Left atrial appendage angiography is associated with the incidence and number of magnetic resonance imaging–detected brain lesions after percutaneous catheter-based left atrial appendage closure

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BACKGROUND Percutaneous catheter-based left atrial appendage closure (LAAC) is a procedure being increasingly performed in patients with atrial fibrillation and high bleeding risk.

OBJECTIVE The purpose of this study was to evaluate the incidence of magnetic resonance imaging (MRI)-detected acute brain lesions (ABLs) as well as potential changes in neurocognitive function after percutaneous LAAC in patients with atrial fibrillation.

METHODS Brain MRI at 3 T was performed within 24 hours before and after LAAC along with neurologic (National Institutes of Health Stroke Scale [NIHSS] score) and cognitive (Montreal Cognitive Assessment [MoCA] test) assessment. Acquired MRI sequences included high-resolution diffusion-weighted imaging as well as fluid-attenuated inversion recovery.

RESULTS Successful device implantation was achieved in all 23 patients (age 74.1 ± 10.5 years; 16 male) using the Amulet (n = 18), Occlutech (n = 3), or LAmbre (n = 2) device. Thirty-seven ABLs were detected by MRI in 12 of 23 patients (52%) after LAAC. The number of periprocedural LAA angiographies was significantly higher in patients with ABL than in those without ABL (1.67 ± 0.65 vs 1.18 ± 0.41; $P = .048$) and was associated with a higher number of ABL ($\rho = 0.615$; $P = .033$). Compared to pre-LAAC assessment, post-LAAC MoCA and NIHSS scores revealed similar results. After LAAC, MoCA test (mean 24.1 ± 4.6 vs 23.2 ± 4.6; $P = .09$) and

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NIHSS score (mean 1.0 ± 1.7 vs 1.2 ± 1.8; $P = .1$) were similar between patients with and those without ABL, respectively.

CONCLUSION MRI-detected ABLs are commonly observed after percutaneous LAAC. The number of LAA angiographies is significantly associated with the number of ABLs; however, the clinical implications of ABL have yet to be determined.

KEYWORDS Bleeding; Brain lesion; Brain magnetic resonance imaging; Left atrial appendage closure; Oral anticoagulation; Silent cerebral lesion

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Introduction

Percutaneous catheter-based left atrial appendage closure (LAAC) is a procedure being performed more frequently, particularly in patients with atrial fibrillation (AF) who have bleeding complications or who are considered at high risk for bleeding while receiving long-term anticoagulation.[1–7] LAAC also is used after electrical left atrial appendage isolation.[8] Beyond the initial learning curve, recent studies have reported a low incidence of device-related complications, including neurologic events.[1,3,9].Although LAAC aims to reduce the risk of AF-related ischemic stroke and systemic embolization, the incidence of periprocedural acute brain lesions (ABLs) after percutaneous LAAC needs to be fully determined. Magnetic resonance imaging (MRI)–detected ABLs have been reported after various cardiac interventional procedures, including coronary interventions and electrophysiologic procedures.[10–14] Although the clinical implications of MRI-detected ABLs on cognitive function are not fully understood, it seems appropriate to examine the frequency and size of such lesions in this more frequently performed cardiac catheter-based procedure. Whereas a reduction in verbal memory function after pulmonary vein isolation was observed in a very small prospective study,[15] the current study included serial neurologic and neurocognitive assessment.

This prospective pilot study aimed to evaluate the incidence of ABLs using high-resolution diffusion-weighted brain MRI at 3 T as well as the potential clinical implications using standardized neurologic and neurocognitive assessment after catheter-based LAAC.

Methods

Twenty-three consecutive patients (age 74.1 ± 10.5 years; 16 male) with paroxysmal (n = 9), persistent (n = 9), or permanent AF (n = 5) were included in this study. All patients were treated with percutaneous LAAC using either the Amulet (St. Jude Medical, Minneapolis, MN), Occlutech (Occlutech, Jena, Germany), or LAmbre (Lifetech Scientific Corp., Shenzhen, China) LAA occlusion device. All patients underwent LAAC because they were considered to have at least 1 relative or absolute contraindication to long-term oral anticoagulation (OAC), such as a history of previous significant bleeding.

This study conformed to the Guiding Principles of the Declaration of Helsinki of 2014. It was approved by the Charité Ethics Committee (EA/084/15) and was registered at the German Clinical Trials Register (No. DRKS00010300).

Pre-, peri-, and postprocedural management

Transesophageal echocardiography (TEE) was performed in all patients before the intervention to assess for intracardiac thrombi. OAC with phenprocoumon was discontinued before the procedure, targeting an international normalize ratio <2. In patients being treated with a novel OAC, the medication was stopped at least 24 hours before the procedure.

LAAC were performed with the patient under conscious sedation using propofol. An arterial line (5Fr) was inserted to provide continuous invasive hemodynamic monitoring. All patients received a single 1.5-g dose of cefuroxime intravenously before the procedure. After femoral venous access was obtained, a transseptal puncture was performed using a nonsteerable SL1 sheath (St. Jude Medical) in conjunction with a BRK-1 needle or the steerable Occlutech sheath under fluoroscopic and TEE guidance. After transseptal puncture, repeated boluses of unfractionated heparin were administered to achieve a target activated clotting time (ACT) >250 seconds. Angiography of the LAA was performed in all patients (right anterior oblique 30°, caudal 20°) using either a pigtail catheter within the LAA or indirect angiography via a steerable sheath, which was positioned at the LAA entrance. For optimal device selection, LAA dimensions were calculated using both fluoroscopy and TEE. For fluoroscopic calculation of LAA dimensions, the angiographic position of right anterior oblique 30°/caudal 20° was used. After the procedure, arterial access was sealed using an arterial vascular closure device in all patients.

OAC was discontinued in all patients after device implantation, and combined treatment with acetylsalicylic acid and clopidogrel was recommended for all patients for a period of 3 months.

Brain MRI

Brain MRI was performed in all study patients within 24 hours before as well as after the LAAC procedure using 3-T MRI (Tim Trio, Siemens AG, Erlangen, Germany). Acquired sequences were high-resolution diffusion-weighted imaging (DWI) (TE = 93 ms; TR = 8,900 ms; matrix size = 192 × 192; field of view = 230 mm; slice thickness = 2.5 mm, 50 slice; b0 = 0 s/mm^2, b1 = 1,000 s/mm^2; gap = 0 mm), 3-dimensional fluid-attenuated inversion recovery (TE = 364 ms; TR = 5,000 ms; TI = 1,800 ms; matrix size = 256 × 256; field of view = 280 mm; slice thickness 1.1 mm, 144 slices), and T2* (TE = 20 ms; TR = 669 ms; matrix size = 320 × 320; field of view = 220 mm; slice thickness = 5 mm, 25 slices; gap = 0.5 mm). All examination results were read by 2 independent

Table 1 Baseline characteristics and serial neurologic and neurocognitive assessment of 23 study patients undergoing LAAC and serial brain MRI

	All patients (n = 23)	Patients with acute brain lesions (n = 12)	Patients without acute brain lesions (n = 11)	*P* value
Age (yrs)	74.1 ± 10.5	74.2 ± 12.2	7.0 ± 8.9	.64*
Male	16 (70)	9 (75.0)	7 (63.6)	.67†
Paroxysmal AF	9 (39.1)	5 (41.7)	4 (36.4)	1†
Persistent AF	9 (39.1)	5 (41.7)	4 (36.4)	1†
Permanent AF	5 (21.7)	2 (16.7)	3 (27.3)	.64†
Diabetes mellitus	10 (43.5)	6 (50.0)	4 (36.4)	.68†
Hypertension	23 (100)	12 (100)	11 (100)	—
CAD	11 (47.8)	6 (50.0)	5 (45.5)	1†
Renal failure	14 (60.9)	7 (58.3)	7 (63.6)	1†
History of stroke	6 (26.1)	4 (33.3)	2 (18.2)	.64†
History of ICB	12 (52.2)	8 (66.7)	4 (36.4)	.22†
Previous GI bleeding	9 (39.1)	4 (33.3)	5 (45.5)	.68†
Phenprocoumon	4 (17.4)	1 (8.3)	3 (27.3)	.32†
Novel oral anticoagulation	7 (30.4)	3 (25)	4 (36.4)	.67†
LA diameter (mm)	21.7 ± 3.9	21.7 ± 3.8	21.8 ± 3.9	.30
LAA flow velocity (cm/s)	0.50 ± 0.23	0.56 ± 0.23	0.43 ± 0.22	.15*
LAA chicken wing	6 (26.1)	2 (16.7)	4 (36.4)	.37
LAA windsock	3 (13.0)	0 (0)	3 (27.3)	.93
LAA cactus	7 (30.4)	5 (41.7)	2 (18.)	.37
LAA cauliflower	7 (30.4)	5 (41.7)	2 (18.)	.37
CHA_2DS_2-VASc score	4.1 ± 1.4	4.2 ± .1.3	4.1 ± 1.5	.80*
HAS-BLED score	3.8 ± 1.1	3.8 ± 1.2	3.73 ± .1,01	.97*
NIHSS score before LAAC	1.0 ± 1.68	0.67 ± 1.23	1.36 ± 2.06	.59*
NIHSS score after LAAC	1.22 ± 1.81	1.00 ± 1.35	1.45 ± 2.25	.95*
MoCA before LAAC	24.05 ± 4.64	23.50 ± 4.98	24.7 ± 4.37	.69*
MoCA after LAAC	23.23 ± 4.60	22.92 ± 5.09	23.60 ± 4.17	.92*

Values are given as mean ± SD or n (%).

AF = atrial fibrillation; CAD = coronary artery disease; HAS-BLED = Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly; ICB = intracranial bleed; GI = gastrointestinal bleed; LA = left atrium; LAA = left atrial appendage; LAAC = left atrial appendage closure; MoCA = Montreal Cognitive Assessment; MRI = magnetic resonance imaging; NIHSS = National Institutes of Health Stroke Scale. * = Student *t* test; † = χ^2 test.

neuroradiologists (JBF, KV), who were blinded to clinical information such as procedure duration and medical history.

Neurologic and cognitive assessment

The National Institutes of Health Stroke Scale (NIHSS) was assessed in all patients by a neurologist within 24 hours before and after LAAC.[16] Cognitive evaluation was performed using the Montreal Cognitive Assessment (MoCA) test.[17]

Statistical analysis

Continuous data are given as mean ± SD or median with first and third quartiles (Q1–Q3). Categorical variables are summarized with absolute and relative frequencies. Continuous data were analyzed using the Student *t* test or Wilcoxon Mann–Whitney test, and categorical data were analyzed using χ^2 analysis or Fisher exact test where appropriate. $P < .05$ was considered significant. Statistical analysis was performed using SPSS statistical software, version 23 (SPSS Inc, Chicago, IL).

Results

Detailed patient characteristics are given in Table 1. Successful LAAC without significant leakage was achieved in all patients using either an Amulet (n = 18), Occlutech (n = 3), or LAmbre (n = 2) device and was confirmed by TEE. Mean procedure time was 64.0 ± 21.1 minutes, and mean fluoroscopy time was 15.4 ± 7.6 minutes. Further procedural details are given in Table 2.

Brain MRI findings

Brain MRI performed within 24 hours before the procedure demonstrated age-related white matter changes (mean 8.9 ± 4.5 per patient) but no apparent lesions on DWI. Cerebral microbleeds were present in 14 of 23 patients (61%) before LAAC. Thirty-seven DWI lesions were detected in 12 of 23 patients (52%) within 24 hours after LAAC, mainly localized in the territory of the middle cerebral artery (Figure 1 and Table 3). Mean volume of these ABLs was 0.076 ± 0.062 mL. New-onset microbleeds were seen in 2 of 23 patients (8.7%) after the procedure. The results of DWI and fluid-attenuated inversion recovery sequence changes are given in Table 3.

The number of periprocedural LAA angiographies was significantly higher in patients with ABL than in patients without ABL (1.67 ± 0.65 vs 1.18 ± 0.41; $P = .048$). A correlation between the number of LAA angiographies

Table 2 Specific procedural details

	Overall group (N = 23)	Patients with acute brain lesions (n = 12)	Patients without acute brain lesions (n = 11)	*P* value
Total heparin dose (IU)	7,065 ± 1,854	7,000 ± 1,692	7,136 ± 2,099	.69*
Mean ACT (s)	291 ± 85.8	310.9 ± 81.1	273.0 ± 94.7	.38*
Time to ACT >250 s (min)	8.54 ± 4.8	8.15 ± 3.5	8.55 ± 3.4	.40
No. LAA angiographies	1.43 ± 0.59	1.67 ± 0.65	1.18 ± 0.41	.048†
No. of device repositioning	0.91 ± 1.24	1.33 ± 1.15	0.45 ± 0.69	.14*
LAA washout	20 (87.0)	10 (83.3)	10 (90.90)	1*
Angiography with pigtail	14 (60.9)	7 (58.3)	7 (63.6)	1*
Contrast agent (mL)	113 ± 38	121 ± 49	105 ± 16	.60*
SR during procedure	8 (35.0)	4 (33.3)	4 (36.4)	1*
Ostial LAA diameter	21.7 ± 3.9	22.1 ± 5.1	21.3 ± 2.1	.62*

ACT = activated clotting time; LAA = left atrial appendage; SR = sinus rhythm.
*Student *t* test; † = χ^2 square.

(Spearman correlation coefficient ρ = 0.615; *P* = .033), and the overall number of ABLs was found.

Neurologic and neurocognitive assessment

No patient reported novel neurologic or cognitive deficits after the procedure. Mean NIHSS score (1.0 ± 1.7 vs. 1.2 ± 1.8; *P* = .1) as well as mean MoCA score (24.1 ± 4.6 vs. 23.2 ± 4.6; *P* = .09) did not differ significantly before or after LAAC.

The MoCA test post-LAAC did not demonstrate significant differences of cognitive function in patients with and those without ABL (mean 23.5 ± 5.0 vs 24.7 ± 4.4; *P* = .70). The NIHSS score was similar in patients with and those without ABL after LAAC (mean 0.67 ± 1.2 vs 1.36 ± 2.1; *P* = .59) (Table 2).

Discussion

The main findings of the present study are as follows. (1) This is the first study to shows that the number of LAA angiographies during LAAC is associated with the incidence and number of ABLs. (2) MRI-detected ABLs after percutaneous LAAC are found in about one-half of all patients. (3)

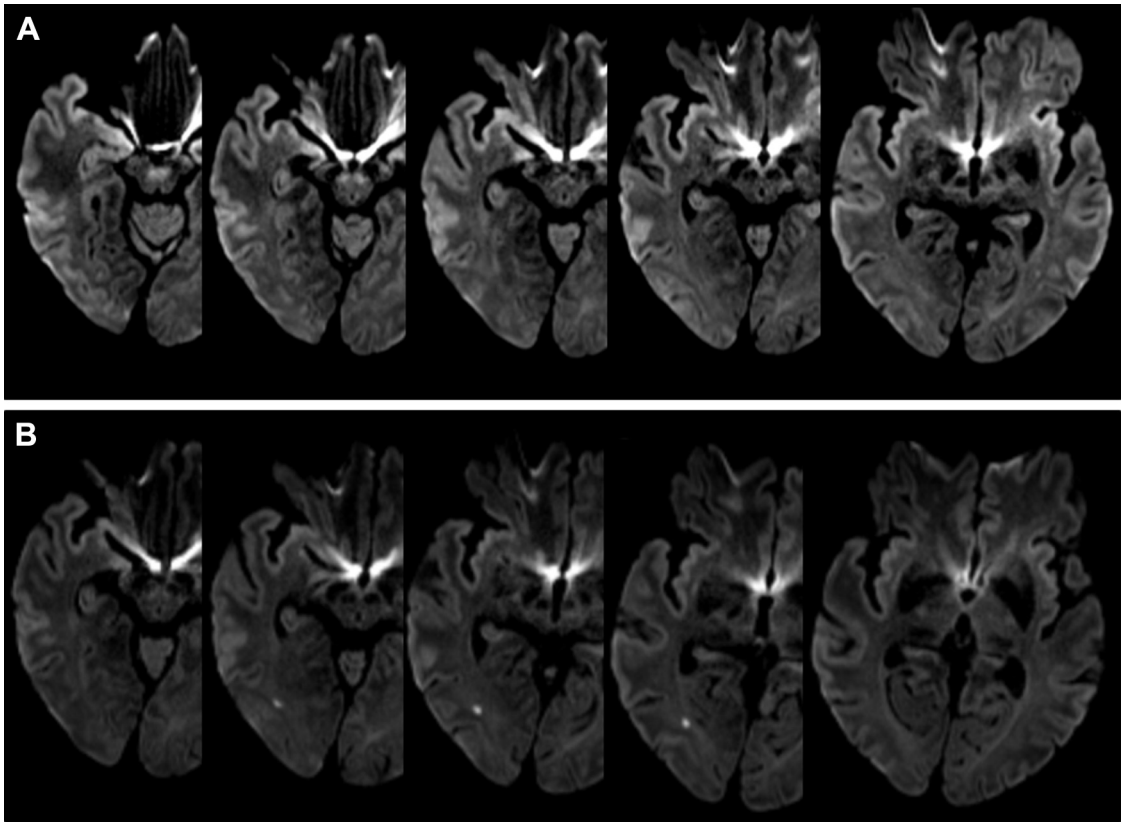

Figure 1 **A:** Preprocedural brain magnetic resonance imaging showing normal diffusion-weighted imaging (DWI). **B:** Postprocedural DWI showing an acute brain lesion in the right temporal lobe.

Table 3 Brain MRI findings in patients with acute brain lesions after LAAC

Patient no.	Age (yrs)	Implanted device	Acute brain lesion (n)	DWI sequence	FLAIR sequence	Location of acute brain lesion(s)	Overall volume of acute brain lesion(s) (mL)
1	87	Amulet	1	+	+	MCA left	0.018
2	88	Amulet	1	+	+	MCA right	0.029
3	82	Amulet	1	+	–	PCA left	0.018
4	47	Amulet	2	+	+	PICA left	0.040
5	72	Occlutech	2	+	+	MCA bilateral	0.032
6	59	Amulet	2	+	+	MCA left/PCA right	0.155
7	71	Amulet	1	+	+	MCA right	0.029
8	80	Amulet	1	+	+	MCA left	0.018
9	64	Amulet	1	+	+	PICA left	0.100
10	83	Amulet	14	+	–	MCA, PCA bilateral, SCA	0.101
11	75	Amulet	8	+	–	MCA bilateral, PCA left	0.291
12	81	Amulet	3	+	+	PCA and MCA left, PICA right	0.061

DWI = diffusion-weighted imaging; FLAIR = fluid-attenuated inversion recovery; LAAC = left atrial appendage closure; MCA = middle cerebral artery; MRI = magnetic resonance imaging; PCA = posterior cerebral artery; PICA = posterior inferior cerebellar artery; SCA = superior cerebral artery.

Although there was no novel neurologic deficit in any single patient or self-reported cognitive dysfunction after LAAC, the clinical impact of LAAC-related ABL has to be further determined.

The incidence of ABLs has been described for several cardiac interventional procedures and for LAAC.[10,18] However, there are discrepancies in the current literature regarding the incidence of ABLs after LAAC. Laible et al[18] found an incidence of 5%, whereas a recently published study reported an incidence of 32% of ABLs after LAAC.[19] Interestingly, the investigators of both studies used similar MRI settings.[18,19] The higher rate of ABLs in our study compared to that reported by other investigators can be explained by applying a high-resolution trace DWI based on an optimized ratio between b = 0 and b = 1,000 s/mm*2 conducted in 6 different directions (see Methods section). This leads to an optimal signal-to-noise ratio and minimized partial volume effects causing an increased detection rate of small lesions compared to standard DWI.[20] The more sensitive imaging modalities might explain why the incidence of ABLs is increased in our study population and nearly double that compared to the findings of other investigators.[19] However, our study for the first time reports that the incidence and number of ABLs were associated with the number of LAA angiographies, thereby raising a hypothesis for a mechanism underlying the observed embolizations.

Although the mechanisms leading to brain lesions during LAAC are not fully understood, several aspects of the procedure may promote brain lesions. During and after transseptal procedures, small air emboli may be caused by flushing the sheath or manipulation of the device during LAAC. Moreover, thrombus formation at the sheath or the device itself may cause ABL.[10–12] Therefore, ACT within 250–350 seconds were targeted in all of our patients. Heparin was administered after the transseptal puncture in this study without heparin administration from the start of the procedure. Currently, there is no general consensus on whether heparin should be administered before or after transseptal punctures. However, even though some centers administer heparin before the transseptal puncture, several centers prefer heparin administration after the transseptal puncture during LAA closure procedures or other electrophysiologic interventions.[5,21] Although ACTs in electrophysiologic procedures are increasingly targeted at >300 seconds, during LAA occluder implantation, a target ACT >250 seconds is still chosen in a large proportion of high-volume centers.[5,22] It might be reasonable to target higher ACTs >300 seconds; however, periprocedural pericardial effusion remains a significant complication of the LAA closure procedure. Further studies are needed to determine the optimal approach in these patients.

Importantly, we did not observe significant differences between ACTs or the time until ACT >250 seconds was reached in patients with and those without ABL (Table 2).

However, the incidence and number of LAA angiographies were associated with the incidence as well as the number of ABLs in the present study. Although LAA thrombi usually are ruled out by TEE before LAAC, small microthrombi cannot be excluded using this imaging modality. Therefore, it seems reasonable that LAA angiography itself is one of the main contributors to ABLs after LAAC, as the LAA is washed out during contrast injection for angiographic visualization. Thus, this finding seems to be of major importance for management of LAAC in the future.

Risk factors for periprocedural acute brain lesions

Factors previously shown to influence the risk of brain lesions during cardiac interventions include left atrial diameter and CHA_2DS_2-VASc score, as well as spontaneous echo contrast within the LAA.[11,13] Finally, procedure times and the peri-interventional anticoagulation regimen have been identified as major risk factors for the occurrence of brain lesions.[11] No significant differences were seen in these parameters or their association with ABL in our study.

Furthermore, LAA morphology has been suggested to be associated with brain lesions and the incidence of clinical stroke or transient ischemic attack.[23,24] In the present study, LAA morphology was not associated with the incidence of ABLs.

Study limitations

This was a prospective single-center pilot study with a limited number of patients. Therefore, final conclusions cannot be definitively drawn, and our results need to be validated in larger studies.

LAA angiography was performed via a pigtail catheter or a transseptal sheath. Although this potentially might influence the incidence of ABLs, there was no significant difference in the use of these LAA angiography modalities between patients with and those without ABLs.

Three different LAAC devices were investigated in an overall limited number of patients in this pilot study. Studies providing more focused evaluation of only 1 device are needed in the future.

It should be emphasized that because of the limited number of patients in this pilot study, the findings of neurocognitive function must be interpreted with caution. Therefore, the clinical impact of ABL after LAAC has to be further determined in future larger studies.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2017.11.015.

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