Late Clinical Outcomes of LAmbre versus Amplatzer Occluders for Left Atrial Appendage Closure

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ORIGINAL ARTICLE

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Late clinical outcomes of lambre versus amplatzer occluders for left atrial appendage closure

Steffen Schnupp MD[1] | Xiao-Xia Liu MD[2,3] | Eric Buffle MD[4] | Steffen Gloekler MD[4,5] | Yamen Mohrez MD[1] | Mohammad Cheikh-Ibrahim MD[1] | Wasim Allakkis MD[1] | Johannes Brachmann MD[1] | Jai-Wun Park MD[6] | Caroline Kleinecke MD[7]

[1]Department of Cardiology, Klinikum Coburg, Coburg, Germany

[2]Department of Cardiology, The 4th Hospital of Harbin Medical University, Harbin, China

[3]Department of Cardiology, Anzhen Hospital, Capital Medical University, Beijing, China

[4]Department of Cardiology, University Hospital of Bern, Bern, Switzerland

[5]Department of Cardiology, Schwarzwald-Baar Klinikum, Villingen-Schwenningen, Germany

[6]Department of Cardiology, Charité Berlin-University Medicine, Campus Benjamin Franklin, Berlin, Germany

[7]Department of Cardiology, Klinikum Lichtenfels, Lichtenfels, Germany

Correspondence
Caroline Kleinecke, MD, Department of Cardiology, Klinikum Lichtenfels Professor Arneth-Straße 2b, 96215 Lichtenfels, Germany.
Email: carolinekleinecke@web.de

Disclosures: None.

Abstract

Introduction: The LAmbre (LifeTech Scientific, Shenzhen, China) is a novel occluder for left atrial appendage closure (LAAC) in patients with atrial fibrillation. This study compares late clinical outcomes of LAmbre and the established Amplatzer devices (Abbott, St Paul, MN).

Methods: Between 2012 and 2018, 265 consecutive patients underwent LAAC with LAmbre and Amplatzer devices at a single center. After a 3:1 propensity score matching, 40 (LAmbre) vs 107 (Amplatzer) patients were compared by the primary efficacy endpoint of all-cause stroke, systemic embolism and cardiovascular/unexplained death, the primary safety endpoint of major periprocedural complications and major bleeding events at follow-up, and the combined hazard endpoint, a composite of all the above-mentioned hazards.

Results: The mean age 75.6 ± 8.9 (LAmbre) vs 75.5 ± 9.0 (Amplatzer) years, CHA_2DS_2-VASc score 4.8 ± 1.7 vs 4.8 ± 1.7 and HAS-BLED score 3.1 ± 0.9 vs 3.2 ± 0.8 were similar. After 3.6 ± 1.9 vs 2.5 ± 1.4 years, the clinical efficacy (12/146, 8.2% [LAmbre] vs 28/266, 10.5% [Amplatzer]; hazard ratio [HR], 0.73; 95% confidence interval [CI], 0.38-1.40; $P = .34$) and safety (5/146, 3.4% vs 14/266, 5.3%; HR, 0.47; 95% CI, 0.14-1.6; $P = .22$), as well as the combined hazard endpoint (15/146, 10.3% vs 36/266, 13.6%; HR, 0.67; 95% CI, 0.36-1.25; $P = .21$) were comparable.

Conclusion: In the presented report, in patients with nonvalvular atrial fibrillation, the LAmbre offered similar long-term efficacy and safety in comparison to Amplatzer devices.

KEYWORDS

Amplatzer, atrial fibrillation, LAmbre, left atrial appendage closure, stroke prevention

Abbreviations: ACP, Amplatzer cardiac plug; AF, nonvalvular atrial fibrillation; BARC, Bleeding Academic Research Consortium; CABG, coronary artery bypass grafting; CE, Conformité Européenne; CI, confidence interval; DRT, device-related thrombus; HR, hazard ratio; LAA, left atrial appendage; LAAC, left atrial appendage closure; OAC, oral anticoagulation; PCI, percutaneous coronary intervention; TEE, transesophageal echocardiography; TIA, transient ischemic attack; VKA, vitamin K antagonist.

Steffen Schnupp and Xiao-Xia Liu contributed equally to this work.

1 | INTRODUCTION

Left atrial appendage closure (LAAC) serves for prevention of stroke in patients with non-valvular atrial fibrillation and contraindications to oral anticoagulation (OAC) or a history of bleeding.[1,2] The most commonly used LAAC devices are the Watchman (Boston Scientific, Marlborough, MA) and the Amplatzer occluders (Abbott, St Paul, MN), with the first- and second-generation Amplatzer cardiac plug (ACP) and Amulet. Randomized trials for the Watchman[3–5] and large, all-comer registries for the Amplatzer[6–8] devices proving their clinical effectiveness in prevention of ischemic and bleeding events, as well as cardiovascular mortality. The LAmbre (LifeTech Scientific, Shenzhen, China) occluder received the CE mark in June 2016. Compared with its competitors, it comes in a wide range of sizes and a steerable sheath to meet the various left atrial appendage (LAA) anatomies.[9,10] Similar to the Amplatzer devices, the LAmbre occluder features a two-part plug-and-disc design: a distal umbrella anchors with hooks in the landing zone of the LAA, and the proximal disc seals the LAA orifice.[10] The sealing effect of the LAmbre is mainly attributable to the disc, in contrast to the Amplatzer devices, which seal the LAA mostly by the lobe and additionally by the disc ("pacifier principle").[11]

Small registry studies showed high implant success rates and acceptable periprocedural complication rates, as well as favorable short-term clinical outcomes of the LAmbre device.[12–16] Another head-to-head comparison demonstrated comparable peri-procedural and clinical outcomes for up to 6 months for LAmbre, Amulet, and Watchman.[17] Currently, a 3-year global post-market surveillance study investigates the performance of the LAmbre device in 500 participants. However, the late clinical outcomes of the LAmbre occluder have not been published yet. (Figures 1 and 2).

Due to the similar design of LAmbre and Amplatzer occluders, we compared long-term clinical efficacy, safety, and net clinical benefit of both devices based on the results of a real-world registry.

2 | METHODS

2.1 | Study cohort

All consecutive patients, who underwent LAAC with LAmbre and Amplatzer devices at the department of cardiology, Klinikum Coburg, Germany were prospectively enrolled in an observational registry

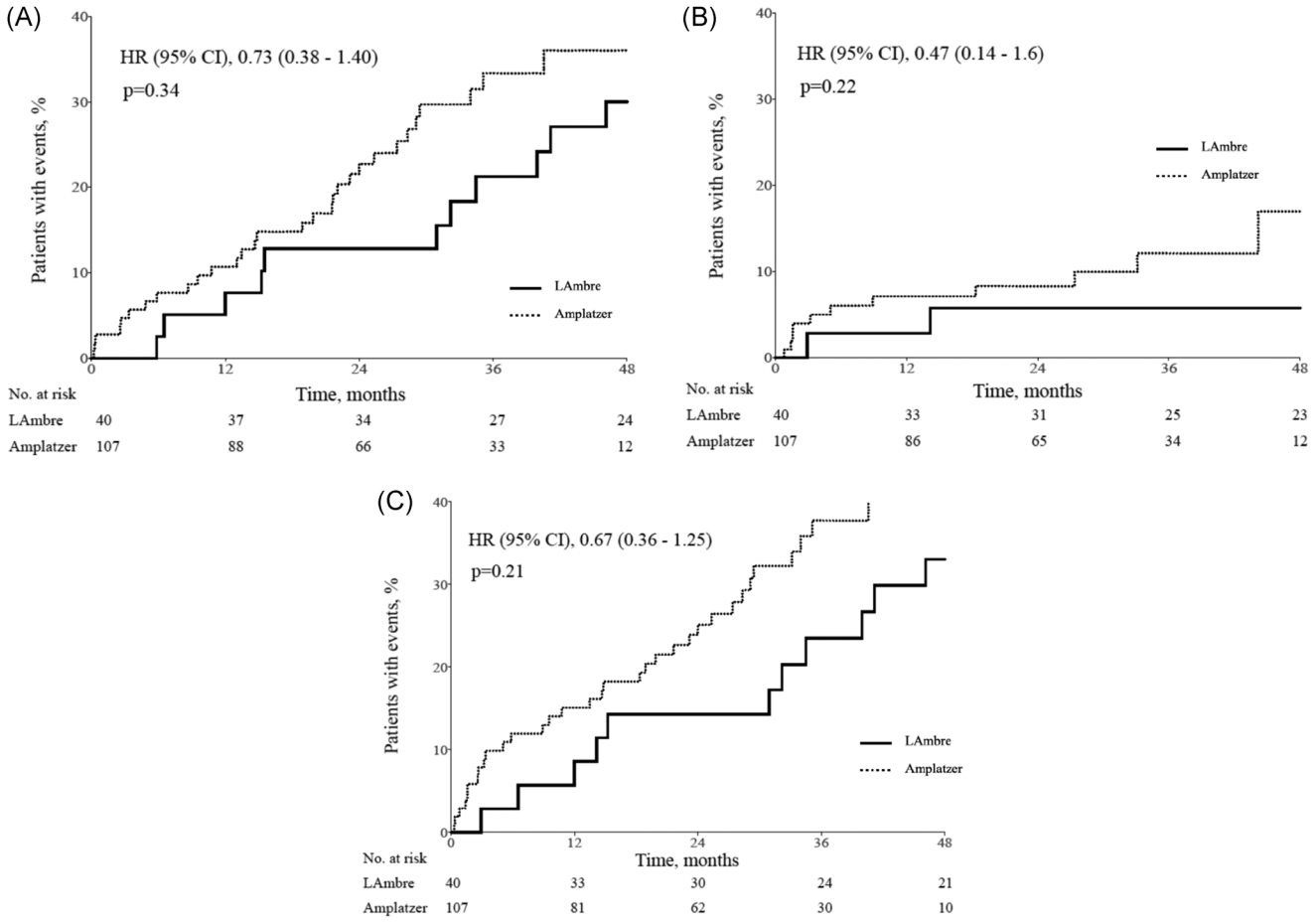

FIGURE 1 Kaplan-Meier curves of the co-primary endpoints of (A) efficacy, (B) safety, and (C) combined hazard endpoint (net clinical benefit) at 48 months

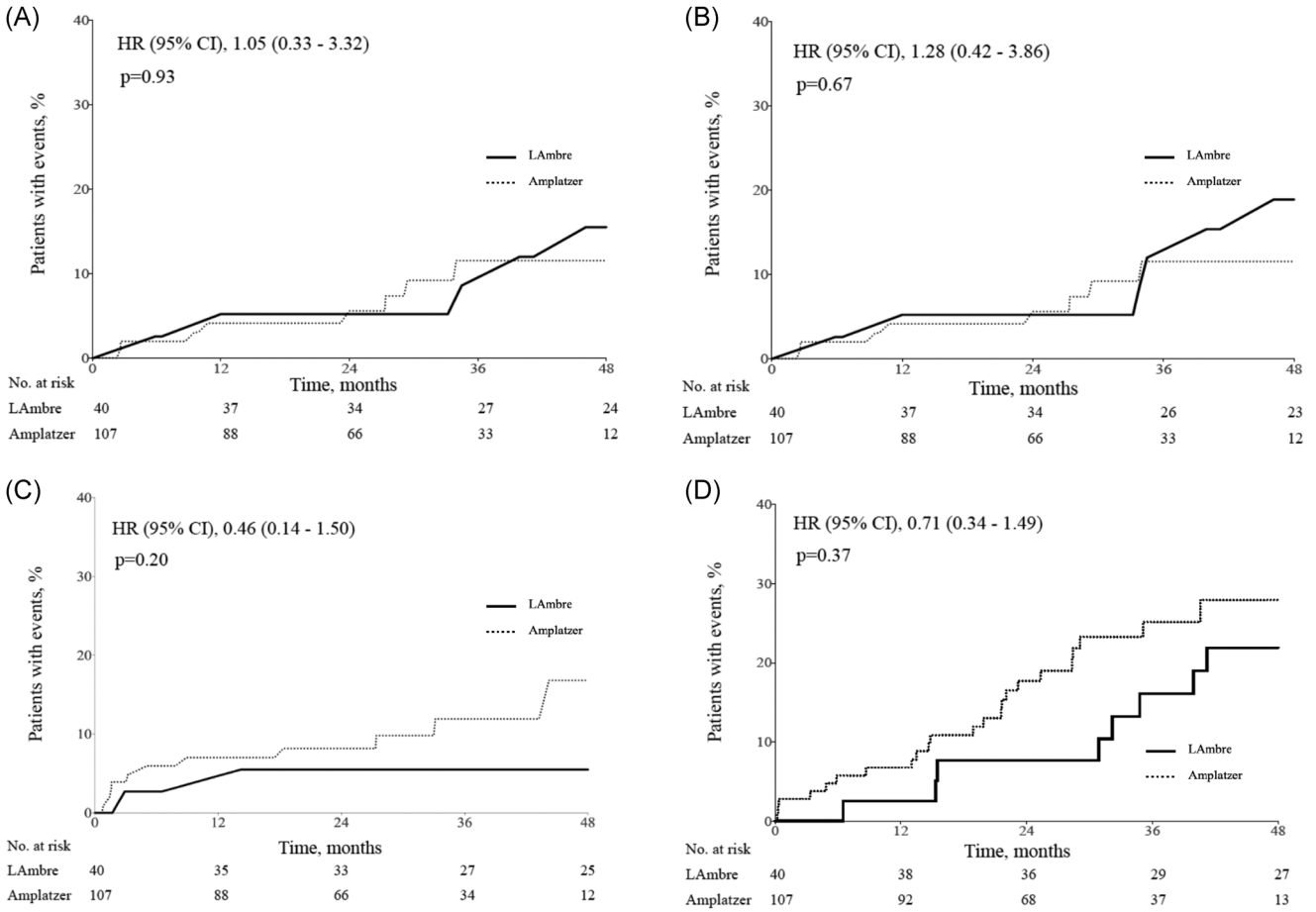

FIGURE 2 Kaplan-Meier curves of (A) all-cause stroke, (B) all-cause stroke and transient ischemic attack, (C) major bleedings, and (D) cardiovascular/unexplained death at 48 month

since 2012. Indications for LAAC were based on current guidelines and expert recommendations.[1,18] Inclusion criteria comprised patients ≥18 years with nonvalvuar atrial fibrillation with a high risk for cardioembolic events (CHA_2DS_2-VASc Score ≥2) and relative or absolute contraindications to OAC. Exclusion criteria were ongoing infection or endocarditis, pregnancy, and reasons for OAC other than atrial fibrillation (AF). Between May and August 2018, clinical follow-up was carried out by patient visits or phone contact and hospital stays. No patient was lost to follow-up. Clinical safety and efficacy events were adjudicated by a clinical event committee of two independent cardiologists and in case of disagreement by a third referee. All analyses were performed according to the intention-to-treat principle. The study complies with the Declaration of Helsinki. It was approved by the local ethical committees, and all patients provided written informed consent before enrollment.

2.2 | LAAC procedure and transesophageal echocardiography follow-up

Device characteristics and procedural aspects were previously described in detail.[10,19] The choice of type and size of the device for LAAC was left to the discretion of the implanting physician. All LAmbre devices were implanted by one highly-experienced operator in LAAC (>500 procedures). In contrast, Amplatzer occluders were implanted by six different operators on different training levels. Most procedures were performed under local anesthesia and in conscious sedation only. Exchange of the transseptal to the delivery sheath was performed for both Amplatzer and LAmbre devices preferably over a stiff guidewire, which was positioned into the left upper pulmonary vein. Occasionally, this maneuver was conducted in the LAA. Transseptal puncture and deployment of the device were guided by transesophageal echocardiography (TEE) and fluoroscopy. The post-procedural antithrombotic therapy consisted of dual antiplatelet therapy with aspirin and clopidogrel for 3 months, followed by aspirin alone. After LAAC with Amplatzer devices, a single TEE was performed after 6 weeks to 3 months to document sufficient LAA closure without device-related thrombus (DRT) or major peri-device leaks (≥5 mm). As LAmbre was a novel device with limited clinical and device-specific experience, a fixed TEE follow-up schedule was performed after 1, 6, and 12 months.

2.3 | Definitions and endpoints

Demographic, clinical, and procedural characteristics, as well as adverse events and endpoints were reported according to the current recommendations of the European Heart Rhythm Association and the European Association of Percutaneous Cardiovascular Interventions,[18] the Bleeding Academic Research Consortium (BARC),[20] the Valve Academic Research Consortium criteria,[21] and the Cardiovascular and Stroke Endpoint Definitions for Clinical Trials.[22] Device success was defined as correct deployment and implantation of the respective LAA occluder. Major periprocedural complications included death (<72 hours after the index procedure), stroke, device embolization, cardiac tamponade or pericardial effusion requiring intervention, major bleeding (>BARC type 3a), need for bailout surgery, need for cardio-pulmonary resuscitation, severe kidney injury, and other relevant complications leading to prolonged hospital stay. The three predefined endpoints were adopted from the PROTECT-AF study[3]: The primary efficacy endpoint was a composite of all-cause stroke, systemic embolism, and cardiovascular/unexplained death. The primary safety endpoint consisted of major periprocedural complications and major bleeding events at follow-up. The combined hazard endpoint (ie, the net clinical benefit) was a composite of all the above-mentioned hazards.

2.4 | Statistical analysis

Statistical analyses were performed with the GraphPad Prism 8 software (GraphPad Inc. La Jolla, CA). Categorical variables are presented as actual numbers and percentages and compared using Fisher's exact test. Continuous variables are summarized as mean ± SD and compared using the Mann-Whitney *U* test. The Kaplan-Meier method was used for graphical assessment of time-dependent events. For comparison of event curves, the logrank (Mantel-Cox) test was used. For the determination of hazard ratio, the Mantel-Haenszel method was applied. Findings were considered statistically significant at the 0.05 level. A propensity score matching was performed using the R software.[23] Among 20 models randomly generated for every combination of caliper values of 0, 1, 0.5, 0.05, and 0.01 and ratios 1:1, 2:1, and 3:1, the best combination was found with a caliper value of 0.5, ratio of 3:1. There was no significant difference in the covariables among the two groups using a univariate logistic regression or unpaired *t* test.

3 | RESULTS

3.1 | Patients characteristics

Between September 2012 and April 2017, 42 and 223 consecutive patients underwent LAAC with LAmbre (from November 2013 to July 2014) and Amplatzer (from September 2012 to April 2017) devices. After the 3:1 propensity score matching, this analysis included 40 LAmbre and 107 Amplatzer patients. It comprised a total of 412 patient-years with a mean follow-up of 3.6 ± 1.9 (LAmbre) vs 2.5 ± 1.4 (Amplatzer) ($P \leq .0001$). Baseline characteristics are shown in Table 1. All relevant baseline characteristics were well comparable both groups, especially age (75.6 ± 8.9 [LAmbre] vs 75.5 ± 9.0 [Amplatzer]; $P = .97$) stroke and bleeding risk (CHA_2DS_2-VASc score 4.8 ± 1.7 vs 4.8 ± 1.7; $P = .96$; HAS-BLED score 3.1 ± 0.9 vs 3.2 ± 0.8; $P = .69$).

3.2 | Procedural characteristics and TEE follow-up

Procedural aspects and TEE follow-up are depicted in Table 2. In the Amplatzer group, 42 (39.3%) patients received the Amplatzer cardiac plug and 65 (60.7%) patients the Amulet device. Device success was high and similar for both occluders (100.0% [LAmbre] vs 99.1% [Amplatzer]; $P = .82$). However, complete sealing of the LAA ostium by the disc could be achieved more often in the Amplatzer group (80% vs 97.2%; $P = .0014$). The rate of major periprocedural

TABLE 1 Baseline characteristics

	LAmbre n = 40	Amplatzer n = 107	*P* value
Age at time of LAAC, y	75.6 ± 8.9	75.5 ± 9.0	.97
Body mass index, kg/m²	28.3 ± 5.1	28.4 ± 5.2	.95
Female sex	16 (40.0%)	45 (42.1%)	.85
Arterial hypertension	32 (80.0%)	89 (83.2%)	.64
Diabetes mellitus	14 (35.0%)	43 (40.2%)	.70
Coronary artery disease	27 (67.5%)	70 (65.4%)	.85
Prior PCI/CAGB	25 (62.5%)	65 (60.7%)	1.0
Left ventricular ejection fraction (EF%)	57.9 ± 9.1	57.2 ± 10.5	.70
Congestive heart failure	16 (40.0%)	44 (41.1%)	1.0
Serum creatinine level, mg/dl	1.2 ± 0.5	1.2 ± 0.5	.87
Prior all-cause stroke	14 (35.0%)	33 (30.8%)	.69
Prior major bleeding	26 (65.0%)	66 (61.7%)	.85
CHA_2DS_2-VASc score	4.8 ± 1.7	4.8 ± 1.7	.96
HAS-BLED score	3.1 ± 0.9	3.2 ± 0.8	.69
Anti-thrombotic medical therapy before LAAC			
Any oral anticoagulation	37 (92.5%)	100 (93.5%)	1.0
Vitamin K antagonist	33 (82.5%)	78 (72.9%)	.28
Non-vitamin K antagonist	6 (15.0%)	25 (23.4%)	.36
Aspirin	3 (7.5%)	10 (9.3%)	1.0
Platelet inhibitor other than aspirin	2 (5.0%)	10 (9.3%)	.51

Note: Categorical variables are expressed as frequencies (n) and percentages (%). Continuous data are reported as mean and standard deviation.

Abbreviations: CABG, coronary artery bypass grafting; LAAC, left atrial appendage closure; PCI, percutaneous coronary intervention.

complications was numerically higher in the LAmbre group but did not differ significantly (7.5% vs 2.8%; $P = .35$). In the LAmbre group, in an 85-year old patient, the stiff 00.35″ guidewire perforated the LAA apex during exchange of the transseptal for the delivery sheath, which at this moment was still located on the right side. The already prepared LAmbre occluder was then successfully implanted. However, surgical repair was needed due to continuous bleeding from the perforation site. After a cardio-pulmonary resuscitation and surgical repair, the circulation could be stabilized, but the patient died 3 days after the procedure due to multiorgan failure. In both groups, no device embolization or peri-procedural stroke occurred. Due to the lack of a controlled design, patient frailty, and logistic reasons, the TEE follow-up rate was not complete (90% for the LAmbre and 67% for the Amplatzer group; $P = .006$). A numerically higher rate of DRT was observed in the LAmbre group (8.1% [LAmbre] vs 1.2% [Amplatzer]; $P = .06$), although statistical significance was not reached. In all three cases with DRT on LAmbre devices, final angiography at the end of the intervention revealed a small peri-device leak <5 mm at the ridge to the left pulmonary veins. Furthermore, in one of those cases, the device was implanted deep into the ostium. In contrast, in the Amplatzer group, DRT occurred on a device, which completely sealed the ostium of the LAA. In the Amplatzer group, one DRT was detected at a 3-month TEE follow-up. It had resolved after 4 weeks under treatment with a vitamin K antagonist (VKA). In the LAmbre group, one DRT was detected after 4 weeks and persisted in further TEE exams. Antithrombotic therapy was not changed to OAC, as it was considered small and nonrelevant. At 5-years of follow-up, the patient had suffered no ischemic event. One DRT (Figure 3B) was detected at a 6-month TEE follow-up. The patient was switched to a lifelong therapy with a VKA as the thrombus did not resolve in further TEE exams. One patient was recovered for a non-disabling ischemic stroke 6 months after LAAC

TABLE 2 Procedural characteristics and TEE follow-up

	LAmbre n = 40	Amplatzer n = 107	*P* value
Amplatzer cardiac plug		42 (39.3%)	
Amulet		65 (60.7%)	
Anesthesia			
Conscious sedation	40 (100.0%)	106 (99.1%)	1.0
General	0 (0.0%)	1 (0.9%)	1.0
TEE guidance	40 (100.0%)	107 (100.0%)	1.0
Fluoroscopy time ± SD, min	12.8 ± 4.9	15.5 ± 9.8	.11
Total contrast volume, ml	102.1 ± 46.8	120.7 ± 70.3	.12
Device success	40 (100.0%)	106 (99.1%)	1.0
Complete occlusion of ostium by disc	32/40 (80%)	104/107 (97.2%)	.0014
Major periprocedural complication	3 (7.5%)	3 (2.8%)	.35
Death	1 (2.5%)	0 (0.0%)	.27
Stroke	0 (0.0%)	0 (0.0%)	1.0
Pericardial tamponade	2 (5.0%)	1 (0.9%)	.18
Major bleeding	2 (5.0%)	2 (1.9%)	.30
Major access vessel complication	1 (2.5%)	0 (0.0%)	.27
Need for bailout surgery	0 (0.0%)	0 (0.0%)	1.0
Device embolization	0 (0.0%)	0 (0.0%)	1.0
Severe kidney injury	0 (0.0%)	1 (0.9%)	1.0
Need for cardio-pulmonary resuscitation	1 (2.5%)	0 (0.0%)	.27
Anti-thrombotic medical therapy post LAAC			
Any oral anticoagulation	0 (0.0%)	0 (0.0%)	1.0
Aspirin	39 (97.5%)	102 (95.3%)	1.0
Platelet inhibitors other than aspirin	39 (97.5%)	106 (99.1%)	.47
TEE follow-up			
TEE performed	36 (90.0%)	72 (67.3%)	.006
Thrombus on device	3 (8.1%)	1 (1.2%)	.06
Peri-device leak (≥5 mm)	1 (2.8%)	1 (1.4%)	.47

Note: Categorical variables are expressed as frequencies (n) and percentages (%). Continuous data is reported as mean and standard deviation.
Abbreviations: LAAC, left atrial appendage closure; TEE, transesophageal echocardiography.

with the LAmbre. TEE revealed DRT (Figure 3A), and the patient was treated with lifelong OAC, as the thrombus persisted in further TEE exams. The rate of major peri-device leaks (2.8% vs 1.4%; $P = .47$) was similar between the groups. Major peri-device leaks were not associated with thromboembolic events in the long-term.

3.3 | Clinical outcomes

Clinical outcomes are listed in Table 3. In 15 patients (37.5%) with the LAmbre occluder, an efficacy or safety event was documented. Four patients suffered two or more events. In the Amplatzer group, an event occurred in 36 (33.6%) patients. More than one event was documented in seven patients. All events are reported per 100 patient-years. Kaplan-Meier curves of the primary endpoints are shown in Figure 1. The primary efficacy endpoint and its components were similar for both groups. There were 12 primary efficacy events among the 40 patients with a LAmbre occluder over 146 patient-years, that is, 8.2% per 100 patient-years versus 28 events among the 107 patients with Amplatzer devices over 266 patient-years, that is, 10.5% per 100 patient-years (hazard ratio [HR], 0.73; 95% confidence interval [CI], 0.38-1.40; $P = .34$). All-cause stroke and systemic embolism occurred in 5/146, 3.4% [LAmbre] vs 10/266, 3.8% [Amplatzer], (HR, 1.05; 95% CI, 0.33-3.32; $P = .93$). Cardiovascular and unexplained deaths were documented in 9/146, 6.2% in the LAmbre group vs 23/266, 8.7% in the Amplatzer group (HR, 0.71; 95% CI, 0.34-1.49; $P = .37$). Also, the primary safety endpoint did not differ significantly between the groups. Safety events occurred in 5 of 40 patients with LAmbre during 146 patients-years, that is, 3.4% per 100 patient-years versus in 14 of the 107 patients with Amplatzer devices during 266 patient-years, that is, 5.3% per 100 patient-years (HR, 0.47; 95% CI, 0.14-1.6; $P = .22$). The rate of major bleeding events was numerically higher in the LAmbre group, although statistical significance was not reached (2/146, 1.4% vs 11/266, 4.1%; HR, 0.46; 95% CI, 0.14-1.50; $P = .20$). Considering all the above-mentioned components of the primary efficacy and safety endpoint, the combined hazard endpoint, that is, the net clinical patient benefit was comparable for both groups (15/146, 10.3% vs 36/266, 13.6%; HR, 0.67; 95% CI, 0.36-1.25; $P = .21$).

4 | DISCUSSION

In this direct comparison, with the limitation of the relatively low numerosity, LAAC with the LAmbre system showed similar long-term efficacy, safety, and net clinical benefit compared with the established Amplatzer devices.

Device success was high for both occluders and similar to other all-comers studies for the LAmbre (99.3%,[12] 100%)[14–16] and Amplatzer devices (ACP: 97.3%,[6] Amulet: 99%).[24] The rate of major periprocedural complications was numerically higher in the LAmbre group, although all LAmbre procedures were performed by a highly skilled operator and even though implantation of LAmbre devices started later in the recruitment phase of the center. In contrast, Amplatzer occluders were implanted by six different operators on different training levels. This observation is less a learning effect, it may be more a chance finding due to the low sample size of the LAmbre group. Other series with the LAmbre reported lower complication rates of 3.3%,[12] 5.9%[16] and 0%.[14,15] Periprocedural adverse events in the LAmbre group comprised two pericardial tamponades and one access vessel complication with the need of surgery. Those complications were not caused by the device itself but related to the procedure. One pericardial tamponade resulted from an LAA perforation with the stiff 00.35″ guidewire, which was placed into the LAA for exchange of the transseptal and delivery sheath. After this incident, this maneuver was abandoned at our center, and exchange of the sheaths is performed preferably via a guidewire in the left upper pulmonary vein. To obviate access site complications, an ultrasound-guided puncture of the common femoral vein is recommended.

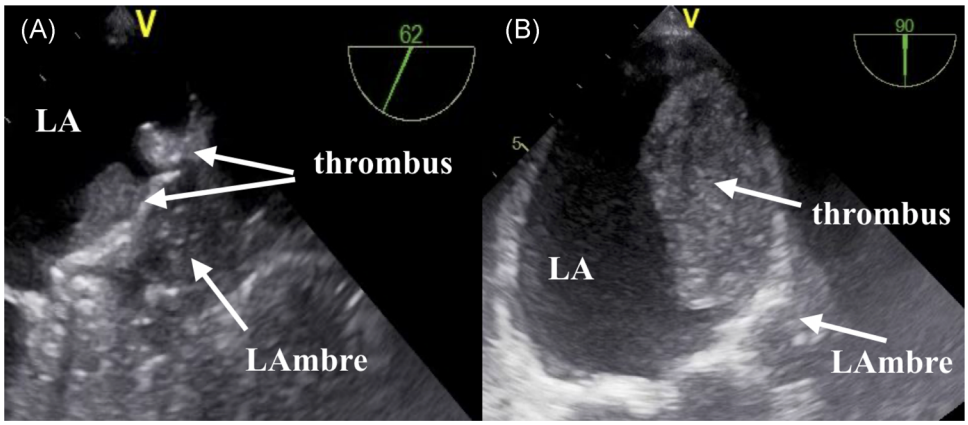

FIGURE 3 Follow-up images of device-related-thrombi: (A) transesophageal echocardiography after 6-mo revealed a sessile thrombus on a 26/32 mm LAmbre; (B) during 6 months follow-up a large thrombus was detected on a 16/30 mm LAmbre. LA, left atrial

TABLE 3 Long-term clinical outcome

	LAmbre n = 40		Amplatzer n = 107		*P* value
	146 Patient-y		266 Patient-y		
Age at follow-up, y, mean ± SD	79.6 ± 8.5		78.5 ± 8.8		.47
Follow-up in y, mean ± SD	3.6 ± 1.9		2.5 ± 1.4		<.0001
	Events/patient-y	**Observed rate**	**Events/patient-y**	**Observed rate**	***P* value**
Primary efficacy endpoint	12/146	8.2 (4.8-13.8)	28/266	10.5 (7.4-14.8)	.34
Primary safety endpoint	5/146	3.4 (1.5-7.8)	14/266	5.3 (3.2-8.6)	.22
Combined hazard endpoint (net clinical benefit)	15/146	10.3 (6.3-1.3)	36/266	13.6 (9.9-18.2)	.21
All-cause death	12/146	8.2 (4.8-13.8)	32/266	12.0 (8.7-16.5)	.23
Cardiovascular/unexplained death	9/146	6.2 (3.3-11.3)	23/266	8.7 (8.7-16.5)	.37
Stroke and TIA (any)	6/146	4.1 (1.9-8.7)	10/266	3.8 (2.1-6.8)	.67
Stroke without TIA (any)	5/146	3.4 (1.5-7.8)	10/266	3.8 (2.1-6.8)	.93
Disabling stroke	4/146	2.8 (1.1-6.8)	4/266	1.5 (0.6-3.8)	.21
Non-disabling stroke	1/146	0.7 (0.1-3.8)	6/266	2.3 (1.0-4.8)	.67
Ischemic stroke	4/146	2.7 (1.1-6.8)	9/266	3.4 (1.8-6.3)	.76
Hemorrhagic stroke	1/146	2.8 (1.1-6.8)	1/266	0.4 (0.1-2.1)	.47
TIA	1/146	0.7 (0.1-3.8)	0/266	0.0 (0.0-1.4)	.27
Systemic embolism	0/146	0.0 (0.0-2.6)	0/266	0.0 (0.0-1.4)	1.0
Any bleeding	5/146	3.4 (1.5-7.8)	21/266	7.9 (5.2-11.8)	.14
Major bleeding	2/146	1.4 (0.4-4.9)	11/266	4.1 (2.3-7.3)	.20
Anti-thrombotic medical therapy at follow-up					
Any oral anticoagulation	6 (15.0%)		10 (9.3%)		.37
Vitamin K antagonists	1 (2.5%)		3 (2.8%)		1.0
Non-vitamin K antagonists	5 (12.5%)		8 (7.5%)		.34
Aspirin	29 (72.5%)		77 (72.0%)		1.0
Platelet inhibitors other than aspirin	4 (10.0%)		12 (11.2%)		1.0

Note: Categorical variables are expressed as frequencies (n) and percentages (%). Continuous data are reported as mean and standard deviation.
Abbreviation: TIA, transient ischemic attack.

With regard to TEE follow-up, the rate of major peri-device leaks was low and comparable for the LAmbre and Amplatzer group. Major peri-device leaks were not associated with DRT or thromboembolic events during follow-up. This observation confirms the results of a study with 339 patients using the ACP for LAAC, which found no association of peri-device leaks and ischemic events.[25] However, the rate of DRT was higher in the LAmbre than in the Amplatzer group, although statistical significance was not reached. Other LAmbre registries documented lower rates of DRT with 1.3%[12] and 0%.[14–16] The known risk factor for the occurrence of DRT is deep implantation of the device into the neck of the LAA, older age, history of stroke, smoking, and female sex.[25–27] A higher rate of incomplete sealing of the LAA ostium by the disc was observed in the LAmbre group. In all three cases with DRT on LAmbre devices, final angiography at the end of the intervention revealed a small peri-device leak <5 mm at the ridge to the left pulmonary veins. Furthermore, in one of those cases, the device was implanted deep into the ostium. At follow-up, those thrombi were sessile and adherent to the surface of the occluder (Figure 3). DRT on LAmbre devices were observed in two females (81 and 68 years) and one male patient (77 years) with high CHA_2DS_2-VASc scores (7, 6, and 4). In those cases, the preoperative TEE showed a dilated LA and dense smoke in the LAA, despite normal systolic left ventricular function. Two patients were switched to lifelong treatment with OAC as the thrombus persisted in further TEE exams. One DRT was considered as nonrelevant, the patient remained asymptomatic under therapy with aspirin alone. Eventually, the high rate of DRT of LAmbre in this study remains unclear and maybe a random finding due to the small sample size of the LAmbre group. As another potential reason, TEE follow-up in the Amulet group was lower and less redundant, which may have led to an underreporting of DRT.

In the present study, the rate of all-cause stroke and systemic embolism at follow-up was similar for both devices but slightly higher than reported in other Amplatzer registries (ACP: 2.3%,[6] 2.9%: Amulet,[24] both devices: 1.56%)[8] and in the 5-year outcomes of the PROTECT-AF and PREVAIL trials (1.7%) for the Watchman occluder.[5]

This can probably be attributed to the higher age and CHA_2DS_2-VASc score of our patient cohort. The rate for ischemic stroke only in the LAmbre group was respectively 2.7 events per 100 patient-years, resulting in a 60% risk reduction for stroke, compared with the expected stroke rate with a mean CHA_2DS_2-VASc score of 4.8 (expected rate of 6.7 events per 100 patient-years).[28] All other LAmbre registries with shorter follow-up times from 6 to 12 months observed low rates of ischemic stroke (0%,[15–17] 1.3%).[12]

The rates of major bleeding events during follow-up were numerically, but not statistically higher in the Amplatzer group. Major bleeding events in the Amplatzer group consisted predominantly of gastro-intestinal bleedings. Although the groups were propensity score-matched, substantial unmeasured confounders may likely persist, like a higher risk for bleeding in the Amplatzer group. Nonetheless, bleeding events rates in our study were low and comparable to other Amplatzer registries (ACP: 2.1%,[6] ACP and Amulet: 2.2%).[8] The 5-year outcomes of the PROTECT-AF and PREVAIL trials reported lower rates of major bleeding events (1.7%).[5] However, those patient cohorts were younger and had fewer co-morbidities. Furthermore, in the PROTECT-AF trial patients with contraindications to warfarin had been excluded, whereas our patient population had a prior major bleeding event in two-third of the cases.

Finally, regarding cardiovascular and unexplained death, as well as all-cause mortality, no significant differences were observed between the LAmbre and Amplatzer group. They are slightly higher than those documented in Amplatzer all-comer registries (cardiovascular death and all-cause mortality: ACP: 1.7% and 6.3%,[6] Amulet: 4.9% and 8.4%,[7] both devices: 2.2%).[8] The 5-year outcomes of the PROTECT-AF and PREVAIL trails with a younger patient cohort and fewer co-morbidities reported overall low rates of cardiovascular death (1.3%) and all-cause mortality (3.6%).[5] The relatively high cardiovascular and all-cause mortality rates of this study are most likely explicable by the elderly, polymorbid and frail patient population.

4.1 | Limitations

The present study is a non-randomized observational, retrospective study and has a small sample size. It was not powered to detect differences in long-term outcomes. Definite conclusions about late clinical efficacy and safety of LAmbre versus Amplatzer occluders need to be confirmed by a randomized, controlled trial. Despite the good comparability of the two groups by the propensity score matching, substantial unmeasured confounders may persist. TEE follow-up was not available for all patients and more incomplete in the Amplatzer group. This may have led to an overestimation or underestimation of device-related thrombi and peri-device leaks.

5 | CONCLUSION

In this single center experience, the LAmbre system compared with Amplatzer devices for LAAC offered comparable peri-procedural and long-term clinical safety and efficacy. These findings have to be confirmed in a prospective randomized trial.

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CONFLICT OF INTERESTS

Jai-Wun Park received consulting fees from LifeTechScientific Corporation, outside the submitted work. Johannes Brachmann reports consulting fees from Abbott, Medtronic, Bayer, Liva-nova, Pfizer, Boston Scientific, Boehringer Ingelheim, and Biotronik. The other authors have no conflict of interests to declare.

ORCID

Caroline Kleinecke http://orcid.org/0000-0002-6814-5236

REFERENCES

1. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37(38):2893-2962.
2. Glikson M, Wolff R, Hindricks G, et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion - an update. *Europace*. 2019.
3. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. *Lancet*. 2009;374(9689):534-542.
4. Holmes DR Jr., Kar S, Price MJ, et al. Prospective randomized evaluation of the Watchman left atrial appendage closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. *J Am Coll Cardiol*. 2014;64(1):1-12.
5. Reddy VY, Doshi SK, Kar S, et al. 5-year outcomes after left atrial appendage closure: from the PREVAIL and PROTECT AF trials. *J Am Coll Cardiol*. 2017;70(24):2964-2975.
6. Tzikas A, Shakir S, Gafoor S, et al. Left atrial appendage occlusion for stroke prevention in atrial fibrillation: multicentre experience with the AMPLATZER Cardiac Plug. *EuroIntervention*. 2016;11(10):1170-1179.
7. Landmesser U, Tondo C, Camm J, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: one-year follow-up from the prospective global Amulet observational registry. *EuroIntervention*. 2018;14:e590-e597.
8. Berti S, Santoro G, Brscic E, et al. Left atrial appendage closure using AMPLATZER devices: a large, multicenter, Italian registry. *Int J Cardiol*. 2017;248:103-107.
9. Kleinecke C, Gomez Monterrosas O, Scalone G, et al. First-in-human experience of left atrial appendage occlusion with the steerable FuStar sheath. *J Interv Cardiol*. 2018;31(4):532-537.
10. Lam YY. A new left atrial appendage occluder (Lifetech LAmbre Device) for stroke prevention in atrial fibrillation. *Cardiovasc Revasc Med*. 2013;14(3):134-136.
11. Meier B, Palacios I, Windecker S, et al. Transcatheter left atrial appendage occlusion with Amplatzer devices to obviate anticoagulation in patients with atrial fibrillation. *Catheter Cardiovasc Interv*. 2003;60(3):417-422.

12. Huang H, Liu Y, Xu Y, et al. Percutaneous left atrial appendage closure with the lambre device for stroke prevention in atrial fibrillation: a prospective, multicenter clinical study. *JACC Cardiovasc Interv*. 2017; 10(21):2188-2194.
13. Park JW, Sievert H, Kleinecke C, et al. Left atrial appendage occlusion with lambre in atrial fibrillation: initial European experience. *Int J Cardiol*. 2018;265:97-102.
14. Chen S, Schmidt B, Bordignon S, et al. Feasibility of percutaneous left atrial appendage closure using a novel LAmbre occluder in patients with atrial fibrillation: initial results from a prospective cohort registry study. *J Cardiovasc Electrophysiol*. 2018;29(2):291-297.
15. Reinsch N, Ruprecht U, Buchholz J, Edel C, Kalsch H, Neven K. Initial experience of percutaneous left atrial appendage closure using the LAmbre device for thromboembolic prevention. *J Cardiovasc Med*. 2018;19(9):491-496.
16. Feng XF, Zhang PP, Sun J, Wang QS, Li YG. Feasibility and safety of left atrial appendage closure using the lambre device in patients with nonvalvular atrial fibrillation with or without prior catheter ablation. *Int Heart J*. 2019;60(1):63-70.
17. Chen S, Chun KRJ, Bordignon S, et al. Left atrial appendage occlusion using LAmbre Amulet and Watchman in atrial fibrillation. *J Cardiol*. 2019;73(4):299-306.
18. Meier B, Blaauw Y, Khattab AA, et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion. *Europace*. 2014;16(10):1397-1416.
19. Berti S, Santoro G, Palmieri C, Meucci F. Tools and techniques clinical: transcatheter closure of left atrial appendage using the Amplatzer Cardiac Plug. *EuroIntervention*. 2013;9(4):524-526.
20. Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation*. 2011;123(23):2736-2747.
21. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *EuroIntervention*. 2012;8(7):782-795.
22. Hicks KA, Mahaffey KW, Mehran R, et al. 2017 Cardiovascular and stroke endpoint definitions for clinical trials. *J Am Coll Cardiol*. 2018; 71(9):1021-1034.
23. Team. RDC. R: A language and environment for statistical computing. https://www.r-project.org/. R Foundation for Statistical Computing, Vienna, Austria. 2018.
24. Landmesser U, Schmidt B, Nielsen-Kudsk JE, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: periprocedural and early clinical/echocardiographic data from a global prospective observational study. *EuroIntervention*. 2017;13(7):867-876.
25. Saw J, Tzikas A, Shakir S, et al. Incidence and clinical impact of device-associated thrombus and peri-device leak following left atrial appendage closure with the Amplatzer Cardiac Plug. *JACC Cardiovasc Interv*. 2017;10(4):391-399.
26. Pracon R, Bangalore S, Dzielinska Z, et al. Device thrombosis after percutaneous left atrial appendage occlusion is related to patient and procedural characteristics but not to duration of post-implantation dual antiplatelet therapy. *Circ Cardiovasc Interv*. 2018;11(3):e005997.
27. Dukkipati SR, Kar S, Holmes DR, et al. Device-related thrombus after left atrial appendage closure: Incidence, predictors, and outcomes. *Circulation*. 2018;138:874-885.
28. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest*. 2010;137(2):263-272.

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