Unfortunately, this patient died later on from kidney failure, not making long-term follow-up possible. After approximately eight months' follow-up, there were no further complications observed. Thus, this experience is very similar to that of largest studies published to date.

The multicenter randomized PROTECT AF¹³ study showed that occlusion of the LAA with the WATCHMAN device was non-inferior to treatment with warfarin and had a higher rate of adverse events (mainly pericardial effusion and gaseous embolism) limited periprocedure period¹³. The European multicenter registration of the ACP reported being a success in 96% of the attempts to implant this device (132 in 137), with serious complications rate of 7% (three gaseous embolisms, two embolizations of the device and five tamponade)¹⁴. This complications rate is virtually the same as that reported at PROTECT AF (7.4%). Although there are differences in population between studies (sample size three times larger and larger percentage of males in the PROTECT AF), it is reasonable to assume that the occurrence of serious complications did not differ substantially between the ACP and the WATCHMAN. Thus, similar to what happened with the PROSPECT AF, it can be speculated that the event rate shall decline with the experience gain of the technique by trained operators.

A key consideration in the clinical use of occlusion of the LAA by catheter is that the risk of the procedure must be weighed against the risk of bleeding from anticoagulation or occurrence of embolism by poor therapeutic control. Among the risks of the procedure, we have gaseous embolism by placing large sheaths, embolization of the device, events related to vascular access and pericardial effusion (with or without cardiac tamponade) 13,14. The stroke can occur during transeptal puncture or by damage of the thin wall of the LAA. Besides the experience gained in the service, complications can be minimized by employing methods of

image as a guide, especially the two and three dimensional TEE. The percutaneous occlusion of the LAA is a technique still under evaluation, not without risks, but with the potential to bring benefits in reducing the incidence of ischemic stroke and mortality in selected patients, such as patients with non-valvular AF with contraindications to oral anticoagulation. Possible bias of this study are the learning curve of the team with the procedure and the restricted use of the device to a selected group of patients.

Another concern relates to the possible role of percutaneous occlusion of the LAA in the genesis of secondary adverse physiological and hemodynamic effects (such as reduced secretion of atrial natriuretic peptide)¹⁵. In thesis, such effects could lead to changes in echocardiographic parameters usually employed to assess cardiac structure and function. In our study, we did not demonstrate significant apparent impact on the cardiac morphophysiology in the short/medium term. Besides not detecting changes in size and function of the LV, there was no apparent influence of the intervention on the left atrial remodeling, despite the fact that four individuals had permanent AF. Anyway, the physiopathological consequences of the implantation of a foreign body in the LAA as well as the future risk of infection should be further elucidated in future studies.

Conclusion

The percutaneous occlusion of the LAA with the ACP is technically feasible in most patients, but are crucial the proper patient selection, execution by trained operators and the use of echocardiography during and after the procedure, to minimize complications and/or treat them immediately. Serious complications can result from intervention and therefore its safety and clinical efficacy should be tested in randomized prospective studies with a larger number of patients. Finally, our data suggest that percutaneous closure of the LAA seems to have no impact on the main echocardiographic parameters of anatomy and function of the heart.

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