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ORIGINAL PAPER

Early results of first versus second generation Amplatzer occluders for left atrial appendage closure in patients with atrial fibrillation

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Abstract
Background Transcatheter left atrial appendage (LAA) occlusion has been proven to be an effective treatment for stroke prophylaxis in patients with atrial fibrillation. For this purpose, the Amplatzer cardiac plug (ACP) was introduced. Its second generation, the Amulet, was developed for easier delivery, better coverage, and reduction of complications.
Aim To investigate the safety and efficacy of first generation versus second generation Amplatzer occluders for LAA occlusion.
Methods Retrospective analysis of prospectively collected data from the LAA occlusion registries of the Bern and Zurich university hospitals. Comparison of the last consecutive 50 ACP cases versus the first consecutive 50 Amulet cases in patients with non-valvular atrial fibrillation. For safety, a periprocedural combined endpoint, which is composed of death, stroke, cardiac tamponade, and bailout by surgery was predefined. For efficacy, the endpoint was procedural success.
Results There were no differences between the two groups in baseline characteristics. The percentage of associated interventions during LAA occlusion was high in (78 % with ACP vs. 70 % with Amulet p = ns). Procedural success was similar in both groups (98 vs. 94 %, $p = 0.61$). The combined safety endpoint for severe adverse events was reached by a similar rate of patients in both groups (6 vs. 8 %, $p = 0.7$). Overall complication rate was insignificantly higher in the ACP group, which was mainly driven by clinically irrelevant pericardial effusions (24 vs. 14 %, $p = 0.31$). Death, stroke, or tamponade were similar between the groups (0 vs. 2 %, 0 vs. 0 %, or 6 vs. 6 %, p = ns).
Conclusion Transcatheter LAA occlusion for stroke prophylaxis in patients with atrial fibrillation can be performed with similarly high success rates with first and second generations of Amplatzer occluders. According to this early experience, the Amulet has failed to improve results of LAA occlusion. The risk for major procedural adverse events is acceptable but has to be taken into account when selecting patients for LAA occlusion, a preventive procedure.

Keywords Anticoagulation · Atrial fibrillation · Left atrial appendage · Closure · Stroke · Bleeding

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Abbreviations

ACP	Amplatzer cardiac plug
AF	Atrial fibrillation
ASA	Acetylsalicylic acid
ASD	Atrial septal defect
DAPT	Dual antiplatelet therapy
GI	Gastrointestinal
INR	International normalized ratio
LAA	Left atrial appendage
LAAO	Left atrial appendage occlusion
MI	Myocardial infarction
NOAC	New anticoagulant drug
OAC	Oral anticoagulation
PAD	Peripheral artery disease
PCI	Percutaneous coronary intervention
PFO	Patent foramen ovale
TAVI	Transcatheter aortic valve implantation
TIA	Transient ischemic attack
VARC	Valve Academic Research Consortium

Introduction

In patients with non-valvular atrial fibrillation (AF) the concept of transcatheter left atrial appendage (LAA) occlusion with the Watchman device (Atritech, Boston Scientific, Natick, MA, USA), has been proven to be non-inferior in short term and superior in longer term with regard to bleeding and stroke prevention and survival in comparison to lifelong oral anticoagulation (OAC) with its documented and sustained risks [1–17]. Amplatzer devices (St. Jude Medical, Plymouth, MN, USA) have been used since 2002 for LAA occlusion [18]. Based on this, a dedicated device, the Amplatzer cardiac plug (ACP), was developed [18–22]. The non-dedicated devices initially used showed high complication rates predominantly due to lack of sufficient anchoring in the LAA with frequent embolizations [20, 21]. With regard to safety and efficacy, the ACP in clinical use in Europe since late 2008, has performed reasonably well [20, 23, 24]. For additional ease of use, expanded size range to better cover large LAAs, and to further reduce adverse events, especially embolization, a second generation of the ACP, the Amplatzer Amulet left atrial appendage occluder has been developed and was released in 2013 [25, 26]. As the first generation ACP, it shows a design with a distal hook-crowned lobe for anchoring in the lumen of the LAA and a proximal disc for excluding the ostium of the LAA according to the pacifier principle. This plug and disc concept is different from the plug only design of other occluders to the end of more complete exclusion of the LAA. Its design is a remnant of the initial use of double disc Amplatzer devices for LAA closure [18]. To test the effects of the modifications, the present study compares the experience of the last 50 ACP with the first 50 Amulet cases of all-comers for LAA occlusion in two Swiss centers.

Methods

Patient population

All patients are recruited from the prospective Bern and Zurich university hospitals registries of transcatheter LAA occlusion for stroke prevention which contain all consecutive patients who underwent LAA occlusion since 2002 in these two centers. Upon availability of the Amulet in January 2013, the last 50 consecutive patients who received an ACP and the first 50 consecutive patients who received an Amulet device were compared, starting with number 214 of our registry. The aggregated experience with LAA occlusion of the 2 centers represents more than 600 cases at present. All patients with non-valvular atrial fibrillation and presumed benefit from protection of embolic events by long-term oral anticoagulation (CHA_2DS_2-VASc score of ≥ 1) were eligible for LAA occlusion and included in the all-comers registries. Given the prospective cohort study character, there were no exclusion criteria. All patients provided written informed consent according to the requirements and approval of the local ethics committees. This study represents a retrospective analysis of prospectively acquired data with prespecified endpoints. Patient baseline characteristics, procedural data, immediate periprocedural outcomes, and available follow-up data were compared.

Data acquisition

Demographic and clinical characteristics, including risk for stroke and major bleeding (CHADS score, CHA_2DS_2-VASc score, HAS-BLED score) [27–30], procedural data, adverse events, and outcome data of in-hospital and follow-up periods were systematically captured. All adverse events underwent adjudication by an independent cardiologist.

Differences between the ACP and Amulet

First and second generation Amplatzer LAA occluders, are made from nitinol meshes with polyester inlays and come in a disc and plug design inspired by the patent foramen ovale (PFO) and atrial septal defect (ASD) occluders. The distal disc has been modified to a more voluminous lobe, body, or plug, which obstructs the LAA neck and anchors within it by the help of stabilizing hooks. The proximal disc, which is connected by a flexible waist to the lobe, covers the ostium, thereby ideally leading to a complete

exclusion of the LAA from blood flow according to the pacifier principle. Due to the occurrence of embolization of the ACP in ≥4 % of cases and of incomplete exclusions of the LAA due to large diameters, the following additional features of the preloaded Amulet for easier preparation and reduction of air embolizations were introduced: the delivery cable was modified to a movable inner 0.014″ core wire to which the screw is attached [31]. The range of the eight sizes available has been extended from 16 mm to a maximum of 34 mm, delivered through 12 or 14 French (F) TorqVue 2 × 45° double-bend sheaths. The protrusion of the discs is 6 mm in the 16–22 mm devices and 7 mm in the 25–34 mm devices. Further, the distal lobe has become more voluminous by increased depth in the larger devices. For better flexibility, the waist length has also been increased. Regarding optimal anchoring for prevention of periprocedural embolizations, beside larger lobes, the stabilizing hooks have been made stiffer (0.0065″ instead of 0.006″). Also, their number has been increased for the larger devices: instead of 6 pairs of hooks for all sizes of ACPs, the 20, 22, and 25 mm Amulets come with eight pairs, and the 28, 31, and 34 mm occluders with 10 pairs of hooks, now equalizing the spacing in between for every size. Finally, to prevent formation of thrombi, the formerly protruding female screw on the proximal disc has been recessed. (Fig. 1).

Procedure of LAA occlusion

All 100 procedures were performed between December 2012 and August 2013 using local anesthesia and fluoroscopic guidance only (with the exception of 2 patients at the University Hospital of Zurich in whom general anesthesia and transesophageal echocardiography (TEE) guidance were used). LAA occlusion was performed either as a single procedure or in the majority of cases in a combined manner together with coronary angiography or intervention, transcatheter valve implantation, PFO or ASD closure, or pulmonary vein isolation. Before or after systemic anticoagulation with generally 5000 units of heparin, the left atrium was accessed through a right femoral venous puncture via either a preexisting PFO or ASD or via a transseptal puncture. Usually an 8F transseptal kit (Mullins transseptal sheath and a Brockenbrough needle, Medtronic Inc., Minneapolis, MN, USA) were used. The obturator of this sheath accepts a 0.035″ wire, like the Backup wire (Boston Scientific, Natick, MA, USA) used to introduce the double-bend Amplatzer TorqVue delivery sheath into the left atrium. To define LAA anatomy, LAA angiography was performed by contrast medium injections through the 12F or 14F delivery sheath still containing the partially retracted obturator in at least the right anterior oblique cranial and caudal projections prior to implantation. Taking for instance the outer diameter of the delivery sheath as a reference, the diameter of the landing zone in the LAA was estimated or measured, aiming for an oversizing of at least 20 %. After deployment, stable position in several views and by sustained tugging on the delivery cable, optimal coverage of the LAA ostium by the disc, and deep enough seating of the lobe within the LAA were ascertained before the device was released. In case of unsatisfactory positioning or anchoring, the plug was not released but resheathed and redeployed in a different angle or depth, or replaced by a more suitable size. On the way out, a preexisting PFO or ASD was closed using the same cable and delivery sheath and Amplatzer PFO or ASD occluders. Transthoracic echocardiography assessed device position and presence or absence of pericardial effusions either at the day of the procedure (in case the procedure was performed on an outpatient basis) or the following day. Oral anticoagulation (OAC) was stopped immediately and patients were discharged on daily acetylsalicylic acid (100 mg) and clopidogrel (75 mg) for at least 1 month. Patients who underwent concomitant radiofrequency ablation of the pulmonary veins and left atrium remained on OAC for 3 months. There were no differences in the sequence or technique of implantation with the exception of the fact, that the Amulet system comes preloaded.

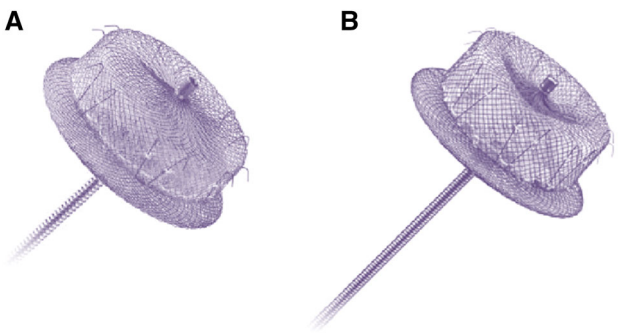

Fig. 1 First and second generation Amplatzer LAA occluders: cardiac plug (**a**) and Amulet (**b**). The Amulet exhibits a deeper distal lobe, a more overriding disc, a longer waist, a recessed female screw, and more and robust anchoring hooks

Follow-up

In all patients, a standardized follow-up examination after 4–6 months was performed: in addition to clinical and neurological examination, TEE was obtained to evaluate seating, peri-device leaks, and freedom from relevant thrombus apposition on the LAA device.

Endpoints and definitions

All endpoints were prespecified in the database and adverse events were adjudicated by an independent cardiologist.

With regard to the efficacy of the procedure, procedural success was defined as implantation of a device. Concerning procedural safety, the combined safety endpoint of all severe adverse events comprised periprocedural death, stroke, cardiac tamponade with need for drainage, and all other events with need for bailout cardiovascular surgery. Since major bleeding occurs mostly due to perforation of the LAA or transseptal puncture with cardiac tamponade and tamponade is already counted as severe adverse event, only overt major bleedings of access sites with hemoglobin drop of 3 to <5 g/dL or requirement of packed red blood cell transfusions were additionally counted (Bleeding Academic Research Consortium, BARC, from type 3a) [32]. According to the classification of the HAS-BLED score, liver disease was defined as: cirrhosis, bilirubin >2× normal, AST/ALT/AP >3× normal, medication usage predisposing to bleeding counted antiplatelet agents, non-steroid antirheumatic drugs and renal disease was defined as need for dialysis, status post transplantation, and a serum creatinine level >200 μmol/L [29]. Need for transcatheter bailout was defined as a composite of need for emergent pericardial puncture and drainage, snaring of an embolized occluder, transcatheter occlusion of leakage in the aortic root due to inadvertent puncture, and recanalization of procedure-associated coronary occlusions.

Statistical analysis

Continuous variables are presented as mean ± SD and were compared using the unpaired Mann–Whitney *U* test. Categorical data are expressed as frequency (percentages) and were compared with Fisher's exact tests. All tests and confidence intervals are two-sided, and an alpha level of 0.05 was chosen to determine statistical significance of differences. Analyses were performed using GraphPad Prism 6 (www.graphpad.com).

Results

Baseline characteristics

Table 1 provides baseline characteristics of the two patient groups. The two groups represent a continuum of prospectively included patients. No differences were detected between the two groups, ensuring good comparability.

Periprocedural data

Table 2 illustrates periprocedural outcome in both groups. Neither procedural nor anatomical characteristics or the frequency of concomitant procedures revealed significant differences between the groups. In procedural success, both groups were comparable. Regarding overall complication rates, the ACP performed insignificantly poorer which was mainly driven by pericardial effusions without need for drainage. The combined safety endpoint was reached by a similar number of patients in both groups: the respective events were: three cardiac tamponades with need for transcatheter drainage in the ACP group. In the Amulet group, one patient died periprocedurally after cardiac tamponade due to procedural tear of the LAA despite emergent surgical drainage. Another two patients suffered from cardiac tamponade with successful transcatheter drainage and one patient needed to undergo periprocedural surgery because of an embolized occluder. Adverse events not included in the combined safety endpoint occurred as follows: ACP group—two device embolizations with successful transcatheter retrieval, seven pericardial effusions without need for drainage, and two inadvertent injuries of surrounding structures (in one case, leakage due to inadvertent aortic root puncture was treated by an 5 mm ASD occluder, in one case, recanalization of an embolically occluded left circumflex coronary artery was performed); Amulet group—two device embolizations treated by transcatheter retrieval and two irrelevant pericardial effusions.

Follow-up

Table 3 illustrates the follow-up data in both groups. Duration from LAA occlusion to follow-up was 127 ± 46 days in the ACP group, 105 ± 48 in the Amulet group, respectively. Both groups were mainly on acetylsalicylic acid or clopidogrel at follow-up. Two patients from the ACP group were on new oral anticoagulants (NOAC) for 3 months time because of concomitant pulmonary vein isolation. There was no neurologic event in the ACP group vs. two neurologic events in the Amulet group. Three weeks after LAA occlusion, a patient suffered a stroke because of a thrombus on the device and one patient had an intra-cerebral bleed being under clopidogrel at the time, resulting in gait abnormality. The patient with stroke was put on OAC. There was one non-related death in the ACP group, 21 days after LAA occlusion. The patient died after a fall-caused hip fracture. There was also one non-related death 24 days after LAA occlusion with concomitant TAVI procedure in the Amulet group during cardiac rehabilitation. One procedure related death occurred in the Amulet group. The patient died after a tear of the LAA. This prompted emergent surgery. However, the patient died on the same day in spite of massive blood transfusion at the intensive care unit.

The transesophageal echocardiography showed good seating of ACP and Amulet devices in all cases (100 %) with no significant difference. The fourteen patients (six in the ACP group, eight in the Amulet group) who refused

Table 1 Baseline characteristics

	ACP *n* (%) or value ($n = 50$)	Amulet *n* (%) or value ($n = 50$)	*p*
Age (years)	72.5 ± 11.5	75.6 ± 9.7	0.15
Body mass index (kg/m^2)	26.0 ± 4.7	26.9 ± 5.2	0.37
$CHADS_2$ score (points)	2.6 ± 1.3	2.8 ± 1.4	0.46
CHA_2DS_2-VASc score (points)	3.9 ± 1.7	4.3 ± 1.7	0.24
HAS-BLED score (points)	2.7 ± 0.9	2.9 ± 1.0	0.29
Risk factors for stroke			
Congestive heart failure	24 (48 %)	23 (46 %)	0.84
Hypertension	45 (90 %)	47 (94 %)	0.72
Age ≥75 years	22 (50 %)	28 (56 %)	0.31
Diabetes	11 (22 %)	7 (14 %)	0.43
Prior stroke, TIA or systemic embolism	11 (22 %)	14 (28 %)	0.64
Vascular disease (prior MI, PAD or aortic plaque)	16 (32 %)	11 (22 %)	0.36
Female gender	14 (28 %)	18 (36 %)	0.52
Risk factors for bleeding			
Hypertension (uncontrolled, >160 mmHg)	0 (0 %)	5 (10 %)	0.06
Renal disease	1 (2 %)	1 (2 %)	1.00
Liver disease	0 (0 %)	0 (0 %)	1.00
Prior stroke	11 (22 %)	13 (26 %)	0.81
Prior major bleeding or predisposition to bleeding	33 (66 %)	28 (56 %)	0.41
Labile INR	0 (0 %)	3 (6 %)	0.24
Age >65 years	37 (74 %)	38 (76 %)	0.85
Medication usage predisposing to bleeding	49 (98 %)	42 (84 %)	0.03
Alcohol use ≥8 units/week	1 (2 %)	3 (6 %)	0.61
Atrial rhythm			
Atrial fibrillation	45 (90 %)	46 (92 %)	1.00
Paroxysmal	33 (56 %)	15 (30 %)	0.0006
Persistent or permanent	22 (44 %)	31 (62 %)	0.108
Atrial flutter	5 (10 %)	4 (8 %)	0.73
Clinical features			
Coronary artery disease	15 (30 %)	13 (26 %)	0.82
Systolic left ventricular ejection fraction	54 ± 12	54 ± 13	0.97
Creatinine (μmol/l)	89 ± 36	100 ± 55	0.24
Left atrial size (PLAX echo, in mm)	46 ± 8	48 ± 7	0.21
Medication before LAA occlusion			
Acetylsalicylic acid	33 (66 %)	32 (64 %)	0.84
Thienopyridine	11 (22 %)	7 (14 %)	0.43
Dual antiplatelet therapy	29 (58 %)	23 (46 %)	0.32
Vitamin K antagonist	37 (74 %)	31 (62 %)	0.28
New oral anticoagulant drug	4 (8 %)	6 (12 %)	0.74
Reason for LAA occlusion			
Prior major bleeding	16 (32 %)	20 (40 %)	0.53
High risk of bleeding	27 (54 %)	27 (54 %)	1.00
High risk of falls or prior falls	6 (12 %)	10 (20 %)	0.28
Instable INR	0 (0 %)	4 (8 %)	0.12
Physician/patient refusal of oral anticoagulation	9 (18 %)	2 (4 %)	0.05
Avoidance of triple therapy after PCI or TAVI	29 (58 %)	23 (46 %)	0.31

INR international normalized ratio, *MI* myocardial infarction, *PAD* peripheral arterial disease, *PLAX* parasternal long axis, *TIA* transient ischemic attack

Table 2 Periprocedural data

	ACP *n* (%) or value ($n = 50$)	AMULET *n* (%) or value ($n = 50$)	*p*
Procedural success[a]	49 (98 %)	47 (94 %)	0.61
Contrast medium (ml)	234 ± 121	215 ± 93	0.409
LAA accessed by transseptal puncture	41 (82 %)	42 (84 %)	0.79
LAA accessed by PFO/ASD	9 (18 %)	8 (16 %)	0.79
LAA orifice diameter (in mm)	25.7 ± 4.1	25.6 ± 5.0	0.914
ACP body diameter	27.8 ± 4.1	28.3 ± 5.0	0.58
Percentage of oversizing	8 % ± 4.5	11 % ± 5.6	0.0043
Ad hoc procedure	9 (18 %)	8 (16 %)	1
Implantation attempts	1.1 ± 0.4	1.1 ± 0.4	1
More than 1 device tried	4 (8 %)	3 (6 %)	1
Concomitant procedures			
LAA occlusion only	11 (22 %)	15 (30 %)	0.49
Coronary angiography	29 (58 %)	27 (54 %)	0.84
PCI	9 (18 %)	11 (11 %)	0.8
ASD or PFO closure	9 (18 %)	8 (16 %)	0.79
TAVI	6 (12 %)	5 (10 %)	0.75
Radiofrequency ablation of atrial fibrillation	5 (10 %)	4 (8 %)	0.21
Hospital stay (days)[b]	2.6 ± 3.7	2.8 ± 4.1	0.81
Same day discharge	7 (14 %)	8 (16 %)	0.73
Periprocedural adverse events			
Any complication	12 (24 %)	7 (14 %)	0.31
Periprocedural death[c]	0 (0 %)	1 (2 %)	0.31
Stroke (any)[c]	0 (0 %)	0 (0 %)	1
Stroke (major)	0 (0 %)	0 (0 %)	1
Air embolism	0 (0 %)	0 (0 %)	1
Device embolization	2 (4 %)	3 (6 %)	0.64
Pericardial effusion (no need for drainage)	7 (14 %)	2 (4 %)	0.08
Cardiac tamponade (need for drainage)[c]	3 (6 %)	3 (6 %)	1
Inadvertent injury of great or coronary arteries	2 (4 %)	0 (0 %)	0.15
Major bleedings of access site	0 (0 %)	0 (0 %)	1
Need for surgery bailout[d]	0 (0 %)	2 (4 %)	0.15
Need for transcatheter bailout[c]	6 (12 %)	5 (10 %)	0.74
Combined safety endpoint[c]	3 (6 %)	4 (8 %)	0.7

ACP Amplatzer cardiac plug, *ASD* atrial septal defect, *LAA* left atrial appendage, *PCI* percutaneous coronary intervention, *PFO* patent foramen ovale, *TAVI* transcatheter aortic valve implantation

[a] Successful placement of an occluder in the LAA at the end of the intervention

[b] Starting at day after intervention

[c] Composite of: death, stroke, tamponade, bailout by surgery

[d] Composite of: Need for emergent pericardial puncture, need for snaring of embolized device, need for transcatheter occlusion of leak in aorta or pulmonary artery due to inadvertent puncture

TEE or were fragile due to comorbidities had transthoracic echocardiography and one had an angiographic follow-up, respectively. One major bleeding in the ACP group was seen. A patient had a hemorrhagic pericardial effusion 14 days after LAA occlusion and needed a hospitalization and drainage. In the Amulet group, there was the patient with an intra-cerebral bleed 6 months after LAA occlusion mentioned above. He was on clopidogrel at the time. He had had acetylsalicylic acid for 3 months prior. One patient in the Amulet group developed a femoral pseudoaneurysm post intervention and needed surgery 19 days after LAA occlusion after inefficient thrombin injection. Four patients of the ACP group had late pericardial effusions but no intervention was needed and the effusion disappeared. One such patient occurred in the Amulet group and he had an irrelevant late pericardial effusion on further follow-up. Three patients in the ACP group had small peri-device leaks of less than 5 mm with no consequence. No leaks were seen in the Amulet group. One ACP device-associated left atrial thrombus was diagnosed but considered not to need (N)OAC. One Amulet device-associated thrombus caused a stroke as mentioned above. The patient was put on OAC and died in the follow-up, the exact cause was not known. Another adherent thrombus was seen for the Amulet device with no therapeutic consequence.

Table 3 Post-procedural data

	ACP n (%) or value ($n = 50$)	Amulet n (%) or value ($n = 50$)	p
Clinical follow-up	45 (90 %)	47 (94 %)	0.72
Neurologic events	0	2 (4 %)	0.49
Bleeding all	1 (2 %)	3 (6 %)	0.62
Major bleeding	1 (2 %)	2 (4 %)	0.30
Death any	1 (2 %)	4 (8 %)	0.36
Death related to LAA occlusion	0	2 (4 %)	0.49
Drugs at follow-up			
Acetylsalicylic acid	45 (90 %)	41 (82 %)	0.38
Thienopyridines	36 (72 %)	34 (68 %)	0.73
Oral anticoagulants	1 (2 %)	0	0.32
Novel oral anticoagulants	1 (2 %)	0	0.32
TEE	33 (66 %)	33 (66 %)	1.0
Correct position	33 (100 %)	33 (100 %)	1.0
Peri-device leak <5 mm	3 (6 %)	0	0.24
Peri-device leak >5 mm	0	0	1.0
Total occlusion by disk	30 (90 %)	33 (100 %)	0.67
Late pericardial effusion	3 (6 %)	1 (2 %)	0.62
Thrombus, any	0	2 (4 %)	0.49
Mobile thrombus	0	1 (2 %)	0.32
Adherent thrombus	0	1 (2 %)	0.32
Need for restart of oral anticoagulation	0	1 (2 %)	0.32
Need for drainage of late pericardial effusion	0	0	1.0
TTE + 1 angiographic follow-up (in Amulet pt)	6 (12 %)	8 (16 %)	0.77
Correct position	6 (100 %)	8 (100 %)	0.77
Total occlusion by disk	6 (100 %)	8 (100 %)	0.77
Late pericardial effusion	1 (2 %)	0	0.31
Thrombus, any	0	0	1.0
Mobile thrombus	0	0	1.0
Adherent thrombus	0	0	1.0
Need for restart of oral anticoagulation	0	0	1.0
Need for drainage of late pericardial effusion	0	0	1.0

LAA left atrial appendage

Discussion

This dual-center cohort study of 100 consecutive patients who underwent transcatheter LAA occlusion for stroke prevention with first and second generation Amplatzer LAA occluders analyzes the differential outcome of both devices. The principal findings are:

1. Comparability of the two patient groups was good and procedural success was similar.
2. The prespecified combined safety endpoint was met by a similar proportion of patients in both groups.
3. The rate of overall periprocedural complications was insignificantly higher in the ACP group, largely driven by non-relevant pericardial effusions.

Limitations

The analysis has several limitations mostly inherent to the limited sample size. The relatively low number of patients and events resulted in low power to detect potentially important differences and low precision is indicated by wide confidence intervals.

Procedural success of the ACP vs. Amulet

In spite of high success rates in previous studies [24, 33, 34] with 96–100 % successful implantations, one of the aims in redesigning the ACP was to further enhance procedural success mainly by preventing embolizations

of devices which may have been undersized, not implanted deeply enough, or not anchored sufficiently [33, 34]. Despite the outlined changes of the second generation device, the Amulet failed to perform better in this respect.

Periprocedural safety of ACP Vs. Amulet

Another rationale behind the modifications of the second generation device was improvement of technical implantation success and better ease of use as well as lowering the rate of severe complications. No air embolism or stroke related to embolizations from the LAA or occluders during the procedure occurred in neither group (Table 2). Looking at the overall rate of complications, there is a trend to a higher incidence in the ACP group, largely driven by more clinically non-significant pericardial effusions. The number of implantation attempts was identical in both groups. This discards poorer anchorage of the ACP with subsequent or primary need of deeper implantation and hereby added risk of perforation of the LAA wall as possible culprit. On the other hand, implantation of the Amulet intuitively may be more cautious fearing injury of the LAA wall by the more voluminous lobe and more and stiffer hooks. Reassuringly, the rate of cardiac tamponade was the same in both groups, waving concerns about increased risks of the more sturdy second generation device. In accordance, the predefined combined safety endpoint of this study, which comprises all severe complications with need for bailout was also reached by a similar rate of patients with a trend in disfavor of the Amulet group. This was driven by two cases who needed urgent surgery (in one case surgical patching due to massive LAA perforation, in another case need for surgical removal of an embolized Amulet occluder from the left atrium). However, in the majority of the cases where adverse events occurred, bailout by transcatheter maneuvers was possible (pericardiocentesis in three and one case per group, respectively, snaring of embolized occluders in two cases per group, implantation of an 5 mm ASD occluder in the aortic root due to inadvertent puncture in an ACP case). As the present study started with case 214 of the registry (i.e. the first of the last 50 ACP cases), the results cannot be explained by a learning curve issue, since all operators of the two high-volume centers were experienced. In contrast, the first 50 ACP implantations (case 33–82) were exclusively performed by the senior author. In this cohort, only one major adverse event, namely a major stroke in a patient with a preexisting thrombus in the LAA. In addition, an urgent need for LAA occlusion due to LAA perforation occurred (2 %), one case of air embolization with transient ischemic attack (2 %), and one pericardial effusion without need for drainage.

Follow-up

Overall regarding death, neurologic events, late pericardial effusions, major bleeding, peri-device leaks or thrombi on device, there seems to be no significant difference between the first and second generation device (Table 2). The trend for higher incidence of pericardial effusion seen periprocedurally for the ACP device appears to persist during follow-up with more late pericardial effusions as also experienced elsewhere [35]. Comparably more neurologic events and major bleedings were recorded in the Amulet group (difference not significant). This may be a result of the small sample size. There seems to be a trend for more peri-device leaks in echocardiographic follow-up for the ACP device compared to the Amulet which could influence long-term neurologic outcome if leaks are considered relevant for thrombus formation and stroke. Thrombus formation on the devices showed no significant difference between the two groups. A better outcome in the second generation device might be expected with larger numbers because of the recessed version of the formerly protruding female screw on the proximal disc.

Do we really need the Amulet?

So far, in this early experience reported in the present study with a limited number of patients, the second generation Amplatzer LAA occluder failed to show a benefit over the first generation device. Nevertheless, some features of the newer device may be of advantage, especially for less experienced operators. On the other hand, for instance in small LAAs, the first generation device may adapt its shape better to a narrow and long neck and thereby reduce injury to the wall. A crucial point in preventing embolizations of both ACPs and Amulets is selecting the appropriate size of occluder for sufficient anchorage. For a definite answer to the question, whether current or further modifications of the Amulet will render the procedure safer and more effective, larger numbers of procedures will be necessary. In addition, more precise specifications about size, shape, and geometry of the LAA may help in selecting the most appropriate type and size of occluder, which will ideally be implanted at the first attempt and result in complete exclusion of the LAA [36, 37]. The extension of the range to larger sizes with the Amulet has come in handy [38].

Conclusions

Transcatheter occlusion of the LAA for stroke prophylaxis in patients with atrial fibrillation can be performed with similarly high success rates with first and second

generations of Amplatzer occluders. In this early experience, the Amulet has failed to improve results of LAA occlusion in comparison to its predecessor, the ACP. The challenging procedure continues to entail a relevant risk for major procedural adverse events which have to be taken into account when selecting patients for the procedure and weighed against the risk of long-term OAC.

Conflict of interest Ahmed A. Khattab and Fabian Nietlispach are consultants to St. Jude Medical, Stefan Windecker has received grants to the institution from St. Jude Medical, and Bernhard Meier is a consultant to and has received grants to the institution from St. Jude Medical.

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