JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 10, NO. 4, 2017

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2016.11.029

Incidence and Clinical Impact of Device-Associated Thrombus and Peri-Device Leak Following Left Atrial Appendage Closure With the Amplatzer Cardiac Plug

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ABSTRACT

OBJECTIVES Routine device surveillance after successful left atrial appendage closure is recommended to evaluate for intermediate to late complications. The aim of this study was to assess the incidence and clinical impact of these complications on cardiovascular events.

METHODS Centers participating in the Amplatzer Cardiac Plug multicenter study were requested to submit their post-procedural transesophageal echocardiograms for independent adjudication. Thirteen of 22 centers contributed all their post-procedural echocardiograms, which included 344 from 605 consecutive patients. These images were submitted to a core laboratory and reviewed by 2 independent experts for peri-device leak, device-associated thrombus, device embolization, device migration, left atrial appendage thrombus, and left atrial thrombus. Clinical events were prospectively collected by each center.

RESULTS Of the 344 transesophageal echocardiograms, 339 were deemed analyzable. Patients' mean age was 74.4 ± 7.5 years, and 67.3% were men. The mean $CHADS_2$ score was 2.7 ± 1.3, the mean CHA_2DS_2-VASc score was 4.3 ± 1.5, and the mean HAS-BLED score was 3.0 ± 1.2. Amplatzer Cardiac Plug implantation was successful in all patients. Periprocedural major adverse events occurred in 2.4%. Median clinical follow-up duration was 355 days (range 179 to 622 days). Follow-up transesophageal echocardiography was performed after a median of 134 days (range 88 to 227 days). Device-associated thrombus was observed in 3.2% and peri-device leak in 12.5% (5.5% minimal, 5.8% mild, 0.6% moderate, 0.6% severe). Neither device-associated thrombus nor peri-device leak was associated with an increased risk for cardiovascular events. Independent predictors of device-associated thrombus were smoking (odds ratio: 5.79; $p = 0.017$) and female sex (odds ratio: 4.22; $p = 0.027$).

CONCLUSIONS Following successful left atrial appendage closure with the Amplatzer Cardiac Plug, the presence of peri-device leak was relatively low, and device-associated thrombus was infrequent. Neither was associated with increased risk for thromboembolism. (J Am Coll Cardiol Intv 2017;10:391–9) © 2017 by the American College of Cardiology Foundation.

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JACC: CARDIOVASCULAR INTERVENTIONS VOL. 10, NO. 4, 2017
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ABBREVIATIONS AND ACRONYMS

ACP = Amplatzer Cardiac Plug

AF = atrial fibrillation

LAA = left atrial appendage

OAC = oral anticoagulation

TEE = transesophageal echocardiographic

TIA = transient ischemic attack

Left atrial appendage (LAA) closure is increasingly performed as an alternative to oral anticoagulation (OAC) for stroke prevention in patients with atrial fibrillation (AF), especially those with contraindications for OAC. The rationale and mechanism of LAA closure in stroke prevention hinge on the observation from transesophageal echocardiographic (TEE) studies that about 91% of thrombi were located in the LAA in the setting of nonvalvular AF (1). These thrombi were implicated as important sources for cardioembolic strokes with AF, and thus, multinational guidelines endorse OAC for patients at high stroke risk on the basis of risk predictions scores, such as CHA_2DS_2-VASc (2,3). However, despite the widespread availability of novel and direct OAC, 30% to 40% of patients with guideline indications for OAC do not receive anticoagulation, because of contraindications, intolerance, high bleeding risk, or patient refusal (4). Thus, local targeted therapy to exclude or excise the LAA as a potential thromboembolic source has been explored since 1949 (5), with the first minimally invasive endovascular device LAA closure performed in 2001 by Sievert (6).

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Although endovascular LAA closure is an attractive alternative to lifelong OAC, with recent randomized trials establishing safety and efficacy in comparison with warfarin (7,8), there remain important device-associated technical requirements post-implantation to minimize long-term thromboembolic risks. In particular, device-associated thrombus and incomplete closure (i.e., presence of peri-device leak) have been implicated as potential causes of late thromboembolic events after initial technically successful LAA closure. Therefore, routine device surveillance at intermediate follow-up (1 to 6 months post-implantation) is strongly recommended, which provides the opportunity to assess for device-associated thrombus, peri-device leak, device positioning, surrounding structures, and pericardial effusion.

The Amplatzer Cardiac Plug (ACP) (St. Jude Medical, Maple Grove, Minnesota) is 1 of the leading endovascular LAA closure devices available globally in >70 countries. The procedural and clinical outcomes of 1,047 patients who underwent ACP implantation at 22 centers were recently reported (9). We sought to assess the incidence and clinical impact of device-associated thrombus and peri-device leak in the subset of patients in this multicenter experience who underwent TEE follow-up after ACP implantation.

METHODS

The primary results of the ACP multicenter experience were previously reported (9). In brief, this study included 1,047 consecutive patients with nonvalvular AF who underwent LAA closure with the ACP at 22 centers in Europe and Canada from December 2008 to November 2013. Data were prospectively collected from each center, transferred to a dedicated database, and analyzed retrospectively. For this substudy, centers participating in the ACP multicenter study were requested to submit their post-procedural transesophageal echocardiograms for independent adjudication. Thirteen of 22 centers contributed all their post-procedural surveillance echocardiograms, which included a total of 344 from 605 consecutive patients. These echocardiograms were submitted to a core laboratory (Cardialysis BV, Rotterdam, the Netherlands) and were reviewed by a clinical events committee. The clinical events committee was composed of independent experts who were not study investigators and not employed by St. Jude Medical. A quorum of 2 experts reviewed and adjudicated all TEE findings. In case of disagreement, a third clinical events committee member would then review and make final decision.

TEE DEFINITIONS. All transesophageal echocardiograms were reviewed in accordance with prespecified definitions for the presence of peri-device leak, device-associated thrombus, device embolization, device migration, LAA thrombus, and left atrial thrombus.

Peri-device leak. Color-flow Doppler was used to assess for residual flow (leak) around the device into the LAA. Peri-device leak was defined as the presence of a color jet around the device lobe that was detected in at least 2 frames in the same location (frames could be nonsequential). The severity of leak was graded as follows: severe, >5-mm-diameter jet; moderate, 3- to 5-mm-diameter jet; mild, 1- to 3-mm-diameter jet; minimal, <1-mm-diameter jet; and none, no visible leak seen on all available views.

Cruz-Gonzalez, Nietlispach, Aminian, Freixa, and Ibrahim are consultants and proctors for St. Jude Medical. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received October 12, 2016; revised manuscript received November 7, 2016, accepted November 17, 2016.

TABLE 1 Baseline Characteristics (n = 339)

Age (yrs)	74.4 ± 7.5
Male	228 (67.3%)
Height (cm)	170.2 ± 9.0
Weight (kg)	79.4 ± 15.7
BMI (kg/m^2)	27.3 ± 4.6
Diabetes mellitus	98 (28.9%)
Hypertension	290 (85.5%)
Smoking	26 (7.7%)
Dyslipidemia	107 (31.6%)
Prior stroke or TIA	122 (36.0%)
Prior TIA	28 (8.3%)
Prior peripheral embolism	19 (5.6%)
Carotid disease	23 (6.8%)
Coronary artery disease	117 (34.5%)
Prior myocardial infarction	45 (13.3%)
Prior PCI	84 (24.8%)
Prior CABG	28 (8.3%)
Congestive heart failure	87 (25.7%)
Renal failure	82 (24.2%)
Paroxysmal AF	118 (34.8%)
Permanent AF	189 (55.8%)
Persistent AF	32 (9.4%)

Values are mean ± SD or n (%).

AF = atrial fibrillation; BMI = body mass index; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

TABLE 2 Baseline Thromboembolic and Bleeding Risks (n = 339)

$CHADS_2$ score	2.7 ± 1.3
CHA_2DS_2-VASc score	4.3 ± 1.5
0	
1	1 (0.3%)
2	6 (1.8%)
3	30 (8.8%)
4	68 (20.1%)
5	86 (25.4%)
6	83 (24.5%)
7	40 (11.8%)
8	16 (4.7%)
9	7 (2.1%)
Annual risk of thromboembolism (%)	5.3 ± 2.6
HAS-BLED score	3.0 ± 1.2
0	
1	4 (1.2%)
2	36 (10.6%)
3	75 (22.1%)
4	121 (35.7%)
5	68 (20.1%)
6	27 (8.0%)
Annual major bleeding risk (%)	5.0 ± 3.7

Values are mean ± SD or n (%).

Device embolization. The device had moved entirely outside of the LAA.

Device migration. The device had moved proximal to the circumflex artery but still within the LAA, typically with the appearance of a noncompressed lobe, flat disc, no separation between disc and lobe, significant or severe leak, and increased mobility of the device.

Thrombus. On TEE imaging, an ACP-associated thrombus or LAA or left atrial thrombus was defined as a well-circumscribed, uniformly consistent, echo-reflective mass of different texture from the ACP, the LAA, or the left atrial wall. A thrombus was defined as mobile when there was clear motion in at least 3 sequential TEE frames.

Device success. Successful LAA occlusion was defined as the absence of moderate or severe leak and no signs of device embolization or migration.

CLINICAL EVENTS AND FOLLOW-UP. All centers provided clinical details for every reported major adverse event. Periprocedural major adverse events within 7 days post-procedure or before hospital discharge were defined according to the Valve Academic Research Consortium criteria (10) and included death, myocardial infarction, stroke, transient ischemic attack (TIA), systemic embolization, air embolization, device embolization, significant pericardial effusion or cardiac tamponade, and major bleeding. Clinical follow-up through patient visit or phone contact was performed according to individual center or operator protocol. Follow-up adverse events were defined according to the Valve Academic Research Consortium criteria and included death (cardiovascular or noncardiovascular), stroke, TIA, systemic embolism, and major bleeding (10). Antithrombotic therapy recommendation by the device manufacturer after LAA closure was aspirin 80 to 100 mg/day and clopidogrel 75 mg/day for 1 to 3 months, followed by aspirin 80 to 100 mg/day for at least another 3 months. However, the choice and duration of antithrombotic therapy were individualized on the basis of physician preference and recorded at admission and last follow-up visit.

STATISTICAL ANALYSIS. Continuous variables are presented as mean ± SD and categorical variables as frequencies and percentages. Variables with skewed distributions are presented as median (interquartile range). Continuous variables were compared using the independent-samples Student *t* test, and categorical variables were compared using the chi-square or Fisher exact test. Stepwise logistic regression was used to assess for univariate and multivariate clinical predictors for device-associated thrombus, peri-device leak, and major adverse events. A 2-sided p value <0.05 was considered to indicate statistical significance. Statistical analyses were

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TABLE 3 Medical Reasons for Percutaneous Left Atrial Appendage Closure (n = 339)

Previous major bleeding	164 (48.4%)
Intracranial bleeding	62 (18.3%)
Gastrointestinal bleeding	62 (18.3%)
Previous minor bleeding	63 (18.6%)
Gastrointestinal bleeding	33 (9.7%)
Thromboembolism on OAC	37 (10.9%)
Liver disease	33 (9.7%)
Easy bruising	35 (10.3%)
Labile INR	26 (7.7%)
High fall risk	29 (8.6%)
PCI with stents	48 (14.2%)
Drug interactions	17 (5.0%)
High HAS-BLED score	76 (22.4%)
Baseline antithrombotic	
None	19 (5.6%)
Aspirin	217 (64.0%)
Clopidogrel/prasugrel/ticagrelor	59 (17.4%)
Warfarin	87 (25.7%)
Direct OAC	9 (2.7%)
Heparin	62 (18.3%)

Values are n (%).
INR = international normalized ratio; OAC = oral anticoagulation; PCI = percutaneous coronary intervention.

TABLE 4 Procedural Results (n = 339)

Procedural success	339 (100%)
Procedural duration (min)	85.5 ± 42.1
Fluoroscopy time (min)	18.2 ± 12.1
Hospital length of stay (days)	2.8 ± 2.4
Procedural anesthesia	
General anesthesia	105 (31.0%)
Sedation only	52 (15.3%)
Local anesthesia only	156 (46.0%)
Procedural imaging	
TEE	240 (70.8%)
ICE	36 (10.6%)
Fluoroscopy only	63 (18.6%)
Via transseptal puncture	308 (90.9%)
Via PFO	31 (9.1%)
Combined procedures:	71 (20.9%)
LAA + PFO closure	23 (6.8%)
LAA + ASD closure	3 (0.9%)
LAA + AF ablation	6 (1.8%)
LAA + coronary angiography	35 (10.3%)
LAA + PCI	19 (5.6%)
LAA + TAVR	3 (0.9%)
LAA + MitraClip	1 (0.3%)
ACP size (mm)	24.2 ± 3.7
16	13 (3.8%)
18	18 (5.3%)
20	25 (7.4%)
22	79 (23.3%)
24	66 (19.5%)
26	55 (16.2%)
28	42 (12.4%)
30	41 (12.1%)
One device attempted	309 (91.2%)
Two devices attempted	27 (8.0%)
Three devices attempted	2 (0.6%)
Four devices attempted	1 (0.3%)

Values are n (%) or mean ± SD.
ACP = Amplatzer Cardiac Plug; AF = atrial fibrillation; ASD = atrial septal defect; ICE = intracardiac echocardiography; LAA = left atrial appendage; PCI = percutaneous coronary intervention; PFO = patent foramen ovale; TAVR = transcatheter aortic valve replacement; TEE = transesophageal echocardiography.

performed using SPSS version 23 (IBM, Armonk, New York).

RESULTS

Of the 344 follow-up transesophageal echocardiograms that were submitted to the core laboratory for evaluation, 339 were deemed analyzable and constituted the cohort of this substudy. Baseline demographics are described in Table 1. Patients' mean age was 74.4 ± 7.5 years, and 67.3% were men. The mean $CHADS_2$ score was 2.7 ± 1.3, the mean CHA_2DS_2-VASc score was 4.3 ± 1.5, and the mean HAS-BLED score was 3.0 ± 1.2 (Table 2). Paroxysmal AF was present in 34.8% of patients, and the remainder had permanent or persistent AF. The majority had contraindications to OAC (Table 3), including 48.4% with prior major bleeding, 18.6% with prior minor bleeding, and 22.4% with HAS-BLED scores ≥3.

ACP implantation was successful in all cases, with a mean ACP size of 24.2 ± 3.7 mm, and 91.2% of patients required only 1 device attempt (Table 4). Combined procedures were carried out in 20.9% of LAA closure cases, including concomitant coronary angiography, patent foramen ovale or atria septal defect closure, AF ablation, or valvular intervention. The mean length of hospital stay was 2.8 ± 2.4 days. Periprocedural major adverse events occurred in 2.4% of patients, including mortality in 0%, stroke in 0.3%, air embolism in 0.3%, cardiac tamponade in 0.9%, device embolization in 0.3%, and major bleeding in 0.9% (Table 5). Median clinical follow-up duration was 355 days (range 179 to 622 days). Cardiovascular death occurred in 0.6% of patients, noncardiovascular death in 2.1%, stroke in 0.9%, TIA in 1.2%, and major bleeding in 1.2%. Antithrombotic therapy use post-LAA closure was available in 255 patients; of these, 159 were on dual-antiplatelet therapy, 79 were on single-antiplatelet therapy, 16 were on OAC, and 1 was receiving no antithrombotic agent post-LAA closure.

Follow-up TEE imaging was performed after a median of 134 days (range 88 to 227 days) (Table 6). There was concordance in all adjudicated cases for

TABLE 5 Amplatzer Cardiac Plug Procedural and Clinical Events (n = 339)

Major procedural (in-hospital or within 7 days) events	
Death	0 (0%)
Stroke	1 (0.3%)
TIA	0 (0%)
Air embolism	1 (0.3%)
MI	0 (0%)
Cardiac tamponade	3 (0.9%)
Device embolization	1 (0.3%)*
Major bleed	3 (0.9%)
Composite procedural major adverse events	8 (2.4%)
Other procedural events	
Pericardial effusion (no intervention required)	14 (4.1%)
Minor bleeding (hematoma)	10 (2.9%)
Mean long-term follow-up (days) and clinical events	428.9 ± 324.8
CV death	2 (0.6%)
Non-CV death	7 (2.1%)
Stroke	3 (0.9%)
TIA	4 (1.2%)
Major bleeding	4 (1.2%)
Minor bleeding	5 (1.5%)

Values are n (%) or mean ± SD. *Embolized device was successfully snared percutaneously.
CV = cardiovascular; MI = myocardial infarction; TIA = transient ischemic attack.

the presence of device-associated thrombus and the presence and degree of peri-device leak by both reviewers. In these adjudicated cases, device-associated thrombus was observed in 3.2% of patients and peri-device leak in 12.5% (Figure 1). Of the 11 cases of device-associated thrombus, TEE imaging was performed at a mean duration of 165 ± 135 days after LAA closure, and 4 cases were mobile thrombi. Seven were treated with dual-antiplatelet therapy post-LAA closure, 3 with clopidogrel alone post-LAA closure, and 1 with OAC post-LAA closure. None of these 11 cases resulted in stroke or TIA over a mean follow-up period of 322 ± 141 days. Of the leaks, 5.5% were graded as minimal, 5.8% as mild, 0.6% as moderate, and 0.6% as severe. There were 2 late device migrations observed (TEE imaging on days 119 and 189) and 2 late device embolizations (TEE imaging on days 54 and 87).

TABLE 6 Adjudicated Transesophageal Echocardiographic Results (n = 339)

Mean follow-up TEE performed (days)	198.2 ± 181.3
Thrombus on device	11 (3.2%)
Peri-device leak (assessed in 311)	
None	272 (80.2%)
Minor (<1 mm)	17 (5.0%)
Mild (1–3 mm)	18 (5.3%)
Moderate (>3 but ≤5 mm)	2 (0.6%)
Severe (>5 mm or multiple jets)	2 (0.6%)

Values are mean ± SD or n (%).
TEE = transesophageal echocardiography.

Neither device-associated thrombus nor peri-device leak (irrespective of severity) was associated with an increased risk for cardiovascular events (stroke, TIA, cardiovascular death, or overall mortality) (Table 7). In univariate and multivariate logistic regression models, only smoking (odds ratio: 5.79; p = 0.017) and female sex (odds ratio: 4.22; p = 0.027) were independent predictors of device-associated thrombus (Table 8). No independent predictors of peri-device leak or cardiovascular events were identified.

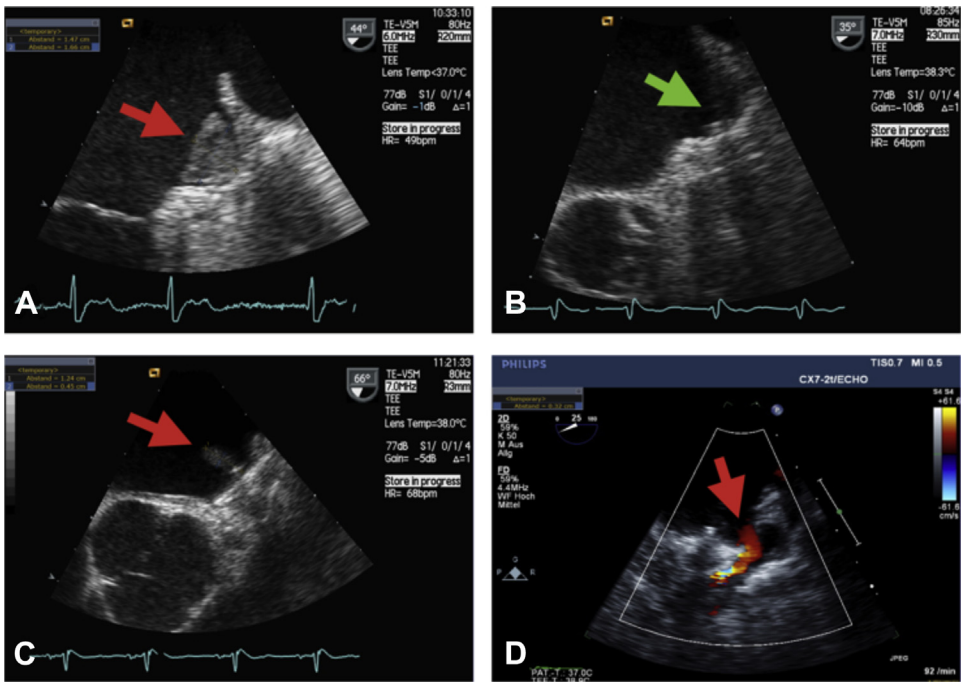
DISCUSSION

In this independently adjudicated TEE substudy of the ACP multicenter experience, we found that the incidence rates of device-associated thrombus and peri-device leak were low, 3.2% and 12.5%, respectively. The presence of neither device-associated thrombus nor peri-device leak was associated with adverse cardiovascular events.

Both device-associated thrombus and peri-device leak are important technical limitations and device-related complications following percutaneous LAA closure. Thrombus on the left atrial side of the device may embolize and cause stroke, TIA, or peripheral embolization. Incomplete LAA closure with peri-device leak results in an open pouch with residual flow into the LAA, which may cause turbulence in blood flow adjacent to the device and stagnant blood in the residual LAA pouch. These may enhance platelet adhesion and thrombus formation at the edge of the device or within the LAA and subsequent embolization of thrombus past the device into systemic circulation.

Device-associated thrombus is thought to occur predominantly on the nonendothelialized portion of the exposed device, especially on protruding structure such as the threaded insert of the WATCHMAN device and the proximal end screw of the ACP. In a pre-clinical study with dogs (n = 9) implanted with WATCHMAN devices, white pannus covered the left atrial surface of the device by 45 days, and the neoendocardial covering was continuous from the left atrial wall to the device, while inside the device and the LAA, there was organizing thrombus and resorbing fibrin (11). In another canine study comparing the WATCHMAN with the ACP (n = 6), there was complete neoendocardial coverage of the WATCHMAN device at 28 days, but the ACP

FIGURE 1 Examples of Device-Associated Thrombus and Peri-Device Leak With Amplatzer Cardiac Plug



(A) Thrombus on the left atrial side of the device **(red arrow)**. **(B)** Thrombus resolved **(green arrow)** following treatment with oral anticoagulation. **(C)** Thrombus on the proximal end screw of the Amplatzer Cardiac Plug **(red arrow)**. **(D)** A 3-mm peri-device leak on color-flow Doppler **(red arrow)**.

had incomplete coverage on the disc surface, especially at the lower edge and end screw (12). Nevertheless, in another larger canine study (n = 10), by 90 days there was complete coverage of the ACP atrial surface by stable mature neointima, with diffuse ingrowth of mature fibrous connective tissue in the device and within the surface neointima (13). These preclinical studies provide some guidance on the duration of antithrombotic therapy prior to complete device endothelialization, but nonetheless, there can be differences in such timing in humans compared with dogs and even among individual humans.

In reported real-world registries with the ACP, varying incidence rates of device-associated thrombus had been reported, ranging from 0% to 16% (14–19). However, these were generally small series involving <50 to 100 patients, and routine device surveillance imaging was not done, so there may have been potential bias of reporting. Even in series in which routine device-surveillance imaging was performed at follow-up, device-associated thrombus incidence could still vary because of differences in implantation technique (e.g., depth of device implantation) and variation in the use of procedural imaging to guide optimal implantation (e.g., lack of procedural imaging to avoid noncoverage of proximal lobes, recesses, and trabeculations that can be the nidus for thrombus formation) (15–19). Therefore, the reported incidence of device-associated thrombus in small series may not accurately reflect the true incidence.

In our series, 13 centers that participated in the ACP multicenter experience contributed all their follow-up TEE images for independent adjudication. With this more rigorous systematic consecutive review of surveillance TEE imaging, we found a 3.2% incidence of device-associated thrombus with the ACP device in a population of predominantly patients with contraindications to OAC who received antiplatelet therapy following LAA closure. Of note, this incidence is slightly lower than the reported 4.4% from the overall 1,047 patient cohort in the ACP multicenter experience, in which not all transesophageal echocardiograms were independently adjudicated (9). This incidence is similar to that reported with the WATCHMAN device in the ASAP (ASA Plavix Feasibility Study With WATCHMAN

Left Atrial Appendage Closure Technology) study, which was reported at 4% for patients with contraindications to OAC treated with dual-antiplatelet therapy post-LAA closure (20). Similarly, the incidence of device-associated thrombus was 4.2% in the PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) study, in which patients eligible for OAC were treated with warfarin for 45 days plus aspirin post-LAA closure (21). In our study, none of the 11 patients with device-associated thrombus had stroke or TIA events, compared with 0.6% to 0.7% in the PROTECT AF and ASAP studies (20,21). In combination, these findings suggest that device-associated thrombus may have low thromboembolic risks, especially if adequately managed with anticoagulation.

Peri-device leak may occur with any percutaneous LAA closure devices, particularly because these devices are circular, whereas LAA ostia are often not round (they may be oval, triangular, footlike, teardrop shaped, etc.) (22). Devices with "single-lobe" designs may have a higher incidence of peri-device leak compared with devices with "lobe and disc" designs, because the latter have 2 layers of barrier between the left atrium and LAA interface. Indeed, the PROTECT AF study showed that WATCHMAN (a single-lobe device) had a 32% incidence of peri-device leak at 12 months (23). In contrast, our study showed a numerically lower peri-device leak incidence of only 12.5% with ACP. The ACP device also has 2 layers of polyester mesh sewn in the lobe and disc, which together with the nitinol compressive seal of the orifice by the lobe and disc may explain the observed lower rate of peri-device leak.

The potential consequences of incomplete seal were exemplified by surgical data in which incomplete closure increased the risk for LAA thrombus and thromboembolic events (24,25). However, incomplete seal with percutaneous devices does not appear to have the same adverse consequences compared with surgical LAA closure. In a post hoc subanalysis of PROTECT AF, the presence of residual peri-device flow into the LAA was not associated with increased risk for thromboembolism (23). Similarly, in our study, the presence of peri-device leak, irrespective of severity, did not increase the risk for thromboembolic events. These findings are reassuring and suggest that leaks <5 mm with percutaneous LAA closure devices are probably safe and do not need further intervention.

The data reviewed here relate to endovascular LAA devices. Epicardial LAA devices, such as the Lariat (SentreHEART, Redwood, California), appear to have different mechanisms of leak and thrombus. In a study that compared the WATCHMAN (n = 219) with the Lariat (n = 259), the prevalence of device-associated thrombus was 3.7% with the WATCHMAN versus 1.6% with the Lariat (p = 0.23). With regard to leak, the WATCHMAN device had a higher incidence of leak (21% vs. 14%, p = 0.019), but more important, the mechanism of leak was different, being peri-device (eccentric) with the WATCHMAN but central (concentric or gunnysack) with the Lariat device (26). The ACP is similar to the WATCHMAN in terms of the mechanism of leak being peri-device.

TABLE 7 Comparison of Clinical Events in Patients With Device-Associated Thrombus or Peri-Device Leak

	Stroke/TIA	Stroke/TIA/CV Death	Stroke/TIA/Death
Device thrombus (n = 11)	0.0%	0.0%	0.0%
No device thrombus (n = 321)	2.1%	2.7%	4.6%
p value	1.00	1.00	1.00
Any leak (n = 39)	2.6%	2.6%	2.6%
No leak (n = 272)	2.2%	2.9%	5.1%
p value	1.00	1.00	0.70
Leak: mild to severe (n = 22)	0.0%	0.0%	0.0%
No leak: mild to severe (n = 289)	2.4%	3.1%	5.2%
p value	1.00	1.00	0.61
Leak: moderate to severe (n = 4)	0.0%	0.0%	0.0%
No leak: mod to severe (n = 307)	2.3%	2.9%	4.9%
p value	1.00	1.00	1.00

Abbreviations as in Table 5.

STUDY LIMITATIONS. Not all centers involved with the ACP multicenter experience provided their follow-up transesophageal echocardiograms to the

TABLE 8 Predictors of Device-Associated Thrombus

	Univariate Model		Multivariate Model	
	Hazard Ratio (95% CI)	p Value	Hazard Ratio (95% CI)	p Value
Age (yrs)	0.98 (0.91–1.06)	0.592		
Female	3.82 (1.10–13.35)	0.036	4.22 (1.18–15.10)	0.027
BMI (kg/m^2)	0.97 (0.84–1.12)	0.686		
Smoking	4.97 (1.24–20.02)	0.024	5.79 (1.37–24.38)	0.017
Hypertension	2.23 (0.59–8.98)	0.231		
Dyslipidemia	0.54 (0.16–1.82)	0.320		
Diabetes	0.48 (0.14–1.59)	0.228		
CHA_2DS_2-VASc score	1.12 (0.76–1.65)	0.573		
$CHADS_2$ score	0.89 (0.55–1.45)	0.644		
HAS-BLED score	0.96 (0.59–1.58)	0.884		
ACP size	0.96 (0.82–1.13)	0.631		

ACP = Amplatzer Cardiac Plug; BMI = body mass index; CI = confidence interval.

core laboratory for independent adjudication. This could have created selection bias for scans that were submitted for adjudication if there were differences in outcomes among centers. We approached all centers to submit their images, but not all centers complied. However, the centers that did participate submitted all follow-up echocardiograms, thus minimizing selection bias on the adjudicated images. Nevertheless, not all patients who underwent ACP implantation at each participating center underwent follow-up TEE imaging, as there were variations in surveillance imaging practices according to centers and physicians. Likewise, there were differences in antithrombotic regimen post-LAA closure according to physician preferences, and not all centers reported the antithrombotic therapy and duration administered. The majority of patients received antiplatelet therapy post-LAA closure, but this may have consisted of dual- or single-antiplatelet therapy, for varying durations. The management of device-associated thrombus, once identified, was also not reported. In addition, TEE visualization of what were deemed thrombus may be due to pannus (general limitation of TEE assessment for thrombus) and may explain the low clinical event rate in this group.

CONCLUSIONS

Following successful LAA closure with the ACP, the presence of peri-device leak was relatively low, and device-associated thrombus was infrequent on adjudicated surveillance TEE imaging. Furthermore, both device-associated thrombus and peri-device leak were not associated with increased risk for thromboembolism. Thus, the clinical impact of these findings appears limited in the setting of routine clinical practice and management.

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PERSPECTIVES

WHAT IS KNOWN? Device-associated thrombus and peri-device leak are recognized potential complications following endovascular LAA closure. However, the incidence and impact of these complications have not been adequately explored with the ACP.

WHAT IS NEW? Our study showed that following ACP implantation, device-associated thrombus was infrequent and peri-device leak was relatively low, and neither was associated with increased risk for thromboembolism.

WHAT IS NEXT? Comparative studies with other LAA closure devices should be performed to assess differences in these events and outcomes.

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KEY WORDS **Amplatzer Cardiac Plug (ACP), device-associated thrombus, left atrial appendage (LAA), peri-device leak**