ORIGINAL ARTICLE

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

José Ramón López Minguez,1 Juan Manuel Nogales Asensio,1 Javier Elduayen Gragera,1 Marco Costa,2 Ignacio Cruz González,3 Federico Gimeno de Carlos,4 José Antonio Fernández Díaz,5 Victoria Martín Yuste,6 Raúl Moreno González,7 Antonio Domínguez-Franco,8 Amparo Benedicto Buendía,9 Jesús Herrero Garibi,10 Felipe Hernández Hernández,11 Vasco Gama Ribeiro12

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 CHADS2 (congestive heart failure, hypertension, age, diabetes, stroke history), CHA2DS2-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 CHADS2 (2.4% vs 9.6%), CHA2DS2-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 CHADS2 (congestive heart failure, hypertension, age, diabetes, stroke history), CHA2DS2-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 proce-
dure, patients were given a wide-spectrum antibiotic (cephalos-
porin), and the procedure was performed under general anaesthetic. Following transseptal puncture, patients were admi-
nistered 100 U/kg heparin. Selective angiography of the LAA
was performed with a volume similar to that of a left coronary
tree, 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 midaxil-
ary line. 2D TOE measurements were taken during the proce-
dure. A preliminary 40°–135° scan with the probe in
mid-oesophageal position was performed to obtain both ostium
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 measure-
ments, 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 admi-
nistered, and treatment was started with 300 mg aspirin (ASA) on
the first day and 100 mg daily thereafter. Clopidogrel was main-
tained for 3–6 months, barring haemorrhagic complications, and
ASA for 6–12 months. If thrombus occurred, subcutaneous enox-
aparin in a therapeutic dose was added for 2 weeks, clopidogrel
was prolonged and the TOE was repeated to check for disappear-
ance. If the result was negative, the decision to prolong the treat-
ment 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 indica-
tive 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 ancho-
rance to the LAA using the tug test.

The main events were death, stroke, serious and relevant haem-
morrhage, and hospitalisation for concomitant conditions, mon-
tored by means of scheduled visits and telephone calls. The
International Society on Thrombosis and Haemostasis defini-
tion was used to define major bleeding: fatal bleeding, and/or symptomatic bleeding in a critical area or organ, such as intracranial,
intraspinal, intracocular, retroperitoneal, intra-articular or peri-
cardial, 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. Minor but relevant
bleeding was defined according to the Academic Research
Consortium guidelines as any bleeding not meeting major cri-
teria but important enough for the patient or the clinician to
merit discontinuation of antithrombotic therapy, albeit tempo-
arily: (1) The patient does not visit the doctor but can suspend
antithrombotic therapy, for example, haematoma, epistaxis, haem-
morrhoidal bleeding, and so on and (2) The patient visits the
doctor and action is needed, for example, suspension of antith-
rombotic 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 χ² 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 begin-
nning 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 CHADS² and HAS-BLED
score, as indicated in the work by Frigeri and colleagues.

Annual risk of bleeding or stroke was based on each patient’s
CHADS² and HAS-BLED score. Observed and expected rates of
thromboembolic and bleeding events were compared using bino-
trial tests. Event-free survival was analysed using the Kaplan–
Meier method. All data were analysed using SPSS V19.0.

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 CHADS²,
CHAD²DS²-VASc and HAS-BLED scores and 25th–75th percent-
ile 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 intraproce-
dure complication rate was 5.38%, with 2.99% being central
and 2.39% vascular due to a punctured artery resulting in arter-
ovenous 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 tran-
sient ischaemic attacks (TIAs) that led 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
subjects, 5.7% major and 4.4% relevant without meeting major
criteria, and 4.4% suffered stroke. Findings from echocardiogra-
phy controls are also shown in Table 2. In all, 13 minimal peri-
implantation events and possible thrombus formation on the
devices in 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,
contrary to the CHADS2 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 reg-
istry and the ASAP with Watchman study) with over 150
patients contraindicated for OACs, and has one of the longest
follow-up periods.12–14

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 group9–9 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
CHADS2-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	hree 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% reduc-
tion with respect to the score-predicted rate (Table 4).2–14

**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 for-
mation 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).3,12–19 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,10 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 indefi-
nite ASA18 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

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

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>74.68±8.58</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥75 years</td>
<td>84 (53.2%)</td>
</tr>
<tr>
<td>≥78 years</td>
<td>63 (39.9%)</td>
</tr>
<tr>
<td>Men</td>
<td>102 (61.1%)</td>
</tr>
<tr>
<td>CHADS2</td>
<td>3 (2–4)</td>
</tr>
<tr>
<td>CHA2DS2-VASC</td>
<td>4 (3–6)</td>
</tr>
<tr>
<td>HAS-BLED</td>
<td>3 (3–4)</td>
</tr>
<tr>
<td>Procedure indication</td>
<td></td>
</tr>
<tr>
<td>Gastointestinal haemorrhage</td>
<td>51 (30.5%)</td>
</tr>
<tr>
<td>Cranial haemorrhage</td>
<td>38 (22.8%)</td>
</tr>
<tr>
<td>Other haemorrhages</td>
<td>28 (16.8%)</td>
</tr>
<tr>
<td>CVA/embolism with OAC</td>
<td>12 (7.2%)</td>
</tr>
<tr>
<td>High risk of bleeding</td>
<td>7 (4.2%)</td>
</tr>
<tr>
<td>Others</td>
<td>32 (19.2%)</td>
</tr>
<tr>
<td>Device size (lobe diameter ranging from 16 to 30)</td>
<td>24 (22–25)</td>
</tr>
<tr>
<td>Need to change device*</td>
<td>6 (3.5%)</td>
</tr>
<tr>
<td>Successful implantation</td>
<td>158 (94.6%)</td>
</tr>
<tr>
<td>Procedural complications</td>
<td>9 (5.38%)</td>
</tr>
<tr>
<td>TIA</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td>Vascular complication</td>
<td>4 (2.39%)</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td>Device migration (percutaneously snared)</td>
<td>1 (0.6%)</td>
</tr>
</tbody>
</table>

Values expressed as: number (percentage), mean±SD or median (25th–75th percentiles).
*Four of the changes were due to a larger size, while the other three to a smaller size.

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

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

ASD, atrial septal defect; 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. 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.

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%. 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%). 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) and in the ROCKET AF study, the risk of thromboembolic events during suspension was more than 6%–8%. 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, 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 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.

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). Annual incidence of gastrointestinal bleeding is around 4.5% in patients taking OAC. Resumption of warfarin leads to bleeding recurrence at 3 months as high as 10%, and even 5.5% without resumption. The 30-day mortality rate following major bleeding due to OAC is significant, ranging from 9.1% to 13%.

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

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

<table>
<thead>
<tr>
<th>Events</th>
<th>12-month (158 patients/year)</th>
<th>Global follow-up (annual event rates, 290 patients/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observed</td>
<td>Expected*</td>
</tr>
<tr>
<td>Death</td>
<td>9 (5.8%)</td>
<td>6.6% HAS-BLED</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>8 (5.2%)</td>
<td>6.6% HAS-BLED</td>
</tr>
<tr>
<td>Total bleeding (major+relevant) Stroke/TIA</td>
<td>15 (9.5%)</td>
<td>9.6% CHADS2</td>
</tr>
</tbody>
</table>

*Expected rates based on Friberg et al 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.

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

<table>
<thead>
<tr>
<th>Study name</th>
<th>Number of patients</th>
<th>CHADS2-VASc</th>
<th>Follow-up (months)</th>
<th>Total stroke/TIA follow-up</th>
<th>Stroke %/year</th>
<th>% Reduction</th>
<th>Death patient/year</th>
<th>Antithrombotic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spanish Unicentre (ACP)</td>
<td>35</td>
<td>3.9±1.89</td>
<td>21.14±10.1</td>
<td>2.85% (1/35)</td>
<td>0% versus 5.45%</td>
<td>5.04%</td>
<td>3–6 m DAPT</td>
<td>3 m indefinite ASA</td>
</tr>
<tr>
<td>Partial ACP European postmarket</td>
<td>145</td>
<td>3.7±1.7</td>
<td>24</td>
<td>2.12% (1/47)</td>
<td>1.24% versus 5.33%</td>
<td>65%</td>
<td>NA</td>
<td>3 m DAPT 3 m ASA</td>
</tr>
<tr>
<td>USA-European ASAP (Watch)</td>
<td>150</td>
<td>4.4±1.7</td>
<td>14.4±3.8</td>
<td>2.6% (4/150)</td>
<td>1.7% vs 7.3%</td>
<td>77%</td>
<td>5%</td>
<td>6 m DAPT</td>
</tr>
<tr>
<td>Canadian (ACP)</td>
<td>52</td>
<td>5 (4–6)</td>
<td>20±5</td>
<td>5.7% (3/52)</td>
<td>1.1% vs 8.6%</td>
<td>87%</td>
<td>5.8%</td>
<td>1–3 or 1–6 m</td>
</tr>
<tr>
<td>Iberian multicentre (current)</td>
<td>167</td>
<td>4 (3–6)</td>
<td>22±8.3</td>
<td>4.2% (7/167)</td>
<td>2.4% vs 9.6%</td>
<td>75%</td>
<td>5.8%</td>
<td>3–6 m DAPT 6 m indefinite ASA</td>
</tr>
<tr>
<td>Average of figures or percentages</td>
<td>549</td>
<td>4.2</td>
<td>20.38</td>
<td>3.54% (16/451)</td>
<td>1.28% vs 7.25%</td>
<td>76%</td>
<td>5.41%</td>
<td></td>
</tr>
</tbody>
</table>

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

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

### Table 5 Details of major bleeding over follow-up

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

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.

Figure 1 Kaplan–Meier event-free survival curves over 24-month follow-up.
bleeding events during the first year are reduced without losing the efficacy of lowering thromboembolic events. This could broaden current indications.

Table 6  Percentage of patients under DAPT and/or at least one antiaggreant treatment at 12 and 24 months of follow-up

<table>
<thead>
<tr>
<th>Patients</th>
<th>1 month</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>158 (100%)</td>
<td>157 (100%)</td>
<td>151 (100%)</td>
<td>148 (100%)</td>
</tr>
<tr>
<td>No APT</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>Only ASA or clopidogrel</td>
<td>14 (8.9%)</td>
<td>26 (16.6%)</td>
<td>111 (73.5%)</td>
</tr>
<tr>
<td>DAPT</td>
<td>138 (87.3%)</td>
<td>128 (81.5%)</td>
<td>33 (21.9%)</td>
</tr>
<tr>
<td>OAC</td>
<td>5 (3.2%)</td>
<td>2 (1.3%)</td>
<td>6 (3.9%)</td>
</tr>
</tbody>
</table>

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

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 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.

Author affiliations
1Hospital Universitario Infanta Cristina, Badajoz, Spain
2Hospital de Coimbra, Coimbra, Portugal
3Hospital Universitario de Salamanca, Salamanca, Spain
4Hospital Clínico Universitario de Valladolid, Valladolid, Spain
5Hospital Puerta de Hierro, Majadahonda, Spain
6Hospital Clínico de Barcelona, Barcelona, Spain
7Hospital Universitario La Paz, Madrid, Spain
8Hospital Virgen de la Victoria, Málaga, Spain
9Hospital de La Princesa, Madrid, Spain
10Hospital de Burgos, Burgos, Spain
11Hospital 12 de Octubre, Madrid, Spain
12Hospital de Oporto, Oporto, Portugal

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Twitter Follow Jesús Herrero-Garibi at @jesusgaribi

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