

# Left atrial appendage occlusion with Amplatzer Cardio Plug is an acceptable therapeutic option for prevention of stroke recurrence in patients with non-valvular atrial fibrillation and contraindication or failure of oral anticoagulation with acenocumarol

La oclusión de la orejuela izquierda con Amplatzer Cardio Plug es una terapia aceptable para prevención del ACV isquémico en pacientes con fibrilación auricular y contraindicación o falla terapéutica con acenocumarol

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## ABSTRACT

Left atrial appendage occlusion (LAAO) appears as a therapeutic option for some atrial fibrillation patients not suitable for oral anticoagulation because an increased hemorrhagic risk or recurrent ischemic events despite anticoagulant treatment. **Methods:** Report of consecutive atrial fibrillation patients treated with LAAO with Amplatzer Cardio Plug because contraindication or failure of oral anticoagulation with acenocumarol. CHA<sub>2</sub>DS<sub>2</sub>VASC, HAS-BLED, NIHSS, mRS, procedural complications and outcome were assessed. Seven patients (73 ± 6 year-old) were treated after intracerebral (n = 5) and gastrointestinal (n = 1) hemorrhages or ischemic stroke recurrence while on acenocumarol (n = 1). **Results:** Mean follow up was 18 months. Baseline CHA<sub>2</sub>DS<sub>2</sub>Vasc y HAS-BLED scores were 5.6 ± 0.7 and 4.1 ± 0.3 respectively. There were no strokes or deaths. There was only one non-serious adverse event. **Conclusion:** LAAO with ACP appears as a feasible therapeutic option for stroke prevention in patients with atrial fibrillation and failure or contraindication to acenocumarol.

**Keywords:** atrial fibrillation, stroke recurrence, intracerebral hemorrhage, oral anticoagulants, Amplatzer Cardio Plug.

## RESUMEN

La oclusión de la orejuela auricular izquierda (OOAI) es una opción terapéutica en pacientes con fibrilación auricular y alto riesgo hemorrágico o recurrencia de accidente cerebrovascular isquémico (ACVi) a pesar del tratamiento anticoagulante. **Métodos:** Reporte de pacientes con fibrilación auricular y contraindicación o fallo terapéutico con acenocumarol tratados con OOA. Se evaluaron escalas CHA<sub>2</sub>DS<sub>2</sub>VASC, HAS-BLED, NIHSS y mRS, complicaciones procedurales y resultados. **Resultados:** Siete pacientes (73 ± 6 años) fueron tratados luego de sufrir hemorragia cerebral (n = 5), gastrointestinal (n = 1) o ACVi recurrente a pesar del tratamiento con acenocumarol. Las escalas CHADS<sub>2</sub>VASC y HAS-BLED fueron 5.6 ± 0.7 y 4.1 ± 0.3 respectivamente. Luego de un seguimiento promedio fue de 18 meses (3-50) no se registraron ACVi o muertes. Se registró sólo un evento adverso no serio. **Conclusión:** La OOA es una opción terapéutica factible para prevenir ACVi en pacientes con fibrilación auricular y fallo o contraindicación para recibir acenocumarol.

**Palabras-clave:** fibrilación auricular, hemorragia intracerebral, anticoagulantes orales, Amplatzer Cardio Plug.

Stroke is the second cause of death and the third cause of disability worldwide<sup>1,2</sup>. Non-valvular atrial fibrillation (NVAF) increases 5 fold the risk of ischemic stroke<sup>3</sup> and it is responsible for 15-30% of all ischemic strokes<sup>4</sup>. NVAF induces the

formation of thrombi in the left atrial appendage (LAA), leading to embolic events<sup>5</sup>. Oral anticoagulation is the main therapeutic strategy for prevention of ischemic stroke in patients with NVAF. However a subgroup of patients presents

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high hemorrhagic risk or suffers recurrent embolic events despite appropriate anticoagulant treatment<sup>6</sup>. Left atrial appendage occlusion (LAAO) may be a therapeutic option to prevent ischemic stroke secondary to NVAF, especially in the above-mentioned subgroups<sup>7,8</sup>.

We report our experience in the use of LAAO as secondary prevention strategy in patients with ischemic stroke and NVAF with contraindication or failure of vitamin K antagonists (VKA).

## METHOD

Review of hospital records of consecutive patients with NVAF treated with LAAO for stroke prevention between January 2011 and March 2015. Amplatzer Cardio Plug (ACP) device was used in all cases. VKA failure was defined as occurrence of cerebral ischemic events attributed to AF during adequate treatment with a VKA. History of previous non-traumatic intraparenchymal cerebral hemorrhage (IPH) or systemic hemorrhage with hemodynamic compromise were considered contraindications for oral anticoagulation. Baseline CHA<sub>2</sub>DS<sub>2</sub>Vasc<sup>9</sup> and HAS-BLED<sup>10</sup> scores were calculated. National Institute of Health Stroke Scale (NIHSS) and modified Rankin scales (mRs) were calculated before treatment and during follow-up. Procedural complications were defined according to the WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation trial (PROTECT AF)<sup>7</sup> as major: ischemic stroke or intracranial hemorrhage (ICH), death, pericardial effusion and device embolism; and minor: groin pseudoaneurysm, arteriovenous fistula, puncture site hematoma, device associated thrombosis and minor bleeding without intervention requirement. Efficacy variables were death, hospitalization and stroke or transient ischemic attack (TIA).

Seven patients (73 ± 6 year-old) with ischemic stroke and NVAF were treated with LAAO because of IPH (n = 5), gastrointestinal hemorrhage with hemodynamic compromise (n = 1) or oral-anticoagulation failure (n = 1). Mean CHA<sub>2</sub>DS<sub>2</sub>Vasc and HAS-BLED scales were 5.6 ± 0.7 and 4.1 ± 0.3 respectively. Average NIHSS and mRs were 4 ± 3.3 (0-9) and 2.8 ± 2 (0-5) respectively before LAAO treatment. Average follow-up was 18 months (3-50). (Table) The etiologies of intraparenchymal hemorrhage (IPH) are also shown in Table.

## RESULTS

LAAO treatment was guided with transesophageal echocardiogram in all cases. After the procedure patients were evaluated for at least 24 hours in the stroke unit by a neurologist and a cardiologist. The day after the procedure

a transthoracic echocardiogram (TTE) was performed in all patients. All subjects initiated aspirin within 24 hours after the procedure. Three days after the procedure, the patient who had been treated because failure of VKA was empirically started on rivaroxaban 20 mg QD. Patients who completed 6 months follow up<sup>6</sup> were studied with a new TTE. It did not show procedure related complications. There were no major complications, ischemic or thromboembolic adverse events. Only one 89 year-old patient presented a groin pseudoaneurysm as a procedure-related adverse event one week after discharge. It resolved with local compression. Average NIHSS and mRs were 2.8 ± 2 (0-6) y 2.7 ± 1.6 (0-4) at last follow-up. Six patients are currently on aspirin and one is on rivaroxaban.

## DISCUSSION

We report technically successful and clinically safe LAAO in 7 NVAF patients not suitable for oral anticoagulants. Our definition of failure of oral anticoagulants was based on VKA use. Novel oral anticoagulants appear as a potentially reasonable alternative to investigate for patients with recurrent strokes while on VKA.

Current data show that mechanical LAAO is an acceptable therapeutic option to prevent ischemic stroke in patients with NVAF. The PROTECT AF trial demonstrated the non-inferiority of LAAO with Watchman device when compared with warfarin for stroke prevention in patients with NVAF<sup>7</sup>. Follow-up data of this study suggest that after 4 years, LAAO was superior to warfarin in terms of efficacy. However, 7.4% of patients had procedure related complications. The Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy (PREVAIL) trial, showed that the procedural risk can be substantially lower<sup>11</sup>. After it, the ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology trial (ASAP) confirmed the usefulness of LAAO with Watchman device in patients with contraindication for oral anticoagulation<sup>12</sup>.

Data about the efficacy of LAAO with ACP for stroke prevention is limited<sup>13</sup>. There is an ongoing trial aimed to compare LAAO with ACP vs warfarin or dabigatran<sup>14</sup> ACP was used for LAAO in one prospective report of 20 patients with NVAF and previous ICH. There were no ischemic or hemorrhagic events after 13.6 ± 8.2 months follow-up. Four minor complications related with the procedure were reported<sup>8</sup>.

Our report adds to the current knowledge of the role of LAAO treatment for prevention of ischemic stroke secondary to NVAF in patients with previous ICH. Patients with other indications were also included. Our patients were older than previous reported and had high and very similar risks of stroke and ICH measured by CHADS<sub>2</sub>Vasc and

**Table.** Patients characteristics.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (years)	63	72	73	78	78	70	89
Gender	Male	Female	Female	Male	Male	Female	Male
CHA <sub>2</sub> DS <sub>2</sub> VASc	5	7	5	5	5	6	6
HAS-BLED	4	5	4	4	4	4	4
Hypertension	Yes	Yes	Yes	Yes	Yes	Yes	No
Diabetes Mellitus	No	Yes	No	No	No	No	No
Left atrial dilation*	Moderate	Mild	Mild	Mild	Mild	Moderate	Moderate
Previous ischemic stroke	1	2	3	1	1	1	1
Indication of LAAO	IPH	IPH	AC failure	IPH	IPH	Gastrointestinal hemorrhage (shock)	IPH
IPH etiology	Hypertensive	Brainstem cavernoma	-	Hypertensive	Hypertensive	-	Amyloid angiopathy
Treatment at IPH	Acenocumarol	Acenocumarol	-	Acenocumarol	Acenocumarol	Acenocumarol	-
Actual treatment	Aspirin	Aspirin	Rivaroxaban	Aspirin	Aspirin	Aspirin	Aspirin
Follow-up (months)	50	22	21	13	10	10	3
Procedure related complications	No	No	No	No	No	No	Goin pseudoaneurism
Death/admission/stroke/TIA	No	No	No	No	No	No	No
NIHSS before treatment	8	9	4	0	5	1	4
NIHSS in the follow-up	2	6	3	0	4	1	4
mRs before treatment	3	5	3	0	5	1	4
mRs in the follow-up	1	3	4	0	4	3	4
Time interval IPH-LAAO	1 year	2 years	-	11 months	11 days	-	70 days
Time interval last stroke-LAAO	45 days	12 days	10 days	26 days	1 days	240 days	11 days
AF subtype	Paroxistic	Paroxistic	Cronic	Paroxistic	Cronic	Cronic	Cronic

LAAO: Left atrial appendage occlusion; IPH: Intraparenchymal hemorrhage; AF: atrial fibrillation; TIA: transient ischemic attack; AC: anticoagulants (acenocumarol); NIHSS: National Institute of Health Stroke Scale. \*Normal: < 20 cm<sup>2</sup>, mild dilation: 20-30 cm<sup>2</sup>, moderate dilation: 30-40 cm<sup>2</sup>, severe dilation > 40 cm<sup>2</sup>.

HAS-BLED scores respectively. In this scenario, data about how to balance both risks in order to decide anticoagulant treatment is scant. No ischemic or hemorrhagic adverse events were detected. Only one patient presented a minor complication related to the puncture site that resolved with medical treatment.

In conclusion, LAAO with ACP is an acceptable therapeutic option for prevention of stroke recurrence in patients with NVAF and contraindication or failure of oral anticoagulation. Our report in an older population with high ischemic and hemorrhagic risks adds to published data about feasibility and efficacy of LAAO with ACP in a selected subgroup of patients.

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