

Hybrid percutaneous treatment of atrial fibrillation: ablation and occlusion of the left atrial appendage. State of the art

Tratamento percutâneo híbrido de fibrilação atrial: ablação e oclusão do apêndice atrial esquerdo. Estado de arte

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INTRODUCTION

Atrial fibrillation (AF) is the most commonly sustained arrhythmia, with an incidence of 2% in the general population, with a lifetime risk of 24% in individuals over 40 years of age¹⁻³.

In the past, this rhythm disorder was considered benign, but now this concept has changed due to increased mortality, and moreover, loss of quality of life because of thromboembolic events. Stroke is a major concern, causing great disability, with an incidence as high as 15% per year in the highest CHA2DS2-VASC score, and 5% in the average patients⁴.

The anatomic source of clots is an anatomic structure called the left atrial appendage (LAA), observed in about 90 % of the cases⁵. This has important consequences and once eliminated, it can theoretically protect patients against thromboembolism.

On the other hand, AF ablation is the accepted treatment for drug refractory, symptomatic patients, the cornerstone is pulmonary vein isolation (PVI). It may be done using radio frequency energy with an ablation catheter point by point, or by cryoenergy, using a specific balloon⁶⁻¹². Other techniques include linear ablation, or different targets like extrapulmonary foci, fractionated electrograms (CAFEs), or nervous plexus ganglia. One thing is clear, when the substrate gets worse, success rates can go down.

About thromboembolism prevention the first line therapy is oral anticoagulation (OAC)¹³ with anti-vitamin K drugs (warfarin or acenocumarol) or NOACs (dabigatran, rivaroxaban or apixaban). But what can we do with those patients with contraindication for OAC? In clinical practice, the most common side effect is bleeding, especially gastrointestinal and intracranial bleeding. Poor compliance, along with drug and dietary interactions^{14,15,16}, are more frequently seen in older patients. There are many scores to evaluate thromboembolism and bleeding risk, but the most widely used are CHA2DS2-VASC and HAS-BLED scores, respectively^{17,18,19,20,21,22}. We must keep in mind that patients who benefit the most from OAC are also the more vulnerable ones with a higher risk for bleeding.

So, what can we do for them? Since LAA is a main source of thrombus formation, its occlusion with devices is a reasonable preventable strategy^{23,24,25,26,27}, there are many devices available on the market, each with different approaches such as endocardial, epicardial, and surgical. The Watchman device, Boston Scientific Inc. Marlborough, MA is the only one approved by the FDA for percutaneous LA closure since 2015. It has proven to be non-inferior to warfarin in stroke prevention and safe for use in this population^{28,29}.

The long-term efficacy of AF ablation proves it is by far the best choice. The numbers vary among centers, but is a consensus that long-term results are still uncertain, more so with persistent AF^{30,31}. This suggests that in patients with high risk for thromboembolism, according to the CHA2DS2-VASC score, guidelines recommend the continuation of long term OAC after catheter ablation³².

If we consider these points: recurrences, the need for OAC maintenance in high risk patients, efficacy and safety of Left atrial appendage occlusion (LAAO) devices, the combination of both therapeutic techniques (LAAO plus AF ablation) seems reasonable to provide a better quality of life to the patients by reducing symptoms (in the best scenario with patient cure, mainly in paroxysmal AF), while reducing the risk of thromboembolism (systemic and stroke) and decreasing hemorrhagic risk due to the absence of OAC in high HAS-BLED scores or the contraindication for anticoagulation.

Two-stage procedures are recommended to perform AF ablation and then close the LAA. Another option is to use the LAAO device first and perform AF ablation later. In this last approach there are many difficulties. Sometimes these patients are not discussed beforehand with an entire team. They had received the occlusion device and AF ablation was later considered as a possible therapy for the arrhythmia, leading to a higher risk of thrombosis, device displacement, leaks, and the impossibility to access some areas because of the mechanical obstacle³³.

When performing a one-stage procedure, we must keep in mind that both procedures have common aspects—the first of them is the left atrial access via transeptal puncture. Other common aspects are the vascular access, general anesthesia, OAC changes before the procedure, hospitalization and stress.

There are not many studies in the literature reporting the use of both therapies together. Some of them are not prospective or randomized, and therefore clear registries are needed.

PATIENTS, METHODS AND RESULTS

In our own experience, in a follow up of 6-29 months about 15% of all patients who had radio frequency (RF) AF ablation were considered for LAA closure at the same time. Sixty percent were female, the average age was 62 years (+- 5), the score CHA2DS2-VASC was 4.3 and HAS-BLED was 4. Seventy-five percent of the patients had previous cerebrovascular ischemic disease, 50% with focal sign, and the rest had behavior disorders (most of them were thought to have psychiatric disorders). Cerebral Magnetic resonance imaging (MRI) was obtained in all of them. Patients with focal signs often showed a single lesion and the others had bilateral infarcts in different territories. (Figures 1 and 2)

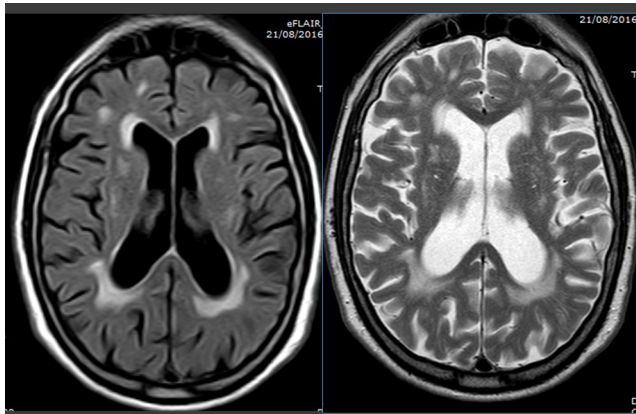


Figure 1: MRI from 78 years old male, with long standing persistent atrial fibrillation, gastrointestinal hemorrhage, and mood changes and transient ischemic attack, under aspirin.

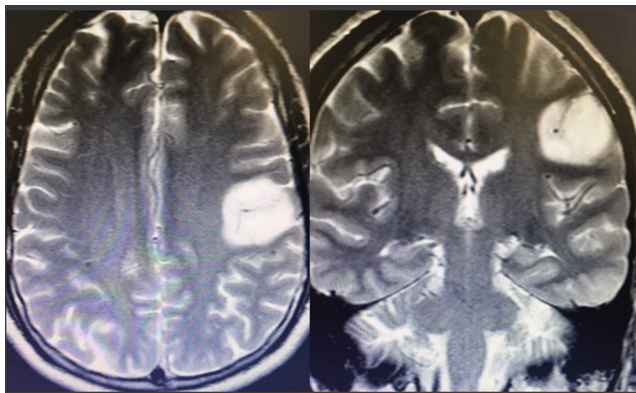


Figure 2: MRI from 43 years old male with permanent atrial fibrillation, 50 minutes from onset of weakness in left facial area and involuntary movement. Under warfarin with INR 2. Familiar restrictive cardiomyopathy.

Under general anesthesia, with continuous transesophageal echocardiography (TEE), there were three femoral venous vascular accesses—two right and one left access. Two transeptal punctures, one inferior and a posterior puncture, was used after ablation to allow placement of the Watchman delivery system. Ablation was performed using a CARTO 3 navigation system, including irrigated catheters with contact force and VisiTag. The RF generator was a Smart Ablate: 30 watts, 42 C for pulmonary vein, and 40 W for ridge applications.

The basic technique used was pulmonary vein isolation (PVI) (Figure 3) with bilateral electric block, while checking for non-PV triggers. The most commonly observed in it was in the superior vena cava. Only one was a redo procedure.

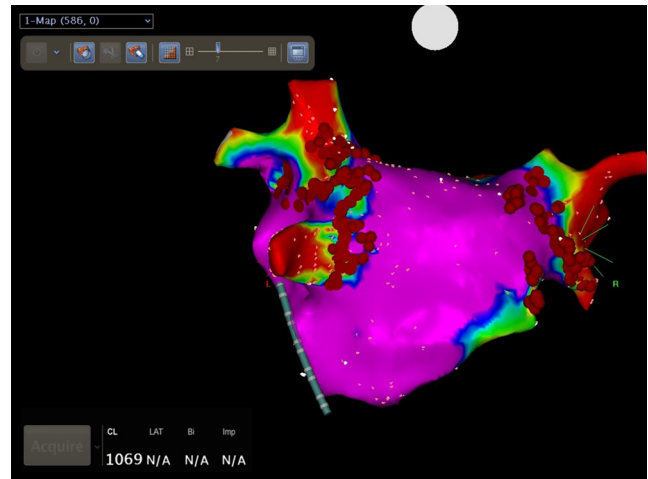


Figure 3: Pulmonary vein isolation using CARTO 3 electroanatomic mapping and irrigated catheters.

After finishing the ablation, a sheath was exchanged with the specific delivery system and the usual LAAO procedure was performed. The choice of the right size device is very important. A cardiac computed tomography (CT) scan was performed in the patients the day before the procedure with three different views. The LAA ostium is usually not circular and often has an irregular shape. It is compared with an angiogram and TEE dimensions taken in real time (Figure 4 and Figure 5). Our choice was to use the biggest size allowed for depth, having a compression of 25% (+/- 3%).

The average total procedure time was 137 minutes (+/- 16 minutes), with 27 min of fluoroscopic time, for both procedures (Figure 6). There were no complications, and the cases shoed 33% of arrhythmia recurrences.

All patients had quality of life improvements. Many of them referred to it as having a “safe feeling.” Other improvements were AF reduction, non—laboratory tests for coagulation control, less hospitalization, and no bleeding events.

After the procedure, OAC was used for 8 weeks, dual antiplatelet therapy was used for 6 months, and aspirin after that. If the patient was bleeding at the time of the procedure or had an absolute contraindication for OAC, no drug was prescribed at all.

Patients were discharged the day after the procedure, followed by a transthoracic echo seven days later, three (Figure 7) and six month TEE was performed, and a CT scan at



Figure 4: Watchman device implant by guiding with transesophageic echo, angiography and CT scan.



Figure 5: Watchman device implant by guiding with transesophageic echo, angiography and CT scan.

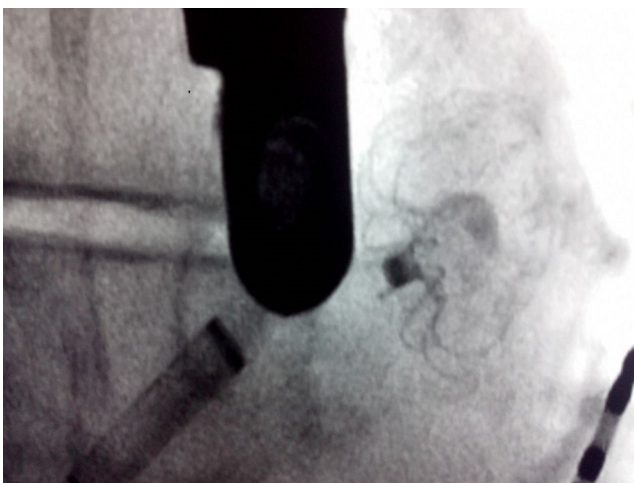


Figure 6: Release Watchman device.

made at Month 12. (Figure 8) No thrombus, displacement or leaks were found at any time.

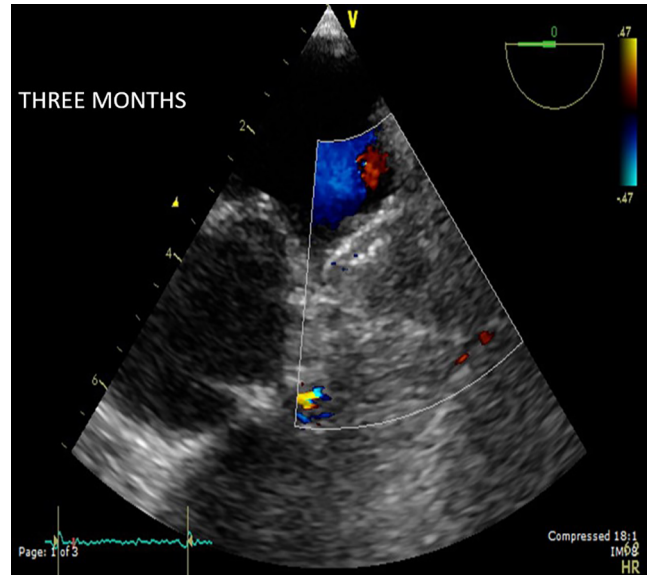


Figure 7: Transesophageic eco control at three months, showing complete sealing of the left atrial appendage with color Doppler.

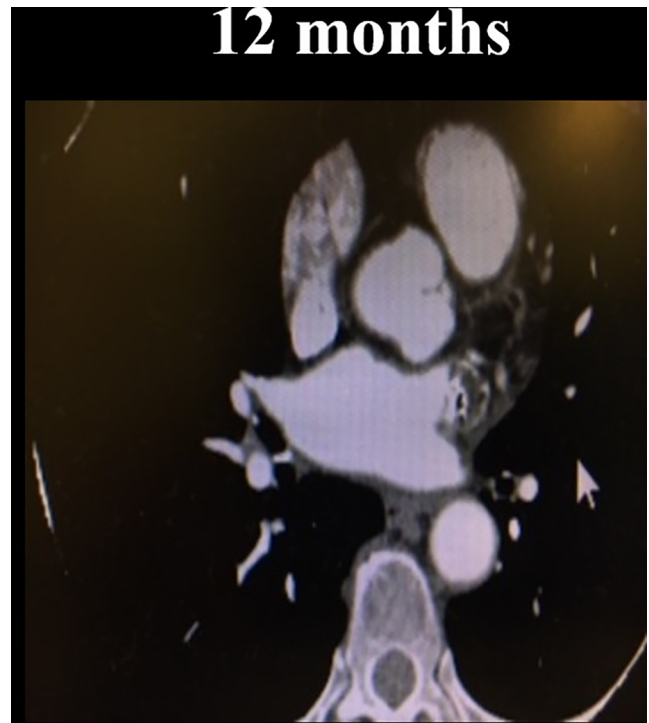


Figure 8: CT scan at 12 months showing no contrast in the left atrial appendage, confirming its exclusion.

DISCUSSION

There are not many research in the literature reporting this progressive and chronic issue, that requires an integral approach to fight symptoms and thromboembolic events especially in most vulnerable populations: the ones with higher risks of stroke, systemic embolism and bleeding.

Turagan et al.³³ studied 60 patients who had implanted a Watchman device, and received RF ablation for rhythm control.

They found 56% of electrically active LAA, but its isolation was not very successful over time. Imaging showed new peri-device leaks in 30% of the cases, with significant leaks (≥ 5 mm) in 10% after radiofrequency ablation (RFA), requiring Accountable Care Organizations maintenance. There were a higher proportion of patients with severe peri-device leaks (≥ 5 mm) after LAA isolation. However, $>50\%$ of those leaks were sealed on follow-up TEE. Their conclusion is that AF ablation is feasible and safe in patients with preexisting Watchman LAAO device and that electrical isolation of the LAA could be difficult and, when attempted, might result in increased risk of short-term peri-device leak and AT/AF recurrence and they suggest an interval of at least 6 months between LAAO and RF ablation.

In a small series of 8 patients published in 2015 by Heeger et al.³⁴, radiofrequency ablation was performed after LAAO 113-1006 days, using Watchman or Amplatzer Cardiac Plug ACP St. Jude Medical, St. Paul, MN, without device interference for targets of RF or periprocedural complications. Only one event of asymptomatic device thrombus occurred, with no leakages, stroke or dislocation, and there was an arrhythmia recurrence of 37%.

But what about LAAO and AF ablation as a one-stage procedure? In 2012 Swann et al.³⁵ studied 30 patients, mean age 62.8 years, who received AF ablation using a multi-electrode with phased RF energy and LAA closure with a Watchman device but of a former generation, 77% had had a previous stroke and 27% had a contraindication for OAC. At 60 days, all patients met the criteria for successful sealing, and they had a 30% recurrence of arrhythmia. Leaks of < 5 mm were present in 10% at implant, 23% at 60 days, and at the 6-month follow-up (FU), 93% were completely sealed. No stroke was observed at the 1-year FU. Their conclusion is that LAA occlusion with the Watchman device and AF ablation may be combined successfully and safely in a single procedure.

Calvo et al.³⁶ evaluated 35 patients of whom 9% had a previous stroke, 48% had bleeding, mean age was 70 years (older than Swann's study). Patients used Watchman and ACP devices. Seventy-eight percent were free of arrhythmia at 13 months FU and 3 patients had a cardiac tamponade. Their conclusion was that the combination of catheter ablation and percutaneous left atrial appendage closure (LAAC) in a single procedure is technically feasible in patients with symptomatic drug-refractory AF, high risk of stroke, and contraindications to OACs, although it is associated with a significant risk of major complications.

In a large series reported by Phillips et al., using the database of two multicenter studies, EWOLUTION and WASP, with 139 patients (12% of them were included in both registries, similar to our experience), 68% with paroxysmal AF, mean age was 64 years (± 7) and 41% had a history of transient ischemic attack (TIA) or stroke. At the time of the procedure, 2.9 % of the patients had peri-device leaks of < 5 mm and none of them had > 5 mm, but at 28 day of FU with the transesophageal echocardiography only 61% had no leaks, 37.1 % were < 5 mms and 1.9 > 5 mm. They did not find any differences between AF ablation techniques or type of energy RF vs. cryoablation and 2.1% had asymptomatic device thrombosis resolution without sequelae with OAC. They had a low incidence of serious complications with 0.7% of tamponade and 1.4% of pericardial

effusion, which may be due to high experience in AF ablation. A very important aspect is that they observed almost no peri-device leaks when Watchman compression was 16% or more. They concluded that these multi-center registries support the feasibility and safety of performing combined procedures of ablation and Watchman LAAC for patients with non-valvular AF and high stroke risk³⁷.

Recently Wintgens et al.³⁸ published a retrospective series with 349 patients with AF RF ablation plus LAAO with the Watchman device. Four percent had leaks < 5 mm at implant, which increased to 28.6% and 0.7% > 5 mm at the 90-day TEE FU. Recurrence of arrhythmias was observed in 51%, with 1.5% of pericardial effusion. One patient suffered a minor stroke several hours after the procedure and 1.1% developed asymptomatic thrombus in the device that was resolved with anticoagulation. During FU, was reported seven ischemic strokes with an annualized stroke risk of 0.7% compared to an expected stroke rate of 3.2% based on CHA2DS2-VASc, off OAC, showing a 78% risk reduction. Best outcomes were seen for higher CHA2DS2-VASc scores, and no benefit for 1 score point. Their conclusion was that in this multicenter analysis of five prospective registries, a hybrid approach combining AF ablation and LAAO is feasible, safe, and successful. Furthermore, it is noteworthy that the long-term outcome shows a clear reduction of the stroke rate despite the AF recurrence observed in more than half of the patients, many of them only on antiplatelet therapy. If cryoablation is considered, Fassini et al.³⁹, published their series of 35 patients, mean age 74 years, in whom they performed AF ablation using cryoenergy and closing the LAA at the same time. They included Watchman and ACP devices in the study. Eighty-six percent of the cases had a previous TIA/stroke, 17% had a major bleeding episode, 28% had arrhythmia recurrence. Leak incidence at 6 months was 14%, which improved at the 12-month FU. The study concluded that cryoablation combined with LAAO appears to be feasible in patients with non-valvular AF associated with high risk of stroke and/or contraindication to antithrombotic prophylaxis.

LESSONS LEARNED

If two stages are preferred, the best option is to perform AF ablation first followed by mechanical closure of the LAA at a second stage.

If only one stage is chosen, one must avoid the mismatch between the real LAA ostium dimension, paying close attention to real-time TEE and angiogram images, as well as to CT scan performed before the ablation. If possible, do it under sinus rhythm and good hydration status to avoid underestimating the ostium size. Once the ostium size is obtained, choose the biggest device allowed according to the LAA depth to reach compression of about 25%. Try to cause the least possible edema of the ridge between LAA ostium and left pulmonary vein. We recommend use more potent and shorter shots (40 W, 15 seconds).

Some questions that still are open are: is one ablation kind of energy better than the other (RF vs. Cryo)? What should we do with leaks in patients with contraindication for anticoagulation? Is the endocardial or epicardial (LARIAT device) approach better for Left atrial appendage occlusion? ⁴⁰.

CONCLUSIONS

According to the references and to our own experience, in patients with non-valvular symptomatic refractory atrial fibrillation, performing a hybrid ablation approach associated with percutaneous mechanical endocardic left atrial appendage closure is feasible and safe in patients with contraindication for anticoagulation.

Peri-device leaks are a potential problem that must be evaluated during the follow up, but the size of the device should be carefully chosen to reduce its incidence.

Prospective registries are required to evaluate long-term outcomes of these therapeutic techniques together.

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