ORIGINAL ARTICLE

Two-year clinical outcome from the Iberian registry patients after left atrial appendage closure

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ABSTRACT

Aims The aim of this study was to observe the percentage of thromboembolic and haemorrhagic events over a 2-year follow-up in patients with non-valvular atrial fibrillation (NVAF) undergoing closure of the left atrial appendage (LAA) with an occlusion device. Observed events and $CHADS_2$ (congestive heart failure, hypertension, age, diabetes, stroke history), CHA_2DS_2-VASc (also adding: vascular disease and sex) and HAS-BLED (hypertension, abnormal liver/renal function, stroke history, bleeding predisposition, labile international normalised ratios, elderly, drugs/alcohol use)-predicted events were compared.

Methods LAA closure with an occlusion device was performed in 167 NVAF patients contraindicated for oral anticoagulants and recruited from 12 hospitals between 2009 and 2013. At least two transoesophageal echocardiograms were performed in the first 6 months postimplantation. Antithrombotics included clopidogrel and aspirin. Patients were monitored for death, stroke, major and relevant bleeding and hospitalisation for concomitant conditions. Mean age was 74.68±8.58, median follow-up was 24 months, 5.38% had intraoperative complications and implantation was successful in 94.6% of subjects. Mortality during follow-up was 10.8%, mostly (9.5%) non-cardiac related. Bleeding occurred in 10.1% of subjects, 5.7% major and 4.4% minor though relevant, and 4.4% suffered stroke. Major bleeding and stroke/transient ischaemic attack events within 2 years (annual event rates, 290 patients/year) were less frequent than expected from $CHADS_2$ (2.4% vs 9.6%), CHA_2DS_2-VASc (2.4% vs 8.3%) and HAS-BLED (3.1% vs 6.6%) risk scores (p<0.001, p=0.003, p=0.047, respectively).

Conclusions LAA closure with an occlusion device in patients contraindicated for oral anticoagulants is a therapeutic option associated with fewer thromboembolic and haemorrhagic events than expected from risk scores, particularly in the second year postimplantation.

INTRODUCTION

In recent years, four new oral anticoagulants (OACs) have shown advantages over warfarin in the prevention of thromboembolic complications in non-valvular atrial fibrillation (NVAF). Although their main advantages (reduction of intracranial haemorrhage and no international normalised ratio (INR) monitoring) are interesting, the risks inherent to their anticoagulant action remain unchanged, and they significantly increase the cost of surgery. The relative reduction in the number of events is striking but less relevant in absolute terms.[1]

Closure of the left atrial appendage (LAA), the site of over 90% of thrombi in these patients, has initially been shown to reduce incidence of intracranial haemorrhage. It is at least as effective as warfarin in reducing thromboembolic events,[2] but might be superior to warfarin in longer follow-up periods.[3][4] LAA occlusion is now starting to appear in treatment guidelines.[5]

The aim of this study was to observe the percentage of thromboembolic and haemorrhagic events over a 2-year follow-up in patients with NVAF undergoing LAA closure with an occlusion device, comparing observed events versus $CHADS_2$ (congestive heart failure, hypertension, age, diabetes, stroke history), CHA_2DS_2-VASc (also adding vascular disease and sex) and HAS-BLED (hypertension, abnormal liver/renal function, stroke history, bleeding predisposition, labile INRs, elderly, drugs/alcohol use)-predicted events.[6–9]

METHODS

The working method used in this and subsequent studies was approved by the independent ethics committees of contributing hospitals, and all patients provided informed consent for this study. All procedures comply with the Declaration of Helsinki. The authors' institutions approved the data analysis.

Patients

Closure of LAA with an ACP device (Amplatzer Cardiac Plug, St Jude Medical, Minneapolis, Minnesota, USA) was performed in 167 patients with NVAF recruited from 12 hospitals between March 2009 and early 2013. Inclusion criteria were one or more of the following conditions: serious haemorrhage during acenocoumarol therapy, prior disease or clinical event that contraindicated OACs or repeated failure to adequately control INR, and haematologist indication to suspend acenocoumarol.

Implantation procedure

All patients underwent a transoesophageal echocardiogram (TOE) 24–48 h prior to the procedure to

rule out the presence of LAA thrombi. One hour prior to procedure, patients were given a wide-spectrum antibiotic (cephalosporin), and the procedure was performed under general anaesthetic. Following transseptal puncture, patients were administered 100 U/kg heparin. Selective angiography of the LAA was performed with a volume similar to that of a left coronary artery, and generally in right anterior oblique (RAO) (20°–20°) caudal and also RAO (30°–10°) cranial views. The calibration reference point was a 23 mm radio-opaque ball on the midaxillary line. 2D TOE measurements were taken during the procedure. A preliminary 40°–135° scan with the probe in mid-oesophageal position was performed to obtain both ostium diameters: minor (usually between 45° and 70°) and major (at approximately 135°). The device was chosen according to the official St Jude Medical scoring table, which is based on the measurement ranges of the ostium of the LAA. As a general rule, the size of the device was based on the length of the longest axis of the TOE, usually the superoinferior axis. These measurements were similar to those obtained by angiography in the right caudal projection. In the case of borderline measurements, the largest size was selected. The same operator carried out the procedure at each hospital, and in all cases transseptal puncture was uncomplicated; these factors, therefore, did not affect the study variables.

Postimplantation treatment and follow-up

At the coordinating hospital, follow-up TOE was performed 1 day after intervention, and then at 1, 3, 6 and 12 months to monitor placement of the device, the presence or absence of interatrial shunting and absence of flow to the LAA, focusing above all on the possible presence of thrombus on the device. In the contributing hospitals, at least two follow-up visits were performed during the 6 months postimplantation. Following implantation, a loading dose (600 mg) of clopidogrel was administered, and treatment was started with 300 mg aspirin (ASA) on the first day and 100 mg daily thereafter. Clopidogrel was maintained for 3–6 months, barring haemorrhagic complications, and ASA for 6–12 months. If thrombus occurred, subcutaneous enoxaparin in a therapeutic dose was added for 2 weeks, clopidogrel was prolonged and the TOE was repeated to check for disappearance. If the result was negative, the decision to prolong the treatment for another week or hospitalise the patient and begin treatment with intravenous heparin was evaluated.

Definition of outcomes

Implantation was successful when the following criteria were met: (a) appropriate distance between the body and the outer disc; that is, the body of the device in the neck of the LAA and the disc covering the ostium, with both standard angiographic views (cranial RAO and caudal RAO) or the short-axis view showing a clear separation between them; (b) lightly compressed body or lobe (tyre shape) without the 'raspberry' effect indicative of excessive compression; (c) absence of flow between the left atrium and the LAA over the device or, failing that, <3 mm on a colour Doppler ultrasound; and (d) proof of firm anchorage to the LAA using the tug test.

The main events were death, stroke, serious and relevant haemorrhage, and hospitalisation for concomitant conditions, monitored by means of scheduled visits and telephone calls. The International Society on Thrombosis and Haemostasis definition was used to define major bleeding: fatal bleeding, and/or symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome, and/or

bleeding causing a fall in haemoglobin level of 20 g/L (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or red cells.[10] Minor but relevant bleeding was defined according to the Academic Research Consortium[11] guidelines as any bleeding not meeting major criteria but important enough for the patient or the clinician to merit discontinuation of antithrombotic therapy, albeit temporarily: (1) The patient does not visit the doctor but can suspend antithrombotic therapy, for example, haematoma, epistaxis, haemorrhoidal bleeding, and so on and (2) The patient visits the doctor and action is needed, for example, suspension of antithrombotic therapy, diagnostic tests and hospitalisation.

Statistical analysis

Continuous variables are expressed as mean±SD or median (25th–75th percentiles), depending on distribution of data. Categorical variables were compared using χ^2 or Fisher's exact test, and numerical variables were analysed using the Student's t test or the Wilcoxon test. The observed incidence of events (number of events during the follow-up period divided by the number of patients per year of follow-up) was calculated per patient and year of follow-up (number of patients at the beginning of the follow-up period multiplied by the mean time of follow-up of those patients expressed in years).

The expected incidence of events in the sample was calculated as the mean of the individual risk of each patient. Each patient was assigned an individual risk according to a score of bleeding and ictus risk depending on his or her $CHADS_2$ and HAS-BLED score, as indicated in the work by Friberg and colleagues.[9]

Annual risk of bleeding or stroke was based on each patient's $CHADS_2$ and HAS-BLED score. Observed and expected rates of thromboembolic and bleeding events were compared using binomial tests. Event-free survival was analysed using the Kaplan–Meier method. All data were analysed using SPSS V.19.0.

RESULTS

Characteristics of the population

Table 1 shows the baseline characteristics of the 167 patients. None were eligible for randomised studies in OAC since these were contraindicated for the reasons listed in table 1. The main indications for LAA occlusion were OAC contraindication or complications, mostly gastrointestinal (30.5%) and neurological (22.8%). Mean age was 74.68±8.58. Median $CHADS_2$, CHA_2DS_2-VASc and HAS-BLED scores and 25th–75th percentile were, respectively, 3 (2–4), 4 (3–6) and 3 (3–4).

Mean follow-up was 24 months (mean 22±8.3 months), giving a follow-up rate of 290 patients per year. The intraprocedure complication rate was 5.38%, with 2.99% being central and 2.39% vascular due to a punctured artery resulting in arteriovenous fistula despite prolonged compression. There was one case of migration during the procedure just after the release of the device that was successfully captured and replaced by a larger device; two cases of cardiac tamponade that were resolved with pericardial puncture; and two intraoperative transient ischaemic attacks (TIAs) that left no sequelae.

Median device size was 24 (25th–75th percentile 22–25). For size 16, the percentage of use was 6.3%; for size 18, 6.3%; for size 20, 11.4%; for size 22, 22.2%; for size 24, 27.8%; for size 26, 16.5%, for size 28, 7% and for size 30, 2.5%. The rate of successful implantation was 94.6%.

Table 2 shows the outcomes of raw clinical events (data not adjusted for patient/year) over the 2-year follow-up in 158 patients with successful implants. Mortality was 10.8%, mostly (9.5%) non-cardiac related. Bleeding was observed in 10.1% of

Table 1 Baseline and procedure-associated characteristics (n=167)

Age (in years)	74.68±8.58
≥75 years: 84 (53.2%); ≥78 years: 63 (39.9%)	
Men	102 (61.1%)
CHADS$_2$	3 (2–4)
CHA$_2$DS$_2$-VASC	4 (3–6)
HAS-BLED	3 (3–4)
Procedure indication	
Gastrointestinal haemorrhage	51 (30.5%)
Cranial haemorrhage	38 (22.8%)
Other haemorrhages	28 (16.8%)
CVA/embolism with OAC	12 (7.2%)
High risk of bleeding	7 (4.2%)
Others	32 (19.2%)
Device size (lobe diameter ranging from 16 to 30)	24 (22–25)
Need to change device*	6 (3.5%)
Successful implantation	158 (94.6%)
Procedural complications	9 (5.38%)
TIA	2 (1.2%)
Vascular complication	4 (2.39%)
Cardiac tamponade	2 (1.2%)
Device migration (percutaneously snared)	1 (0.6%)

Values expressed as: number (percentage), mean±SD or median (25th–75th percentiles).
*Three of the changes were due to a larger size, while the other three to a smaller size.
CVA, cerebrovascular accident; HAS-BLED, hypertension, abnormal liver/renal function, stroke history, bleeding predisposition, labile international normalised ratios, elderly, drugs/alcohol use; OAC, oral anticoagulant; TIA, transient ischaemic attack.

subjects, 5.7% major and 4.4% relevant without meeting major criteria, and 4.4% suffered stroke. Findings from echocardiography controls are also shown in table 2. In all, 13 minimal peri-prosthetic leaks were detected that did not meet the <3 mm significance criterion, together with 18 cases of minimal small atrial septal defect shunts (detected by the existence of flow-passage through the interatrial septum by eco-colour Doppler examination), which gradually disappeared on subsequent controls.

Table 3 shows observed events and CHADS$_2$, CHA$_2$DS$_2$-VASc and HAS-BLED-predicted events at 12 and 24 months (expressed as annual event rates, 290 patients/year).

Significant differences in stroke events were observed during the first year, whereas major bleeding events were only observed during the second year. Tables 4 and 5, respectively, show the comparative reduction in stroke following LAA occlusion,

Table 2 Raw clinical events and echocardiographic findings during follow-up in 158 successfully implanted patients

Clinical events	
Death	17 (10.8%)
Major bleeding	9 (5.7%)
Minor relevant bleeding	7 (4.4%)
Total bleeding events	16 (10.1%)
Stroke/TIA	7 (4.4%)
Some event	30 (19.0%)
Echocardiographic findings	
Device thrombus	13 (8.2%)
Small residual ASD	18 (11.4%)
Leak	13 (8.2%)

ASD, atrial septal defect; TIA, transient ischaemic attack.

contrary to the CHADS$_2$ score expected rate, and the types of haemorrhage occurring over follow-up, mainly gastrointestinal. Figure 1 shows the Kaplan–Meier event-free survival curve.

Table 6 shows the percentage of patients under dual platelet therapy and/or at least one antiaggregant treatment at 12 and 24 months of follow-up.

DISCUSSION

This study in LAA occlusion with an occlusion device is one of only three similar studies (together with the European ACP registry and the ASAP with Watchman study) with over 150 patients contraindicated for OACs, and has one of the longest follow-up periods.[12] [13]

The main finding is that the reduction in the rate of events such as stroke or bleeding versus the score-predicted rate in this patient group[6–9] is significant as of the first and second year postimplantation, respectively.

Reduction of expected events during follow-up

In the first year, significant difference between observed and CHADS$_2$-predicted stroke and TIA rate was observed despite peri-implantation events and possible thrombus formation on the devices in the first few months. Incidence, therefore, was 3.9% (or 5.2% including peri-implantation events) versus 9.6% expected rate. Nevertheless, at 2 years when expressed as annual event rates, 290 patients/year, this was 2.4% versus 9.6% score-predicted rate (p<0.001).

In the ASAP study, all-cause stroke or systemic embolism occurred in four patients (2.3% per year): ischaemic stroke in three patients (1.7% per year) and haemorrhagic stroke in one patient (0.6% per year).[13] In other series, stroke and TIAs are usually separated, but in general the approximate mean percentage of stroke/TIA ranged from 2% to 3% per year, a 70% reduction with respect to the score-predicted rate (table 4).[2] [12] [14–19]

Thrombus formation on the device usually occurs around the delivery cable attaching screw, but improvements in design and implantation techniques (faster, 100 U/kg heparin following transseptal puncture, activated clotting time (ACT) monitoring) will probably reduce incidence of thrombi. Most of them are located over the upper quadrant between the screw and the left lateral ridge; they are not usually greater than 5–10 mm and respond well to treatment with low molecular weight heparins for 2 weeks. Once the device is endocardiolised, thrombus formation is virtually nil.

In this series, thrombus formation on the device occurred in around 8% of patients, similar to other studies where it ranges from 5% to 17% depending on the strictness and definition of the TOE follow-up protocol (inclusion/exclusion of mural thrombus).[5] [12–19] More importantly, thrombus rate is higher when dual antiplatelet therapy (DAPT) is withdrawn in the first 2 months, and usually falls with the addition of a 2–3-week course of enoxaparin.[14] [18] [19] Nevertheless, information on post-implantation antithrombotic therapy is somewhat contradictory. In the PROTECT AF study in the Watchman device,[2] warfarin was administered for the first 45 days, followed by DAPT. In other studies, DAPT is administered for 3 months, followed by a further 3 months with ASA alone,[14–17] [19] while others report good results with DAPT for only 6 weeks, following by indefinite ASA[18] suggesting that DAPT is more effective than aceno-coumarol or warfarin.[18]

One of the most interesting findings in this series is the reduced incidence of bleeding, which was significant between the first and second years following withdrawal of antiplatelet drugs. Bleeding at 2 years was 10.4% (16 patients), of which

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Table 3 Observed versus expected events at 12- and 24-month follow-up, adjusted for patient/year

Events	12-month (158 patients/year)			Global follow-up (annual event rates, 290 patients/year)		
	Observed	Expected*	p Value	Observed	Expected*	p Value
Death	9 (5.8%)			17 (5.8%)		
Major bleeding	8 (5.2%)	6.6% HAS-BLED	0.400	9 (3.1%)	6.6% HAS-BLED	0.047
Total bleeding (major+relevant)	15 (9.5%)			16 (5.5%)		
Stroke/TIA	6 (3.9%)	9.6% CHADS₂	0.007	7 (2.4%)	9.6% CHADS₂	<0.001
		8.3% CHA₂DS₂-VASc	0.025		8.3% CHA₂DS₂-VASc	0.003

*Expected rates based on Friberg et al[9] using event rates not adjusted for reduction by aspirin.
HAS-BLED, hypertension, abnormal liver/renal function, stroke history, bleeding predisposition, labile international normalised ratios, elderly, drugs/alcohol use; TIA, transient ischaemic attack.

4.4% were relevant (minor) (seven patients) and 5.7% major (nine patients) versus a HAS-BLED-predicted rate of 6.6% major bleeding events (NS). This is to be expected since during the first 6 months patients were given antiplatelet agents, and the BAFTA and ACTIVE studies have shown that bleeding with antiplatelet drugs is equivalent to bleeding with OAC, particularly among elderly patients.[20 21] Nevertheless, in the second year, when most patients no longer took antiplatelet drugs, the bleeding rate in this series (when expressed as annual event rates, 290 patients/year) remained practically unchanged (3.1% vs HAS-BLED-predicted 6.6% (p=0.047)). These findings are wholly consistent with the longer follow-up period of the PROTECT AF study, in which the balance of events in favour of the implant was more noticeable during the second year.[3]

Relevant bleeding events are not usually shown when reporting major bleeding, which is on average 3%–3.6% versus minor relevant bleeding, with an annual rate that can exceed 10%.[1] Lack of information leads to underestimation of the percentage of patients requiring suspension of therapy and the effect this can have. This is very important since real-life studies that include patients who would otherwise be excluded from randomised series have shown that in follow-up of less than 2 years, up to 51.4% of patients had to suspend anticoagulant therapy due to intercurrent conditions (procedures, falls, etc) or haemorrhagic complications (34%),[22 23] incidence of the latter being higher with higher CHADS₂ and HAS-BLED scores. These studies showed that the risk of stroke during suspension periods increased (OR=1.60)[22 23] and in the ROCKET AF study, the risk of thromboembolic events during suspension was more than 6%–8%.[24] Suspension after 2 years is due to bleeding problems and poor compliance. In the PROTECT AF study, for example, 16% did not resume warfarin after 2 years,[3] and the situation is no better with new OACs, as shown by the 21% rate reported in the RELY study in dabigatran.

Furthermore, the fact that studies in LAA occlusion devices usually include patients contraindicated for OACs and that the annual rate of major bleeding in patients not included in randomised studies[25] is closer to 7% than the 3%–3.6% found in these studies is widely ignored. In a review of 994 patients treated with warfarin with some kind of bleeding, less than 70% would have been eligible for a clinical trial, and the risk of bleeding increases dramatically with more exclusion criteria.[26]

Most bleeding observed during follow-up in this series was gastrointestinal. Approximately 58% of bleeding with dabigatran was gastrointestinal, and incidence was higher than with warfarin (p<0.001).[27] Annual incidence of gastrointestinal bleeding is around 4.5% in patients taking OAC.[28] Resumption of warfarin leads to bleeding recurrence at 3 months as high as 10%, and even 5.5% without resumption.[28] The 30-day mortality rate following major bleeding due to OAC is significant, ranging from 9.1% to 13%.[27]

Procedural safety
Safety events have fallen to less than half the rate reported in the PROTECT AF study and Continued Access Protocol register, the European ACP register and postmarket

Table 4 Observed and expected events at 1 year in different studies in LAA occlusion patients contraindicated for OAC

Study name	Number of patients	CHA₂DS₂-VASc	Follow-up (months)	Total stroke/TIA follow-up	Stroke %/year	% Reduction	Death patient/ year	Antithrombotic therapy
Spanish Unicentre (ACP)[14]	35	3.94±1.89	21.14±10.1	2.85% (1/35)	0% versus 5.45%		5.04%	3–6 m DAPT 3 m indefinite ASA
Partial ACP European postmarket	145	3.7±1.7	24	2.12% (1/47)	1.24% versus 5.33%	65%	NA	3 m DAPT 3 m ASA
USA-European ASAP (Watch)[13]	150	4.4±1.7	14.4±8.6	2.6% (4/150)	1.7% vs 7.3%	77%	5%	6 m DAPT
Canadian (ACP)[15]	52	5 (4–6)	20±5	5.7% (3/52)	1.1% vs 8.6%	87%	5.8%	1–3 or 1–6 m
Iberian multicentre (current)	167	4 (3–6)	22±8.3	4.2% (7/167)	2.4% vs 9.6%	75%	5.8%	3–6 m DAPT 6 m indefinite ASA
Average of figures or percentages	549	4.2	20.38	3.54% (16/451)	1.28% vs 7.25%	76%	5.41%	

ACP, Amplatzer Cardiac Plug; ASA, aspirin; DAPT, double antiplatelet therapy; LAA, left atrial appendage; OAC, oral anticoagulant; TIA, transient ischaemic attack.

Table 5 Details of major bleeding over follow-up

	Type of haemorrhage	Reason for implantation	Gender	Age	HAS-BLED	Time since implantation (months)	Treatment
1	Upper gastrointestinal bleeding	Gastrointestinal haemorrhage	F	68	3	3	ASA and clopidogrel
2	Upper gastrointestinal bleeding	Gastrointestinal haemorrhage	F	78	4	24	ASA and clopidogrel
3	Cerebral haematoma	Cerebral haemorrhage	M	73	3	6	ASA
4	Upper gastrointestinal bleeding	Ischaemic CVA	M	73	4	3	ASA
5	Lower gastrointestinal bleeding	Lower gastrointestinal bleeding	M	83	3	6	ASA and clopidogrel
6	Lower gastrointestinal bleeding	Lower gastrointestinal bleeding	M	70	4	12	Nothing
7	Lower gastrointestinal bleeding	Severe anaemia	F	78	4	12	ASA
8	Lower gastrointestinal bleeding	Lower gastrointestinal bleeding	M	84	4	3	ASA and clopidogrel
9	Lower gastrointestinal bleeding	Lower gastrointestinal bleeding	M	65	4	1	ASA and clopidogrel

ASA, aspirin; CVA, cerebrovascular accident; F, female; HAS-BLED, hypertension, abnormal liver/renal function, stroke history, bleeding predisposition, labile international normalised ratios, elderly, drugs/alcohol use; M, male.

surveillance.[29] [30] However, recent studies in populations similar to this series in highly experienced hospitals continue to report rates of between 4% and 8%. The ASAP and the Canadian study reported 8.7% and 5.8%, respectively, although most events were resolved with few sequelae or none at all.[13] [15] A complication rate of around 5.38% is average. Vascular complications in most studies range from 1% to 2.5%. For example, the ASAP study reported 2% vascular problems and 3.8% major bleeding due to haematoma at the puncture site, while other events such as 1.2% perioperative TIA, 1%–2% cardiac tamponade and 0.6% device migration are at the lower end of the rates reported in leading studies. The authors believe that after accidental puncture of the femoral artery the needle should not be withdrawn and compression applied immediately, but rather the introducer should remain in the artery and compression or percutaneous closure performed at the end of the procedure as programmed as otherwise arteriovenous haematomas and/or fistulas can form.

Regarding study limitations, this study recruited 167 patients from 12 hospitals, thereby including patients from hospitals with varying experience in the procedure. Nevertheless, most sites started and included cases under a common monitor, a factor that the authors believe ensures homogeneity. Instead of being randomised, event comparison is score-based; however, the scores used have been thoroughly validated in the literature. Finally, the methodological approach applied during the follow-up period could have been more exhaustive than that used in routine practice and in highly experienced groups.[17]

In conclusion, these findings show that LAA closure with an occlusion device in patients contraindicated for OAC is a reasonably safe therapeutic option associated with fewer thromboembolic and haemorrhagic events than those expected from risk scores, particularly after the first year postimplantation following endothelialisation and withdrawal of antiplatelet therapy.

New studies with longer follow-up periods and early discontinuation of DAPT would be of great interest to verify whether

Figure 1 Kaplan–Meier event-free survival curves over 24-month follow-up.
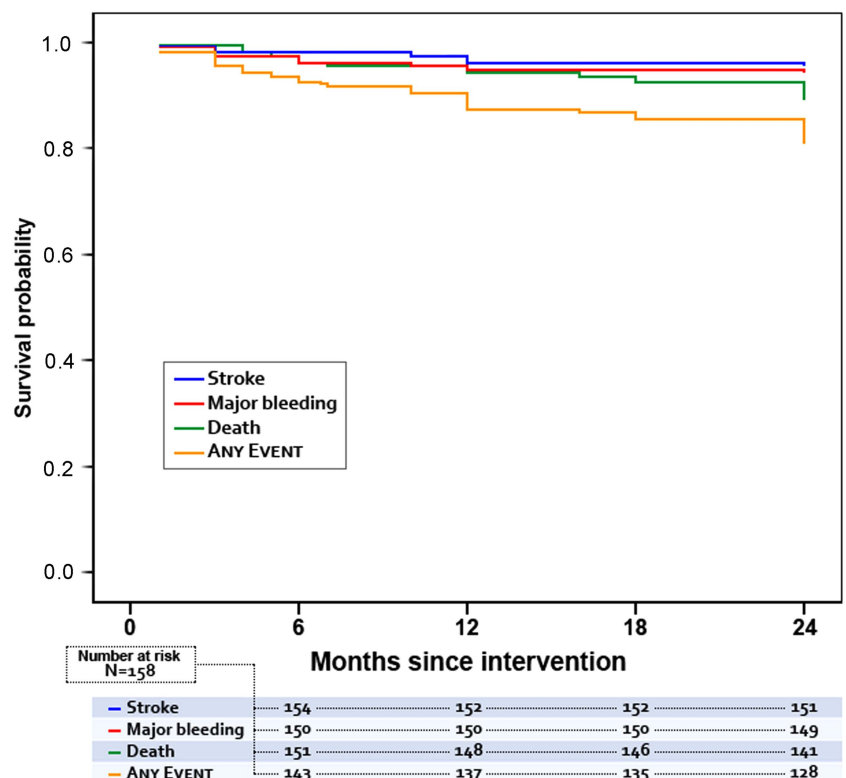
Table 6 Percentage of patients under DAPT and/or at least one antiaggregant treatment at 12 and 24 months of follow-up

	Discharge	1 month	6 months	12 months
Patients	158 (100%)	157 (100%)	151 (100%)	148 (100%)
No APT	1 (0.6%)	1 (0.6%)	1 (0.7%)	5 (3.4%)
Only ASA or clopidogrel	14 (8.9%)	26 (16.6%)	111 (73.5%)	130 (87.8%)
DAPT	138 (87.3%)	128 (81.5%)	33 (21.9%)	7 (4.7%)
OAC	5 (3.2%)	2 (1.3%)	6 (3.9%)	6 (4.1%)

APT, antiplatelet therapy; ASA, aspirin; DAPT, dual antiplatelet therapy; OAC, oral anticoagulation.

bleeding events during the first year are reduced without losing the efficacy of lowering thromboembolic events. This could broaden current indications.

Key messages

What is already known on this subject?
Left atrial appendage closure has been shown not to be inferior to oral anticoagulants (OACs) in the treatment of patients with non-valvular atrial fibrillation, and some studies suggest it could be a good alternative for patients contraindicated for OACs due to high risk of haemorrhage.

What might this study add?
The reduction of events in this population with respect to expected outcomes based on risk scores is significant in the first year for stroke (53% at 12 months and 73% at 24 months) and in the second year for haemorrhage (53%).

How might this impact on clinical practice?
Left atrial appendage closure is shown to be an effective treatment for patients contraindicated for OACs. However, with current antithrombotic therapy similar haemorrhagic complications can occur in the first year, suggesting the need to seek alternative antithrombotic treatment and maximise vigilance for this complication during this period.

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