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ORIGINAL RESEARCH

Impact of Silent Cerebral Embolism during and after Left Atrial Appendage Occlusion on Long-Term Cognitive Function

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BACKGROUND: Left atrial appendage occlusion (LAAO) was associated with a high incidence of procedure-related silent cerebral embolism (SCE). There are limited data regarding the long-term cognitive trajectory of patients undergoing LAAO. The aim of our study was to comprehensively assess the acute and long-term impact of SCE during and after LAAO.

METHODS: Consecutive patients with atrial fibrillation referred for LAAO from the First Affiliated Hospital with Nanjing Medical University between February 2021 and February 2023 were included. All patients underwent magnetic resonance imaging and cognitive assessments before and within 48 hours after the procedure. These evaluations were also repeated at 45-day, 3-month, 6-month, and 1-year follow up.

RESULTS: Out of 75 patients included in the final analysis, 29 (38.7%) patients suffered from new SCE during LAAO. Patients with SCE exhibited a significant decline in cognitive function (Mini-Mental State Examination) immediately after the procedure (P<0.001), which was not reversible during 1-year follow-up (P<0.001). Additionally, with time going on, the gap in cognitive function between patients with and without SCE became wider (SCE × 1 year: B=−4.81 [95% CI, −5.58 to −4.05]; P<0.001). New-onset SCE was detected in 11 (14.7%) patients during the follow-up magnetic resonance imaging, which also showed a decline in cognitive function (P=0.004). The results in Montreal Cognitive Assessment scores were consistent with Mini-Mental State Examination.

CONCLUSIONS: LAAO-related SCE is associated with a marked impairment in cognitive function immediately after the procedure and is irreversible over a 1-year follow-up. New magnetic resonance-detected SCE during follow-up after LAAO would also be associated with a decline in cognitive function.

Key Words: anticoagulation ■ atrial fibrillation ■ cognitive function ■ left atrial appendage ■ silent cerebral embolism

Since the initial reports of silent cerebral embolism (SCE) of catheter-based interventions,[1–3] the awareness of SCE and its clinical implication has been significantly heightened. It is now widely recognized that SCE can occur in a variety of procedures involving the left heart system, including ablation for left ventricular premature ventricular contractions,[4] left atrial appendage occlusion (LAAO),[5] transcatheter aortic valve replacement,[6] and left-sided Wolff-Parkinson-White syndrome among others.[7] Although SCE are neurologically silent and radiologically reversible,[8,9] their clinical impact needs to be further investigated, followed by the optimization of periprocedural and long-term management. Accumulating evidence

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CLINICAL PERSPECTIVE

What Is New?

- Periprocedural silent cerebral embolism during left atrial appendage occlusion is associated with immediate cognitive decline post-procedure which remains irreversible over a 1-year follow-up period.
- Even after successful left atrial appendage occlusion, patients continue to face a 15% risk of new silent cerebral embolism, and an immediate decline in cognitive function has also been observed.

What Are the Clinical Implications?

- Percutaneous left atrial appendage occlusion has a high incidence (38.7%) of procedure-related silent cerebral embolism, measures should be taken to reduce the incidence of silent cerebral embolism regarding device refinement and skillful catheter manipulation.
- Periprocedural and long-term anticoagulation and antithrombotic strategies of patients with left atrial appendage occlusion should be further optimized.

Nonstandard Abbreviations and Acronyms

ACT	activated clotting time
LAAO	left atrial appendage occlusion
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
SCE	silent cerebral embolism

has linked SCE to an increased risk of long-term cognitive decline and dementia.[10,11] However, the acute and long-term impacts of peri-procedural SCE have not been fully grasped, with clear consensus on the implications of these magnetic resonance imaging (MRI)-detected lesions remaining elusive.[12–14]

LAAO, in particular, has become a prominent and crucial measure for stroke prevention in patients with atrial fibrillation.[15] Strikingly, our preliminary research indicated a surprisingly high incidence of periprocedural SCE during LAAO procedures (54.8%),[5] raising concerns about its potential clinical impacts. We presume that any brain parenchyma impairment would have functional impact, conspicuous or occult. The immediate and long-term cognitive outcomes of LAAO-related SCE should be investigated due to its high incidence.

However, there remained a significant knowledge gap in research regarding the long-term postprocedural cognitive trajectory of patients undergoing LAAO, particularly for those who experienced LAAO-related SCE. Prospective data on the development of new brain lesions in patients with atrial fibrillation (AF) after LAAO are also lacking. Consequently, our study aimed to fill this void by conducting frequent and comprehensive follow-ups, which included detailed MRI scans and cognitive function assessments, to establish the dynamic trajectory of cognitive impact of periprocedural SCE and to detected the residual risk of thromboembolism after LAAO. These findings are intended to provide valuable insights for refining periprocedural and postprocedural management for patients receiving LAAO.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

This prospective, observational study was performed at the First Affiliated Hospital of Nanjing Medical University between February 2021 and February 2023. Ethical approval was granted by the ethical committee of the First Affiliated Hospital of Nanjing Medical University, number 2022-SR-228. All enrolled patients provided written informed consent.

Consecutive patients with AF indicated to receiving Watchman implantation were enrolled. The inclusion criteria were as follows: (1) ≥18 years of age; (2) previous ischemic stroke or a CHA2DS2-VASc score ≥3; (3) unwilling or unable to take oral anticoagulant; (4) without baseline severe neurological or neurocognitive impairment (such as severe hemiplegia or limb dysfunction, vision/hearing impairments and impairment of understanding, expression or emotional regulation) and have the capacity to complete the cognitive function assessments; and (5) no contraindications to craniocerebral MRI scans.

Anticoagulation Strategy and Routine Preprocedural Examinations

All patients received uninterrupted anticoagulation therapy with rivaroxaban (15 mg) for at least 3 weeks before the procedure. The administration of rivaroxaban was sustained throughout the duration of the procedure. Left atrial thrombi were routinely screened by transesophageal echocardiography before the procedure. Patients routinely underwent preprocedural intracranial and carotid MR angiography screenings to exclude significant large artery atherosclerosis or stenosis.

Intravenous weight-adjusted heparin (100 IU/kg) was administered immediately after transseptal puncture and supplemented as needed to maintain a target activated clotting time (ACT) of ≥250 to 300 s during the whole procedure.[16,17] ACT was monitored every 10 to 15 minutes.

After the procedure, patients received a combination of oral anticoagulation using rivaroxaban (15 mg) and aspirin (100 mg) for 45 days and switched to clopidogrel (75 mg) and aspirin (100 mg) upon confirmation of adequate device stability and no significant peridevice leak or device-related thrombus at the 45-day transesophageal echocardiography until 6 months. After the 6 months, only aspirin 100 mg was continued indefinitely.

LAAO Procedures

The Watchman implantation technique has been previously described and the Watchman devices were all advanced, anchored and released in a standard way.[16] All procedures were performed under conscious sedation. The entire procedure including transseptal puncture, device positioning and releasing was guided by a combination of fluoroscopy intracardiac echocardiogram.

MRI Acquisition and Analysis

During hospitalization, all patients underwent a craniocerebral MRI with a 1.5-T unit and 2 mm slice thickness on the day before LAAO and within 48 hours after LAAO. Within 1 year after discharge, patients would also complete MRI examinations during each follow-up visit as part of the standard follow-up protocol. The detailed imaging protocol and definition of SCE have been previously described.[5] MR images were independently interpreted by 2 junior neuroradiologists who were blinded to the clinical characteristics of patients. In cases of discrepancy between their analysis, the data would be submitted to a senior neuroradiologists to make the final decision. All lesions were documented in terms of number, size, location, and changes observed.

Cognition Function Assessment

Cognitive function was measured by the same physician (blinded to the clinical and MR results) at baseline, within 48 hours after the procedure and at each follow-up visit within 1 year in all patients using the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) Chinese version.[18,19] MMSE and MoCA were conducted face to face, with trained investigators carrying out the assessments in strict accordance with established guidelines and protocols within 5 to 10 minutes and 10 to 15 minutes, respectively. The total score of both MMSE and MoCA was 30. Cognitive function of different domains was evaluated according to items of MoCA, including visuospatial and executive, naming, attention and concentration, language, abstraction, recall 5 words, and orientation to time and place. To maintain the accuracy of the evaluation, different alternative versions of test items were used for each cognitive function assessment during follow-up.

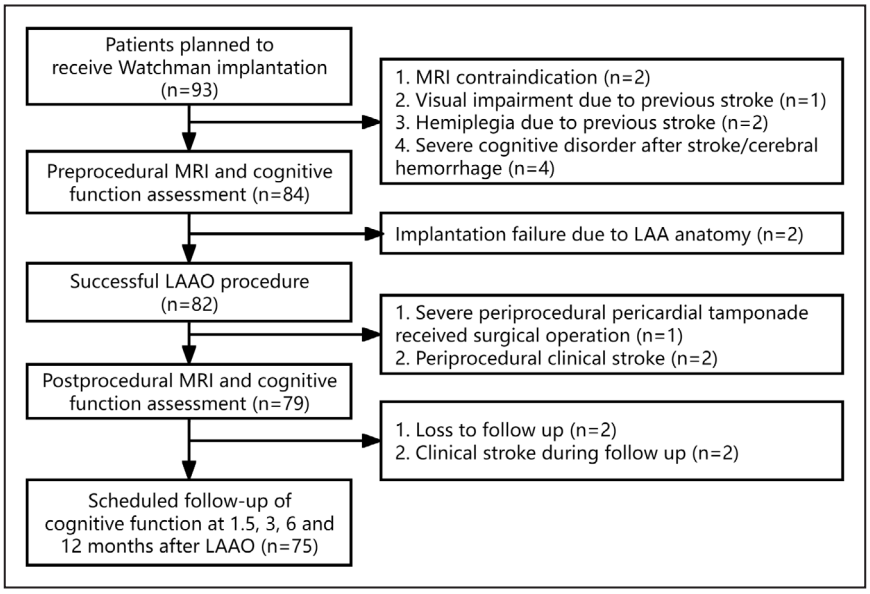

Figure 1. Flow chart.
LAA indicates left atrial appendage; LAAO, left atrial appendage occlusion; and MRI, magnetic resonance imaging.

Table 1. Baseline Characteristics

	Overall (n=75)	New SCE (n=29)	No SCE (n=46)	*P* value
Male sex	55 (73.3%)	22 (75.9%)	33 (71.7%)	0.900
Age, y	67.25±7.56	66.21±8.22	67.91±7.13	0.345
Body mass index, kg/m^2	24.75±2.98	24.53±2.56	24.88±3.23	0.616
Education				
Without education	3 (4.0%)	1 (3.4%)	2 (4.3%)	0.809
Primary school (≤6 years)	21 (28.0%)	7 (24.1%)	14 (30.4%)	
Secondary and above (>6 y)	51 (68.0%)	21 (72.4%)	30 (65.2%)	
Hypertension	49 (65.3%)	20 (69.0%)	29 (63.0%)	0.783
Coronary artery disease	25 (33.3%)	9 (31.0%)	16 (34.8%)	0.933
Diabetes	18 (24.0%)	7 (24.1%)	11 (23.9%)	1.000
Previous stroke	66 (88.0%)	28 (96.6%)	38 (82.6%)	0.149
Heart failure	1 (1.3%)	0 (0.0%)	1 (2.2%)	1.000
Paroxysmal atrial fibrillation	32 (42.7%)	13 (44.8%)	19 (41.3%)	0.952
CHA_2DS_2-VASc score	4.25±1.30	4.10±1.08	4.35±1.42	0.430
HAS-BLED score	2.35±0.76	2.31±0.66	2.37±0.83	0.746
Echocardiogram				
Left atrium diameter, mm	44.45±4.27	44.21±5.29	44.61±3.53	0.694
Left ventricular end diastolic dimension, mm	47.88±3.25	47.38±3.12	48.20±3.32	0.292
Left ventricular ejection fraction, %	62.55±3.67	62.31±3.86	62.71±3.58	0.646

SCE indicates silent cerebral embolism.

Neurological Examinations

Detailed neurological physical examinations were performed before and after LAAO by an experienced neurologist blinded to the clinical and MR results.

Follow-Up

The 1-year routine follow-up strategy included repeated transesophageal echocardiography at 45-day and 1-year follow-up, repeated neurological physical examinations, cognition function assessments, and MR scans at 45-day, 3-month, 6-month, and 1-year follow-up. A designated physician was responsible for conducting regular online follow-ups beyond the outpatient reviews. Patients were also required to promptly report any adverse events, including stroke, transient ischemic attack, major bleeding event, all-cause mortality, etc.

Statistical Analysis

Statistical analyses and visualization were performed using R, the statistical programming language (version 4.2.2).

Descriptive statistics were conducted using means±SD for continuous variables and proportions for categorical variables. Categorical variables were compared by the chi-square test or continuous correction chi-square test, and normally distributed continuous variables were compared using *t* test. We grouped the patients based on whether new SCE occurred after LAAO procedure and compared the baseline characteristics between the 2 groups.

Within each group, we used a paired *t* test to compare the differences in cognitive function at various time points to the baseline. Subsequently, we used a 2 independent samples *t*- est compared the differences in cognitive function between the 2 groups at each time point, which was used to assess intergroup differences. Given the potential correlation in repeated measures of cognitive function within individuals, we employed a generalized estimating equation model to address the correlations across time points (post-procedure, 45-day, 3-month, 6-month and 1-year follow-up), allowing for a more reliable exploration of the effect of SCE on cognitive function. First, in the Model 1, we adjusted the baseline cognitive function and time effects to explore the average effect of SCE on cognitive function. Subsequently, Model 2 extended this by introducing an interaction term between time and SCE to examine their combined effect. Finally, to further validate the reliability of the model, we adjusted all baseline data in Models 3 and 4 based on Models 1 and 2.

The analysis was performed with R package 'geepack' (version 1.3.3), which obviates the need for imputation of missing values. The calculated *P* values were considered significant at $P<0.05$.

Table 2. Within-Group and Between-Group Comparison of Cognitive Function

	Overall (n=75)	*P* value (within group)	No SCE (n=46)	*P* value (within group)	New SCE (n=29)	*P* value (within group)	*P* value (between group)
Baseline							
MMSE scores	25.57±3.02		25.24±2.95		26.10±3.11		0.230
MoCA total scores	21.57±3.36		20.98±3.01		22.52±3.72		0.053
Within 48 h after							
MMSE scores	24.64±3.26	<0.001	25.39±2.99	0.254	23.45±3.36	<0.001	0.011
MoCA total scores	19.91±3.49	<0.001	21.17±2.69	0.451	17.90±3.71	<0.001	<0.001
45 d follow-up							
MMSE scores	25.82±3.40	0.197	26.83±2.74	<0.001	23.96±3.74	0.001	0.001
MoCA total scores	22.20±3.54	0.099	23.64±2.80	<0.001	19.57±3.26	<0.001	<0.001
3 mo follow-up							
MMSE scores	26.02±3.42	0.233	27.52±2.01	<0.001	24.00±3.91	<0.001	<0.001
MoCA total scores	22.45±4.12	0.298	24.41±2.85	<0.001	19.80±4.15	<0.001	<0.001
6 mo follow-up							
MMSE scores	26.56±3.55	0.026	28.28±1.97	<0.001	23.50±3.74	0.001	<0.001
MoCA total scores	23.24±4.82	0.013	25.79±2.50	<0.001	18.86±4.74	<0.001	<0.001
12 mo follow-up							
MMSE scores	26.56±3.31	0.004	28.09±2.15	<0.001	24.14±3.42	<0.001	<0.001
MoCA total scores	23.12±4.49	0.003	25.50±2.99	<0.001	19.34±3.85	<0.001	<0.001

MMSE indicates Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; and SCE, silent cerebral embolism.

RESULTS

In total, 93 patients with AF admitted for LAAO procedures were consecutively enrolled, of whom 79 completed both preprocedure and postprocedure MRI as well as cognitive assessments. Two individuals were lost to follow-up (1 in the group with new SCE and 1 in the group with no SCE, missing rate: 3.3% (1/30) versus 2.1% (1/47), *P*=0.682), and 2 experienced clinical strokes during the follow-up period. A total of 75 patients were included in the final statistical analysis (Figure 1).

Baseline Characteristics

Participant characteristics are presented in Table 1, stratified by the incidence or absence of new SCE on postprocedural MRI. Overall, the analytic sample (N=75) consisted of 20 (27%) women. The mean age was 67.25±7.56 years, with an average body mass index of 24.75±2.98 kg/m2. Most of the participants were educated to secondary school or higher (68%). In addition, most of participants had persistent AF (57%) and a history of previous stroke (88%). No patient had significant large artery atherosclerosis or stenosis preprocedurally. No patients were identified with cerebral amyloid angiopathy (based on routine preprocedural intracranial and carotid MR angiography screenings) or with a history of hypertensive hemorrhages.

Cognitive function assessments were administered to all participants within 24 hours before the procedure, yielding an average MMSE score of 25.57±3.02 and an average MoCA score of 21.57±3.36. The baseline characteristics of the 2 groups were comparable, including CHA_2DS_2-VASc score (*P*=0.430), HAS-BLED score (*P*=0.746), education levels (*P*=0.809), baseline MMSE scores (*P*=0.230), and baseline MoCA scores (*P*=0.053).

MRI Results

In MRI conducted within 48 hours after LAAO, new-onset SCE was detected in 29/75 (38.7%) patients, with a total of 90 lesions identified; the average lesion number was 3.10±2.79. Of these, 88 lesions were no longer visible in the 45-day follow-up MRI (indicating lesion resolution). Additionally, 11/75 (14.7%) patients evaluated developed new-onset SCE during the follow-up, with a total of 16 new lesions. The average lesion number was 1.45±0.82. None of the patients exhibited stroke-related neurological symptoms. The distribution of SCEs during and after LAAO were shown in Figure S1.

Within-Group and Between-Group Comparison of Cognitive Function

The results for within-group and between-group comparisons at each time point were summarized in

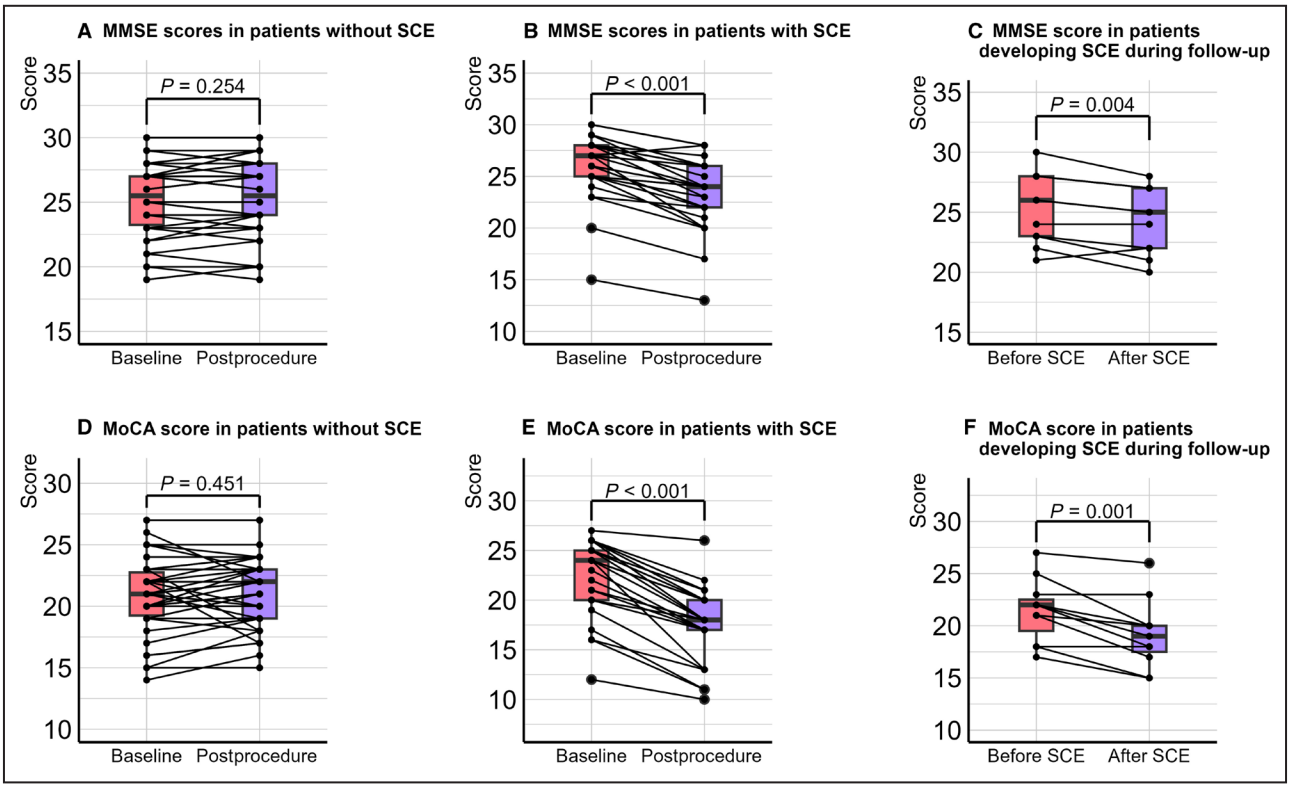

Figure 2. Acute impact of SCE on cognitive function.
Patients without SCE during LAAO showed no significant cognitive decline after the procedure (**A, D**). Patients with new SCE during LAAO showed significant cognitive decline after the procedure (**B, E**). Patients with new-onset SCE detected by the follow-up MRIs after LAAO also showed a drop in cognitive function (**C, F**). LAAO indicates left atrial appendage occlusion; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; MRI, magnetic resonance imaging; and SCE, silent cerebral embolism.

Table 2. Among all LAAO participants, the postprocedural MMSE scores decreased significantly compared with preprocedural levels (24.64±3.26 versus 25.57±3.02, *P*<0.001), then gradually recovered, surpassing preprocedural levels at the 6-month follow-up (*P*=0.026), and higher than baseline levels at 1-year follow-up (26.56±3.31 versus 25.57±3.02, *P*=0.004). In participants without periprocedural SCE, MMSE scores showed no decline (*P*=0.254) after LAAO and even improved compared with baseline during follow-up (*P*<0.001). Conversely, in patients with new SCE, MMSE scores decreased significantly after LAAO (*P*<0.001) and remained lower than baseline during the whole follow-up period (*P*<0.001). Similar results were also observed in MoCA scores. Additional results for specific scoring items are detailed in the Table S1.

Between-group comparisons were then executed. At each time point (postprocedure, 45-day, 3-month, 6-month, and 1-year follow-up), patients with new SCE exhibited lower MMSE and MoCA scores compared with patients without new SCE. Furthermore, 11 individuals experienced new MR-detected SCE during follow-up after discharge. We also compared the cognitive function before and after the occurrence of SCE, revealing a significant decline on cognitive function immediately after SCE (MMSE score: 25.36±2.94 versus 24.36±2.77, *P*=0.004; MoCA score: 21.45±3.01 versus 19.18±3.25, *P*=0.001) (Figure 2).

The Effects of SCE on Cognitive Function

Table 3 presented results for the generalized estimating equation model. In the multivariable generalized estimating equation model, SCE was inversely correlated with MMSE scores (B=−3.27 [95% CI, −3.67 to −2.86]; *P*<0.001). The results for MoCA scores were consistent with MMSE scores (B=−5.29 [95% CI, −5.89 to −4.70]; *P*<0.001). In the same model, the results of time effects suggested that overall cognitive function in the postoperative population initially declined and then gradually improved. We also included 5 interaction terms (SCE × each time point) in the fully adjusted model in order to examine the time change trend of cognitive function difference between the 2 groups. After LAAO, the interpretations of the generalized estimating equation analysis results were essentially based on the SCE and 5 postprocedure follow-up time point interaction terms, which estimated the additional

Table 3. Generalized Estimating Equations Analyses for the Comparisons of Differential Changes in Cognition Between the Group With New SCE and the Group With No SCE During Follow-Up

Outcomes	Variables	Model 1		Model 2	
		B (95% CI)	*P* value	B (95% CI)	*P* value
MMSE scores baseline	SCE	−3.27 (−3.67 to −2.86)	<0.001	−0.12 (−0.47 to 0.23)	0.496
	Time point				
	Post procedure	−0.93 (−1.34 to −0.52)	<0.001	0.15 (−0.1 to 0.41)	0.243
	45 d	0.30 (−0.31 to 0.91)	0.328	1.76 (1.35 to 2.17)	<0.001
	3 mo	0.57 (−0.05 to 1.18)	0.071	2.24 (1.76 to 2.72)	<0.001
	6 mo	0.92 (0.26 to 1.57)	0.006	2.62 (2.10 to 3.13)	<0.001
	1 y	0.99 (0.34 to 1.64)	0.003	2.85 (2.37 to 3.33)	<0.001
	Interaction term				
	SCE × post procedure			−2.81 (−3.43 to −2.18)	<0.001
	SCE × 45 d			−3.89 (−4.96 to −2.81)	<0.001
	SCE × 3 mo			−4.17 (−4.98 to −3.36)	<0.001
	SCE × 6 mo			−4.45 (−5.23 to −3.67)	<0.001
	SCE × 1 y			−4.81 (−5.58 to −4.05)	<0.001
MoCA scores baseline	SCE	−5.29 (−5.89 to −4.7)	<0.001	−0.31 (−0.78 to 0.17)	0.205
	Time point				
	Post procedure	−1.67 (−2.34 to −0.99)	<0.001	0.2 (−0.3 to 0.69)	0.442
	45 d	0.54 (−0.22 to 1.31)	0.164	2.77 (2.28 to 3.26)	<0.001
	3 mo	0.81 (−0.05 to 1.67)	0.064	3.25 (2.62 to 3.87)	<0.001
	6 mo	1.52 (0.56 to 2.48)	0.002	4.12 (3.53 to 4.72)	<0.001
	1 y	1.55 (0.57 to 2.52)	0.002	4.52 (3.99 to 5.06)	<0.001
	Interaction term				
	SCE × post procedure			−4.82 (−5.69 to −3.94)	<0.001
	SCE × 45 d			−5.86 (−6.77 to −4.94)	<0.001
	SCE × 3 mo			−6.3 (−7.33 to −5.26)	<0.001
	SCE × 6 mo			−6.86 (−8.15 to −5.58)	<0.001
	SCE × 1 y			−7.69 (−8.74 to −6.65)	<0.001

Model 1 was adjusted for the following variables: SCE, time, baseline MMSE/MoCA scores, age, sex, body mass index, atrial fibrillation type, hypertension, coronary artery disease, diabetes, stroke, heart failure, CHA2DS2-VASc score, HAS-BLED score, left atrium diameter, left ventricular end diastolic dimension, and left ventricular ejection fraction. Model 2 included all adjustments from Model 1, with the addition of an interaction term between SCE and time.

MMSE indicates Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; and SCE, silent cerebral embolism.

difference in the potential outcomes at same point in the group with new SCE compared with the group with no SCE. First, the improvement in MMSE scores became more pronounced with longer follow-up time, reaching its peak at the final follow-up (1 year: B=2.85 [95% CI, 2.37– 3.33]; *P*<0.001). However, this improvement was attenuated in patients with new SCE, resulting in an increasing gap in MMSE scores between these patients and patients without new SCE (SCE × 1 year: B=−4.81 [95% CI, −5.58 to −4.05]; *P*<0.001). We observed similar results in the model with MoCA score as the outcome, which confirmed the reliability of the findings. The overall trend of cognitive function of the 2 groups assessed by MMSE and MoCA was showed in Figure 3 and the subitem of MoCA was showed in Figure S2. The full results of the models were in the Table S2, which included some models with MoCA-specific project scores as the result.

DISCUSSION

This prospective, observational study was the first to focus on the dynamic changes in cognitive function following LAAO, with 6 cognitive assessments and 6 MRI examinations conducted periprocedural and throughout the first year after LAAO. The main findings are as follows: (1) periprocedural SCE was associated with a significant decline in postprocedural cognitive function that appeared to be nonreversible over the 1-year follow-up period; and (2) there remained a 15% incidence of SCE during follow-up even after LAAO, which was also associated with a significant cognitive decline.

Neurocognitive Trajectory After LAAO

In our study, patients undergoing LAAO experienced a transient decline in postprocedural cognitive function, as

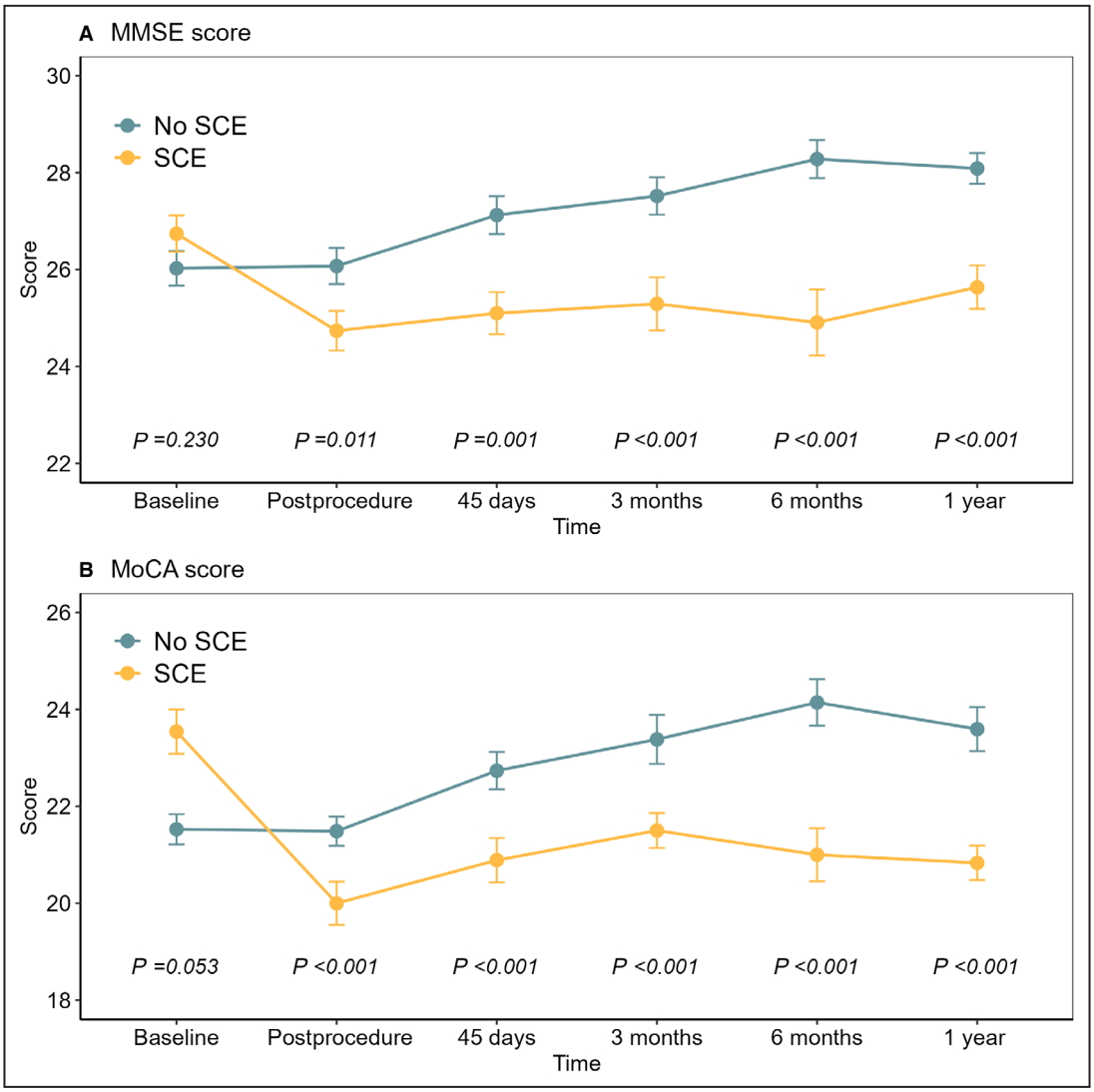

Figure 3. Changes in neurocognition.
The yellow line is the cognitive function curve of patients with SCE, the dark green line is the cognitive function curve of patients without SCE, and the horizontal coordinate is the time point: before procedure, 48 hours after procedure, 45 days, 3 months, 6 months, and 12 months after procedure. **A**, results of MMSE scores and (**B**) results of MoCA scores. The *P* values showed the between-group differences (group with new SCE vs group with no SCE) at each time point. MMSE indicates Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; and SCE, silent cerebral embolism.

consistently reflected by MMSE and MoCA scores. This initial decline gently reversed during follow-up, culminating in a statistically significant cognitive improvement at 6 months. This initial cognitive decline might be attributed to a multitude of factors, including anesthesia, preprocedural fasting, blood loss, microembolism, and surgical trauma, which closely resembled the neuropsychological findings after AF ablation[13] and cardiac surgeries.[20]

Patients with LAAO-related SCE (38.7%) demonstrated a significant postprocedural cognitive decline, which was irreversible throughout the 1-year follow-up. Conversely, patients without SCE showed no significant cognitive decline after LAAO, and their cognitive function even consistently improved during follow-up. These observations indicate that SCE might be a more critical factor in the reduction of cognitive function associated with LAAO when compared with other factors.

Although previous studies have reported negative outcomes in cognitive function after LAAO, a slight decline in mean MMSE/MoCA scores aligned with our findings.[21,22] Such statistically negative findings might be due to the small sample size. Likewise, minor increases were also observed in mean MMSE/MoCA scores at 3-month and 1-year follow-up.[15,22] However, higher SCE incidence (48%–52% versus 39%)caused

by lower periprocedural target ACT level (250 s versus 300 s) might have suppressed the overall trend for cognitive improvement, thereby diminished the observable cognitive benefits in patients without SCE.[17]

Neurocognitive Impact of New MR-Detected SCE During Follow-Up

Even after successful LAAO (without displacement or leaks), 15% of patients developed new SCE during follow-up, which was associated with further cognitive decline. This phenomenon underscores a persistent residual risk of thromboembolism in patients with AF even after the procedural safeguard of LAAO. With a 15% incidence of SCE under the recommended dual antiplatelet therapy regimen, the importance of post-LAAO anticoagulation management is underscored. The causal relationship of AF and long-term dementia had been shown by previous studies.[23,24] Although the evidence of LAAO in the prevention of disaster thromboembolism is clear,[25] AF-related microembolism still exists in patients with LAAO. This emphasizes the urgency of optimizing post-LAAO antithrombotic strategies to mitigate this risk.

Future Directions

Considering the adverse association between procedure-related SCE and acute and long-term cognitive function, it is important to recognize and take measures to minimize the risk of SCE. Our previous studies identified risk factors for SCE during LAAO, including LAAO placement time, periprocedural ACT levels, and CHA_2DS_2-VASc score.[5] Elevating the target ACT level from 250 s to 300 s could significantly reduce the incidence of periprocedural SCE.[17] Therefore, we should closely monitor ACT levels during the procedure while balancing the risk of bleeding and embolism to optimize anticoagulation intensity. Furthermore, fully assessing the morphology of LAA before LAAO to improve the success rate of a single release and reduce procedure duration might also be of great importance. Moreover, for patients with a high risk of thromboembolism or preexisting cognitive impairments, decision-making should be shared to better select the right patients for right procedure.

On the other hand, the study indicated that the overall population undergoing LAAO, and patients having LAAO without SCE, showed gradual improvement in long-term cognitive function. This suggests that repeated cognitive function assessments as a form of training might have a learning effect beneficial for enhancing certain aspects of cognitive function in patients. Therefore, for patients with AF who already have mild cognitive impairment or those with new SCE, regular cognitive function training might delay or reduce the occurrence of cognitive dysfunction. However, further studies are needed to confirm its effectiveness.

The high incidence of SCE and its impact on cognition function in patients with AF after LAAO also serve as an indication of the importance of standardized post-LAAO antithrombotic therapy. Larger randomized controlled trials are urgently needed to further investigate the optimal antithrombotic regimen after LAAO.

Limitations

First, this is a prospective single-center study with a relatively small sample size, which might limit the ability to generalize our results to other occlusive devices and other anticoagulants. Second, because the follow-up period of this study was 1 year, it is uncertain whether patients with SCE would recover some cognitive abilities over a longer term. Third, this is a cohort study without a control group, which may affect the clarity of the specific risk of SCE associated with LAAO.

CONCLUSIONS

In conclusion, procedure-related SCE during LAAO was associated with a marked and acute impairment in cognitive function and appeared nonreversible over a 1-year follow-up. The incidence of new MR-detected SCE during the follow-up after LAAO was 15%, which could be also associated with a significant decline in cognitive function.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S2
Figures S1–S2

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