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ORIGINAL RESEARCH

1-Year Clinical Outcomes and the Impact of Procedural Configurations in Left Atrial Appendage Occlusion Patients

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ABSTRACT

BACKGROUND The clinical performance of left atrial appendage occlusion (LAAO) as a procedure and the long-term impact of its varied implantation configurations and anticoagulation regimens remain unclear.

OBJECTIVES This study sought to provide data in routine practice from a prospective multicenter registry.

METHODS A total of 3,096 consecutive patients from 39 Chinese centers undergoing LAAO were enrolled between April 1, 2019, and October 31, 2020.

RESULTS The baseline CHA_2DS_2-VASc and HAS-BLED scores were 4.0 ± 1.8 and 2.4 ± 1.2, respectively; mean age was 69 ± 9 years. One-year follow-up was completed in 3,013 (97.8%) patients. The ischemic endpoint of death, stroke, and systemic embolism occurred in 133 (4.51%) patients, and life-threatening, disabling, or major bleeding occurred in 71 (2.36%) patients. After inverse probability of treatment weighting, no significant association was found between anesthesia type (moderate sedation vs general anesthesia) or image guidance (transesophageal/intracardiac echocardiography vs fluoroscopy) and ischemic or bleeding events. In 1,295 (42.0%) cases, LAAO combined with catheter ablation was associated with a significantly lower rate of death, stroke, or systemic embolism than LAAO only (3.5% vs 5.2%, inverse probability of treatment weighting HR: 0.68; 95% CI: 0.47-0.99). The most common post-LAAO antithrombotic regimen was warfarin/direct oral anticoagulant monotherapy for 45 days, followed by single-/dual-antiplatelet therapy (38.1%).

CONCLUSIONS In Chinese centers, patients undergoing LAAO had low rates of ischemic and bleeding events at 1 year. Combining LAAO with catheter ablation was associated with a lower rate of ischemic events than LAAO only. (Registry to Evaluate Chinese Real-World Clinical Outcomes in Patients With Atrial Fibrillation Using the Watchman Left Atrial Appendage Closure Technology [RECORD]; NCT03917563) (JACC Asia. 2024;4:777-790) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CA = catheter ablation

CTA = computed tomography angiography

DAPT = dual-antiplatelet therapy

DOAC = direct oral anticoagulation

DRT = device-related thrombus

ICE = intracardiac echocardiography

IPTW = inverse probability of treatment weighting

LAA = left atrial appendage

LAAO = left atrial appendage occlusion

OAC = oral anticoagulation

RCT = randomized controlled trial

SE = systemic embolism

TEE = transesophageal echocardiography

Percutaneous left atrial appendage occlusion (LAAO) is a nonpharmacologic stroke prevention strategy for patients with nonvalvular atrial fibrillation (AF) who have contraindications or are unsuitable for long-term oral anticoagulation (OAC).[1,2] However, the pivotal randomized controlled trials (RCT)[3-5] and registries[6-11] investigating LAAO were mostly conducted in U.S. or European sites and primarily enrolled White populations (between 92% and 94%). The RECORD (Registry to Evaluate Chinese Real-World Clinical Outcomes in Patients With Atrial Fibrillation Using the Watchman Left Atrial Appendage Closure Technology; NCT03917563) was a real-world cohort study that enrolled approximately 3,000 Chinese patients, documenting the safety and efficacy profiles of LAAO as a procedure. We have reported that, at 30 days, the periprocedural rate of death, stroke, and systemic embolism was 0.5%.[12]

According to expert consensus on percutaneous LAAO, transesophageal echocardiography (TEE) or intracardiac echocardiography (ICE) is recommended as the standard imaging guidance.[13] However, LAAO planning and guidance[14,15] have evolved over time, with a greater understanding of the complex and variable anatomy of the left atrial appendage and how imaging should guide intervention. In the 30-day report of RECORD,[12] we observed that LAAO was guided by fluoroscopy alone in 16.0% of cases. In addition, we also found that 42.0% underwent LAAO combined with radiofrequency ablation or cryoablation for AF (combined procedure treatment), despite the recent Society for Cardiovascular Angiography and Interventions/Heart Rhythm Society Expert Consensus Statement on LAAO,[16] which suggests that combined procedures of LAAO with structural interventions or pulmonary vein isolation should not be routinely recommended because of a lack of evidence. The long-term clinical performance of LAAO as a procedure and the impact of these varied procedural configurations and treatment strategies remain debated and require further documentation.

The RCTs[3,4] have stipulated the antithrombotic regimens post-LAAO and were subsequently supported by guidelines.[2] Briefly, patients undergoing LAAO were discharged on warfarin and aspirin for 45 days; if there was no leak of >5 mm, antithrombotic strategies could switch to dual-antiplatelet therapy (DAPT) for 6 months, followed by aspirin thereafter. Although more than one-half of LAAO patients (57.7%) in the United States were discharged with aspirin plus (direct) OAC ([D]OAC)[17] and most patients (73%) in Europe were prescribed without (D)OAC,[8] RECORD observed substantial deviations from the standardized protocols: 78.9% of Chinese patients received (D)OAC monotherapy in the initial 45 days. Whether these varied regimens are associated with different long-term outcomes is unclear.

To address these gaps in knowledge, in the current study, we report the 1-year clinical outcomes of RECORD, explored their associations with procedural techniques, and investigated the anticoagulation patterns at discharge, 45 days, 6 months, and 12 months.

METHODS

STUDY POPULATION. The study outline has been previously described in detail.[12] In brief, RECORD (NCT03917563) was a multicenter, prospective cohort study that included 3,096 patients from 39 centers in China, conducted between April 1, 2019, and October 31, 2020. Consecutive patients from each participating center who received the left atrial appendage (LAA) closure device (Watchman generation 2.5) and were of legal age to provide informed consent were recruited in this registry. Patients who were participating in other trials, declined to provide informed consent, or refused to participate were excluded. Peri- and intraprocedural techniques and

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postprocedural medications were left to the operator's discretion. A total of 159 operators, with varying levels of experience implanting the device, participated in the study.

This cohort study adhered to the international standards for scientific research and the principles of the Declaration of Helsinki. Central (Ethics Committee of Xijing Hospital) or local Ethics Committee approval was obtained in all participating centers. All participants provided informed consent before the procedure.

OUTCOMES. Events, including any death, stroke, systemic embolism (SE), transient ischemic attack, readmission, device-related thrombosis, peridevice leak, and bleeding events, were collected. The rates of device/technical/procedural success, periprocedural complications, and adverse events at 30 days post-LAAO have been reported previously.[12] Death, stroke, SE, and bleeding were adjudicated by an independent Clinical Event Committee comprising 5 physicians with expertise in electrophysiology and/or interventional cardiology. The adjudication of events was based on the definitions outlined in the consensus document on percutaneous LAAO: the Munich consensus document on definitions, endpoints, and data collection requirements for clinical studies.[18] Bleeding was evaluated by both the Munich consensus document criteria[18] and the Bleeding Academic Research Consortium criteria.[19] Anticoagulation patterns were recorded at discharge, 45 days, 6 months, and 12 months post-LAAO.

FOLLOW-UP. Follow-up visits were scheduled at 45 days (±14 days), 6 months (±30 days), and 12 (±30 days) months after the LAAO procedure. These visits were preferably conducted onsite; however, if patients were unable or unwilling to visit the outpatient clinic, the scheduled visit could be conducted via telephone, with the exception of the 45-day and 1-year visits. Similar to the previous study,[8] the timing of LAA imaging follow-up was recommended at 45-day and/or 12-month visits, based on each institution's standard practice.

STATISTICAL ANALYSIS. The sample size was determined by the objective of consecutively enrolling all available cases at each participating center during the 18-month study enrollment course to provide sufficiently precise estimates of rare adverse events, rather than based on power requirements for a formal hypothesis test. The initial sample size was set at 1,050. However, this target was quickly achieved, and the Steering Committee then decided to continue enrollment until the planned study period concluded. Eventually, 3,086 participants were enrolled.

Continuous variables with normal distribution are expressed as the mean ± SD and were compared using Student's *t*-test, and those with a skewed distribution are described as the median (IQR) and were assessed by the Wilcoxon rank sum test. Categorical data are presented as absolute numbers and proportions and were compared using the Fisher exact test. All reported outcomes were based the first occurrence of the event and were estimated using the Kaplan-Meier method. Cox proportional hazards regression models were used to estimate HRs for each outcome at the specified timepoints. The proportional hazards assumption was checked using Schoenfeld residuals and visual assessment of log(−log) plots, and the assumption was met in all models. To reduce confounding bias related to baseline characteristics when comparing procedural configurations, 2 statistical approaches were applied: multivariable adjustment and inverse probability of treatment weighting (IPTW). The variables included in the multivariable adjustment or IPTW are provided in the Supplemental Appendix. There was no formal correction for multiple testing, taking into account the observational nature of the study.[20] Analyses were performed using SAS version 9.4 (SAS Institute) and R project version 4.1 (R Foundation). A 2-sided *P* value of <0.05 was considered statistically significant.

RESULTS

BASELINE CHARACTERISTICS. From April 1, 2019, to October 31, 2020, a total of 3,569 consecutive patients planned for LAAO were screened across the 39 participating centers. After applying exclusions (Supplemental Figure 1), 3,096 participants were enrolled in the study. Of these, 3,082 participants successfully received an LAAO implant, and 3,013 (97.8%) completed the 1-year follow-up (2,778 through clinic visits and 235 through phone contact). Among them, 1,831 (65.9%) underwent computed tomography angiography (CTA) or TEE examinations.

Baseline demographics are summarized in **Table 1**, categorized by the occurrence of death, stroke, and systemic embolism (SE). The mean age of participants was 69.1 ± 9.4 years, and 42.5% were female. The mean CHA_2DS_2-VASc score was 4.0 ± 1.8, and the mean HAS-BLED score was 2.4 ± 1.2. Procedures were performed under moderate sedation in 41.6% of cases. Intraprocedure image guidance was performed using TEE in 81.0% of cases, fluoroscopy alone in 16.0%, and ICE in 3.1%. In 42.0% of cases, the

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TABLE 1 Baseline Characteristics

	Total (N = 3,082)	Death, Stroke, and SE (-) (n = 2,949)	Death, Stroke, and SE (+) (n = 133)	*P* Value
Demographic characteristics				
Age, y	69.1 ± 9.4	68.93 ± 9.3	73.26 ± 9.2	<0.001
≥75 y	908 (29.5)	842 (28.6)	66 (49.6)	<0.001
Male	1,771 (57.5)	1,689 (57.3)	82 (61.7)	0.363
Body mass index, kg/m^2	24.83 ± 3.5	24.85 ± 3.5	24.34 ± 4.0	0.122
Heart rate, beats/min	81.91 ± 20.4	81.85 ± 20.4	83.35 ± 22.2	0.408
Diabetes	714 (23.2)	669 (22.7)	45 (33.8)	0.004
Previous stroke or TIA	1,411 (45.8)	1,331 (45.1)	80 (60.2)	0.001
Ischemic stroke or TIA	1,373 (44.5)	1,297 (44.0)	76 (57.1)	0.004
Hemorrhagic stroke	106 (3.4)	101 (3.4)	5 (3.8)	0.524
Hypertension	2,120 (68.8)	2,012 (68.2)	108 (81.2)	0.007
Coronary artery disease	875 (28.4)	833 (28.2)	42 (31.6)	0.464
Previous PCI	326 (10.6)	303 (10.3)	23 (17.3)	0.023
Previous CABG	46 (1.5)	41 (1.4)	5 (3.8)	0.066
Vascular disease[a]	1,674 (54.3)	1,589 (53.9)	85 (63.9)	0.029
Current smoker	333 (10.8)	318 (10.8)	15 (11.3)	0.923
Alcohol abuse	168 (5.5)	163 (5.5)	5 (3.8)	0.494
Chronic heart failure	462 (15.0)	429 (14.5)	33 (24.8)	0.002
LVEF, %	60.05 ± 8.3	60.12 ± 8.3	58.53 ± 9.6	0.040
Abnormal thyroidal function	132 (4.3)	132 (4.5)	0 (0.0)	0.057
Abnormal renal function	72 (2.3)	61 (2.1)	11 (8.3)	<0.001
Abnormal liver function	51 (1.7)	46 (1.6)	5 (3.8)	0.110
Bleeding history or predisposition[b]	313 (10.2)	293 (9.9)	20 (15.0)	0.079
Concomitant use of drugs	1,034 (33.5)	975 (33.1)	59 (44.4)	0.009
Classification of AF				0.743
Paroxysmal	1,245 (40.4)	1,196 (40.6)	49 (36.8)	
Persistent	1,270 (41.2)	1,211 (41.1)	59 (44.4)	
Long-standing persistent (>1 y)/permanent	567 (18.4)	542 (18.4)	25 (18.8)	
$CHADS_2$ score	2.3 ± 1.4	2.3 ± 1.4	3.1 ± 1.4	<0.001
CHA_2DS_2-VASc score	4.0 ± 1.8	3.9 ± 1.8	4.9 ± 1.8	<0.001
HAS-BLED score	2.4 ± 1.2	2.4 ± 1.2	3.1 ± 1.1	<0.001
ATRIA score	6.2 ± 3.0	6.2 ± 3.0	7.6 ± 2.5	<0.001
Procedural characteristics				
Recaptured (≥2 times) before release	252 (8.2)	240 (8.1)	12 (9.0)	0.840
Devices used	3,187 (1.03 per patient)	3,053 (1.04 per patient)	134 (1.01 per patient)	0.003
Device size, mm				
21	188 (6.1)	180 (6.1)	8 (6.0)	
24	634 (20.6)	615 (20.9)	19 (14.3)	
27	918 (29.8)	877 (29.7)	41 (30.8)	
30	714 (23.2)	679 (23.0)	35 (26.3)	
33	633 (20.5)	603 (20.4)	30 (22.6)	
Anesthesia				0.111
General anesthesia	1,799 (58.4)	1,712 (58.1)	87 (65.4)	
Moderate sedation	1,283 (41.6)	1,237 (41.9)	46 (34.6)	
Imaging guidance				0.759
TEE/ICE	2,590 (84.0)	2,480 (84.1)	110 (82.7)	
Fluoroscopy	492 (16.0)	469 (15.9)	23 (17.3)	
Combined procedures				
Radiofrequency ablation/cryoablation	1,295 (42.0)	1,251 (42.4)	44 (33.1)	0.041
Cryoablation	350 (11.4)	337 (11.4)	13 (9.8)	
Radiofrequency ablation	945 (30.7)	914 (31.0)	31 (23.3)	
Others[c]	154 (5.0)	150 (5.1)	4 (3.0)	0.383

Values are mean ± SD, or n (%). N = 3,082 except for body mass index (n = 2,842), LVEF (n = 2,774), $CHADS_2$ score (n = 3,065), CHA_2DS_2-VASc score (n = 3,065), HAS-BLED score (n = 3,068), and ATRIA score (n = 3,068). [a]Vascular disease includes previous myocardial infarction, peripheral artery disease, or aortic plaque, defined according to the CHA_2DS_2-VASc score. [b]Bleeding history or predisposition includes previous major hemorrhage or anemia or severe thrombocytopenia, defined according to the HAS-BLED score. [c]Others included atrial septal defect/patent foramen ovale occlusion (n = 78), percutaneous coronary intervention/percutaneous transluminal coronary angioplasty (n = 54), pacemaker implantation (n = 8), percutaneous mitral valvuloplasty (n = 5), transcatheter aortic valve replacement (n = 2), femoral artery stent implantation (n = 1), implantation of vena cava filter (n = 1), splenic artery angiography (n = 1), renal angiography (n = 1), radiofrequency ablation of supraventricular tachycardia (n = 1), and electrocardiogram event recorder implantation (n = 1).

AF = atrial fibrillation; CABG = coronary artery bypass graft; ICE = intracardiac echocardiography; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; SE = systemic embolism; TEE = transesophageal echocardiography; TIA = transient ischemic attack.

percutaneous LAAO was combined with 1-stage radiofrequency ablation or cryoablation.

CLINICAL OUTCOMES AT 1-YEAR FOLLOW-UP. At 1 year, the composite endpoint of death, stroke, and systemic embolism occurred in 133 (4.51%) patients, consisting of 68 (2.31%) deaths, 52 (1.79%) ischemic strokes, 24 (0.82%) hemorrhagic strokes, and 4 (0.13%) systemic embolisms (**Table 2**). Device-related thrombus (DRT) occurred in 45 (2.48%) patients. Complete sealing was achieved in 75.5% of patients (Supplemental Table 1). The results of subgroup analyses according to demographic risk factors are shown in Supplemental Figure 2. At the 1-year follow-up, the AF recurrence rate was 27.5% in patients who had undergone 1-stage radiofrequency ablation or cryoablation.

IMPACTS OF THE VARIABLE COMPONENTS OF PROCEDURAL PERFORMANCE. The baseline characteristics according to procedural configurations of LAAO are provided in Supplemental Table 2, and the impact of these procedural configurations on 1-year clinical outcomes are shown in **Table 3**, **Figure 1**, and the **Central Illustration**. There was no significant difference between general anesthesia or moderate sedation or between imaging guidance by fluoroscopy or TEE/ICE regarding the ischemic endpoint of death, stroke, or SE; or the bleeding endpoint of any life-threatening, disabling, or major bleeding; or the net adverse event by combining the ischemic and bleeding outcomes (**Figures 1A to 1F**). Compared with site-reported complete sealing of the LAA during the procedure, incomplete sealing was associated with a higher risk of the net adverse event, including death; stroke; SE; or life-threatening, disabling, or major bleeding (5.7% vs 8.5%; HR_{IPTW}: 1.55; 95% CI: 1.01-2.39; $P = 0.044$) (**Figure 1I**).

In addition, we found that the Kaplan-Meier curve, which showed the cumulative event rate of death, stroke, or SE, began to diverge at 6 months between the strategies of combining LAAO with catheter ablation (CA) and performing LAAO only. The combined procedure strategy was associated with a significantly lower rate of death, stroke, or SE at 1 year (3.5% vs 5.2%; HR_{IPTW}: 0.68; 95% CI: 0.47-0.99; $P = 0.044$) (**Figure 1J**). Exploratory analyses showed that LAAO plus CA in patients with AF diagnosed within 1 year (AF ≤1 year) was associated with the lowest rates of death, stroke, and SE compared with LAAO plus CA in the AF > 1-year group and LAAO only group (3.1% vs 4.0% vs 5.2%; $HR_{adjusted\ vs\ LAAO\ plus\ CA\ in\ AF\ >1\ year}$: 1.26; 95% CI: 0.69-2.28; $P = 0.452$; $HR_{adjusted\ vs\ LAAO\ only}$: 1.66; 95% CI:1.01-2.71; $P = 0.044$) (Supplemental Table 3, Supplemental Figure 3).

TABLE 2 Clinical Events at 1 Year After LAAO

	Events	Event Rates (95% CI)
Death, stroke, systemic embolism	133/3,082	4.51 (3.76-5.26)
Death; stroke; systemic embolism; any life-threatening, disabling, or major bleeding	177/3,082	5.95 (5.09-6.80)
Death; stroke; systemic embolism; BARC 2, 3, or 5 bleeding	221/3,082	7.42 (6.47-8.36)
Individual components		
Death	68/3,082	2.31 (1.76-2.85)
Cardiovascular death	61/3,082	2.08 (1.56-2.60)
Undetermined death	32/3,082	1.12 (0.73-1.50)
Noncardiovascular death	7/3,082	0.23 (0.06-0.40)
Stroke	74/3,082	2.54 (1.96-3.11)
Ischemic stroke	52/3,082	1.79 (1.30-2.28)
Hemorrhagic stroke	24/3,082	0.82 (0.49-1.15)
TIA	10/3,082	0.34 (0.13-0.54)
Systemic embolism	4/3,082	0.13 (0.00-0.26)
Readmission	954/3,082	31.84 (30.15-33.49)
Device-related thrombus	45/1,831	2.48 (1.76-3.19)
Incomplete sealing	449/1,831	24.52 (22.57-26.56)
Peridevice leak of 0-5 mm	439/1,831	23.98 (22.08-25.99)
Peridevice leak of ≥5 mm	10/1,831	0.55 (0.30-1.04)
Bleeding		
LAAO Munich consensus classification		
Any life-threatening, disabling, or major bleeding	71/3,082	2.36 (1.81-2.90)
Life-threatening or disabling bleeding	32/3,082	1.09 (0.71-1.46)
Major bleeding	39/3,082	1.27 (0.87-1.67)
Minor bleeding	47/3,082	1.60 (1.15-2.06)
BARC classification		
Type 2, 3, or 5	117/3,082	3.92 (3.22-4.62)
Type 3 or 5	48/3,082	1.61 (1.16-2.06)
Type 5	12/3,082	0.41 (0.18-0.65)
Type 3	36/3,082	1.20 (0.81-1.59)
Type 3a	4/3,082	0.13 (0.00-0.27)
Type 3b	12/3,082	0.39 (0.17-0.61)
Type 3c	20/3,082	0.68 (0.38-0.97)
Type 2	69/3,082	2.32 (1.77-2.86)

Event rates were provided based on Kaplan-Meier estimates. Patients who did not complete the 1-year follow-up were censored at the last contact.

BARC = Bleeding Academic Research Consortium; LAAO = left atrial appendage occlusion; TIA = transient ischemic attacks.

Compared with the absence of DRT, the presence of DRT was associated with a 3.7-fold increase in the risk of death, stroke, and SE (11.4% vs 2.9%; $HR_{adjusted}$: 3.72; 95% CI: 1.46-9.46; $P = 0.006$) (Supplemental Table 4, Supplemental Figure 4). The temporal relationship between DRT and the occurrence of death; stroke; SE; and any life-threatening, disabling, or major bleeding events is illustrated in Supplemental Figure 5.

ANTITHROMBOTIC MEDICATIONS. Antithrombotic medication regimens varied among patients (**Figure 2**, **Central Illustration**). We identified 5 major patterns (mutually exclusive categories, accounting for 87.9%

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TABLE 3 The 1-Year Clinical Outcomes According to Procedural Configurations

		Crude		Multivariable Adjusted		IPTW Adjusted	
	Events /Total (%)	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Death, stroke, and systemic embolism							
Moderate sedation	46/1,283 (3.7)	Ref		Ref		Ref	
General anesthesia	87/1,799 (5.1)	1.35 (0.95-1.94)	0.096	1.32 (0.92-1.88)	0.133	1.20 (0.73-1.96)	0.476
Fluoroscopy	23/492 (5.1)	Ref		Ref		Ref	
TEE/ICE	110/2,590 (4.4)	0.90 (0.57-1.40)	0.630	0.83 (0.53-1.31)	0.423	0.62 (0.37-1.03)	0.063
Complete sealing	115/2,770 (4.4)	Ref		Ref		Ref	
Incomplete sealing	18/312 (6.0)	1.40 (0.85-2.30)	0.187	1.36 (0.83-2.24)	0.223	1.44 (0.87-2.39)	0.158
LAAO only	89/1,787 (5.2)	Ref		Ref		Ref	
LAAO plus ablation	44/1,295 (3.5)	0.68 (0.47-0.98)	0.037	0.67 (0.47-0.97)	0.032	0.68 (0.47-0.99)	0.044
Any life-threatening, disabling, or major bleeding							
Moderate sedation	27/1,283 (2.1)	Ref		Ref		Ref	
General anesthesia	44/1,799 (2.5)	1.16 (0.72-1.88)	0.534	1.16 (0.72-1.87)	0.545	0.78 (0.44-1.39)	0.393
Fluoroscopy	6/492 (1.2)	Ref		Ref		Ref	
TEE/ICE	65/2,590 (2.6)	2.06 (0.89-4.76)	0.090	1.94 (0.84-4.50)	0.121	1.47 (0.59-3.65)	0.406
Complete sealing	61/2,770 (2.3)	Ref		Ref		Ref	
Incomplete sealing	10/312 (3.2)	1.48 (0.76-2.89)	0.250	1.50 (0.77-2.92)	0.237	1.38 (0.68-2.79)	0.368
LAAO only	43/1,787 (2.5)	Ref		Ref		Ref	
LAAO plus ablation	28/1,295 (2.2)	0.90 (0.56-1.44)	0.656	0.88 (0.55-1.43)	0.613	0.99 (0.61-1.62)	0.973
Death; stroke; systemic embolism; any life-threatening, disabling, or major bleeding							
Moderate sedation	66/1,283 (5.3)	Ref		Ref		Ref	
General anesthesia	111/1,799 (6.4)	1.20 (0.89-1.63)	0.236	1.18 (0.87-1.61)	0.277	0.98 (0.63-1.52)	0.922
Fluoroscopy	28/492 (6.1)	Ref		Ref		Ref	
TEE/ICE	149/2,590 (5.9)	1.00 (0.67-1.50)	0.983	0.93 (0.62-1.4)	0.739	0.73 (0.46-1.16)	0.184
Complete sealing	151/2,770 (5.7)	Ref		Ref		Ref	
Incomplete sealing	26/312 (8.5)	1.56 (1.03-2.36)	0.037	1.55 (1.02-2.35)	0.040	1.55 (1.01-2.39)	0.044
LAAO only	115/1,787 (6.7)	Ref		Ref		Ref	
LAAO plus ablation	62/1,295 (4.9)	0.74 (0.55-1.01)	0.060	0.72 (0.53-0.99)	0.043	0.73 (0.53-0.99)	0.048

ICE = intracardiac echocardiography; IPTW = inverse probability of treatment weighting; LAAO = left atrial appendage occlusion; Ref = reference; TEE = transesophageal echocardiography.

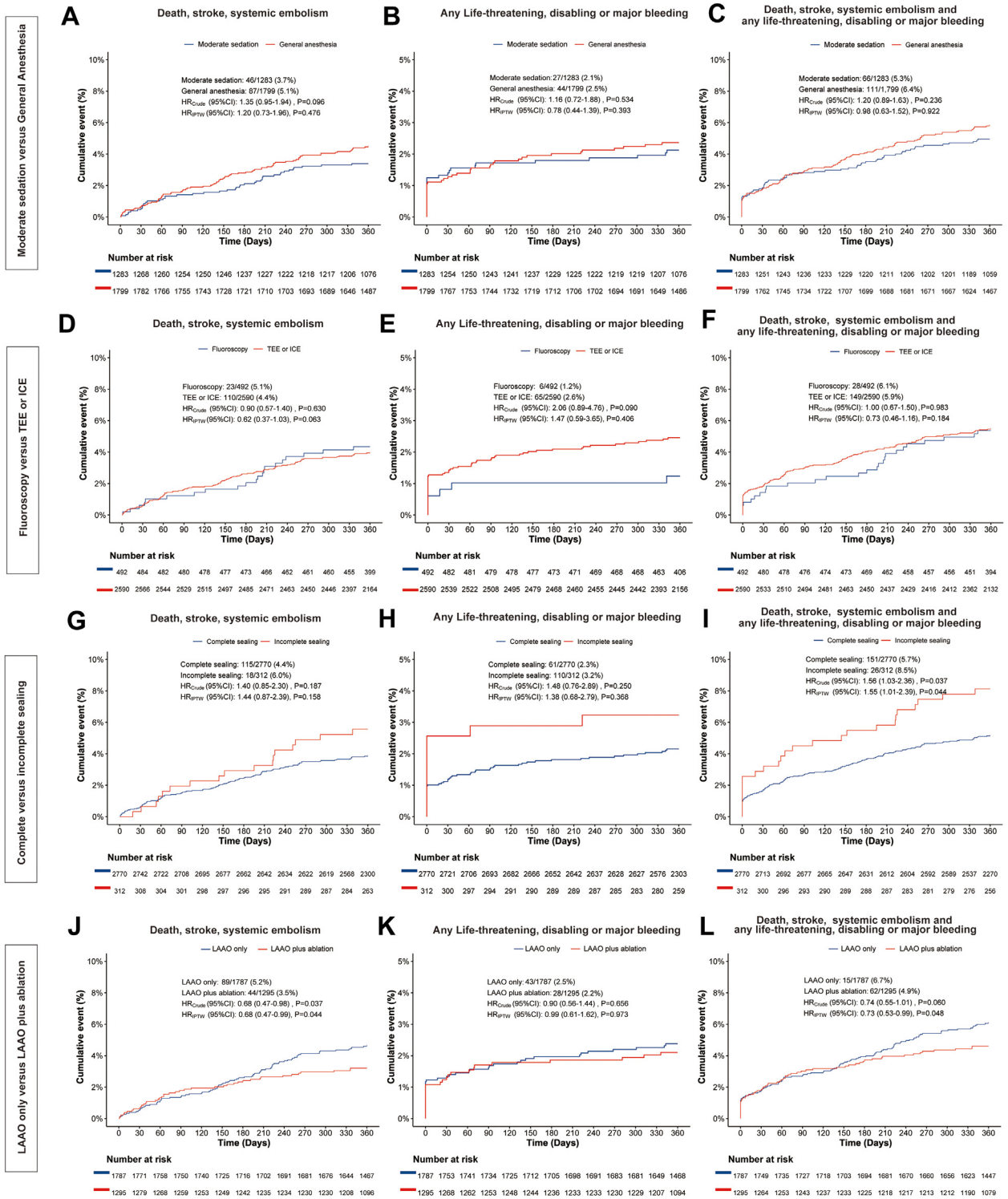
of the total population), presented in ascending order of the mean CHA_2DS_2-VASc score for each group (**Table 4**). The baseline characteristics of these groups are shown in Supplemental Table 5. The most common strategy (38.1%) was OAC | APT | APT, which corresponds to being discharged on warfarin or DOAC, switching to single-antiplatelet therapy or DAPT at 45 days, and continuing this regimen at the 6-month follow-up. The unadjusted rate of death; stroke; SE; or any life-threatening, disabling, or major bleeding was lowest among those treated with OAC | APT | APT (3.5%), followed by OAC + APT | APT | APT (4.5%), OAC | OAC | APT (5.0%), OAC | OAC | OAC (12.0%), and APT | APT | APT (12.3%).

Only 5.1% of patients received post-LAAO antithrombotic medications following the recommendations of the European Society of Cardiology AF guideline. Exploratory analyses showed no significant difference between the OAC | APT | APT and OAC + APT | APT | APT groups regarding ischemic events. However, in patients with a HAS-BLED of ≥3, the OAC | APT | APT regimen was associated with lower rates of life-threatening, disabling, or major bleeding events (1.1% vs 4.8%; $HR_{adjusted}$: 4.55; 95% CI: 1.31-15.81; $P = 0.017$) (Supplemental Table 6). Compared with OAC | APT | APT, the OAC | OAC | APT regimen was associated with a higher risk of life-threatening, disabling, or major bleeding (1.2% vs 2.5%; $HR_{adjusted}$: 0.50; 95% CI: 0.25-0.99; $P = 0.047$), whereas the risk of death, stroke, and SE was numerically similar (2.9% vs 3.0%; $HR_{adjusted}$: 1.05; 95% CI: 0.61-1.78; $P = 0.867$) (Supplemental Table 7). The patterns of antithrombotic medication, stratified by the presence or absence of coronary artery disease, are shown in Supplemental Figure 6.

DISCUSSION

In the real world, LAAO planning, guidance, and postprocedure antithrombotic medication strategies have evolved over time, often outpacing the guidelines[21]; however, supporting evidence remains

FIGURE 1 **Impacts of the Variable Components of Procedural Performance**



Kaplan-Meier curves showing the impact of various procedural components: (A to C) moderate sedation vs general anesthesia, (D to F) fluoroscopy vs TEE/ICE, (G to I) complete vs incomplete sealing, and (J to L) LAAO only vs LAAO plus ablation. These curves illustrate the composite endpoint of death, stroke, and systemic embolism; the endpoint of any life-threatening or major bleeding; or the composite endpoint of death, stroke, and systemic embolism and any life-threatening or major bleeding. ICE = intracardiac echocardiography; LAAO = left atrial appendage occlusion; TEE = transesophageal echocardiography.

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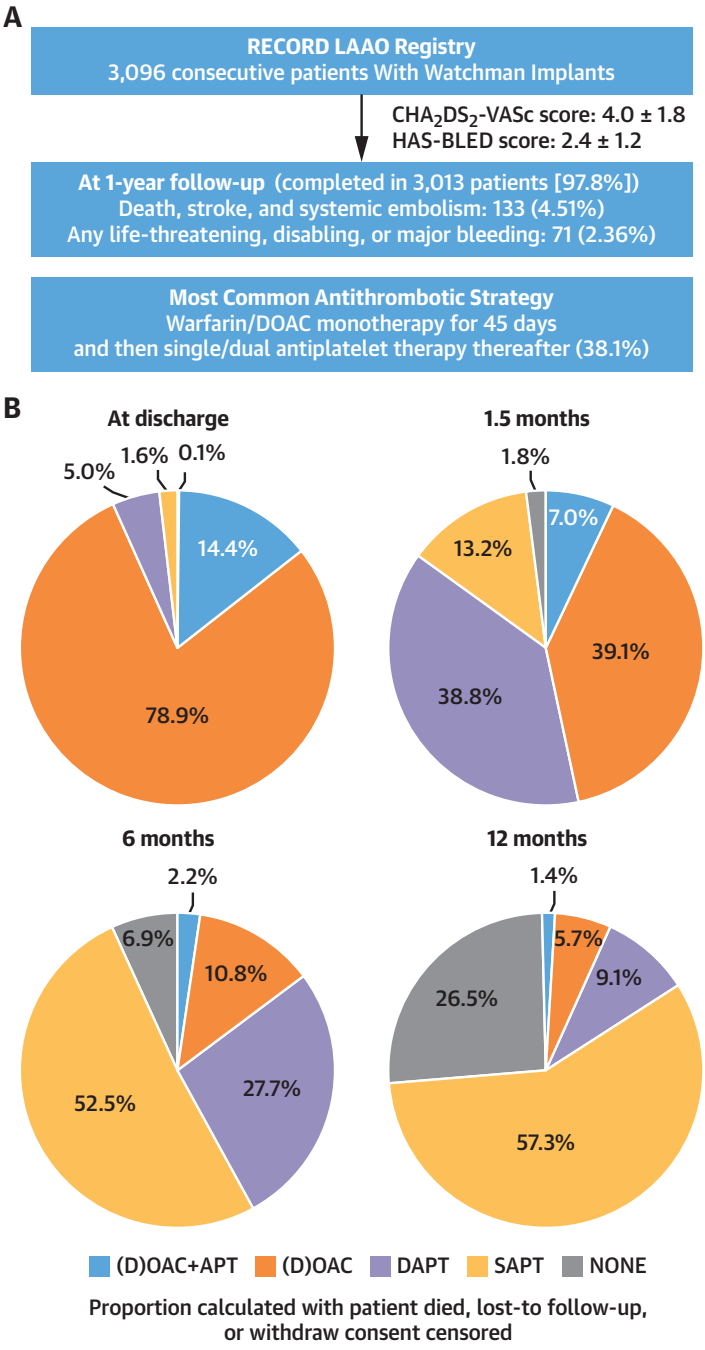
CENTRAL ILLUSTRATION **Procedure Configurations, Medications, and Outcomes Post-Left Atrial Appendage Occlusion**



Gao C, et al. JACC Asia. 2024;4(10):777–790.

(A) Brief study flow chart. A total of 3,096 patients were included in RECORD (Registry to Evaluate Chinese Real-World Clinical Outcomes in Patients With Atrial Fibrillation Using the Watchman Left Atrial Appendage Closure Technology), and 97.8% completed the 1-year follow-up. The cumulative event rate of death, stroke, or systemic embolism occurred in 4.5% of patients at 1 year. (B) Pie charts showing the type of antithrombotic medication of patients at discharge and 1.5, 6, and 12 months postprocedure. Warfarin or DOAC monotherapy was used in ~80% of patients at discharge, and single-antiplatelet therapy was used in ~60% of patients at 12 months postprocedure. (C) The impact of the periprocedural configurations is shown by the forest plot. Although the type of anesthesia or the type of imaging guidance had nonsignificant impact on the prognosis of patients at 12 months postprocedure, complete sealing (in comparison with incomplete sealing) and LAAO in combination with catheter ablation (in comparison with LAAO only) were both associated with lower risk of net adverse cardiovascular events (a composite endpoint including death; stroke; systemic embolism; and any life-threatening, disabling, or major bleeding). APT = antiplatelet therapy; DAPT = dual antiplatelet therapy; (D)OAC = (direct) oral anticoagulants; FU = follow-up; ICE = intracardiac echocardiography; IPW = inverse probability of treatment weighting; LAAO = left atrial appendage occlusion; SAPT = single-antiplatelet therapy; TEE = transesophageal echocardiography.

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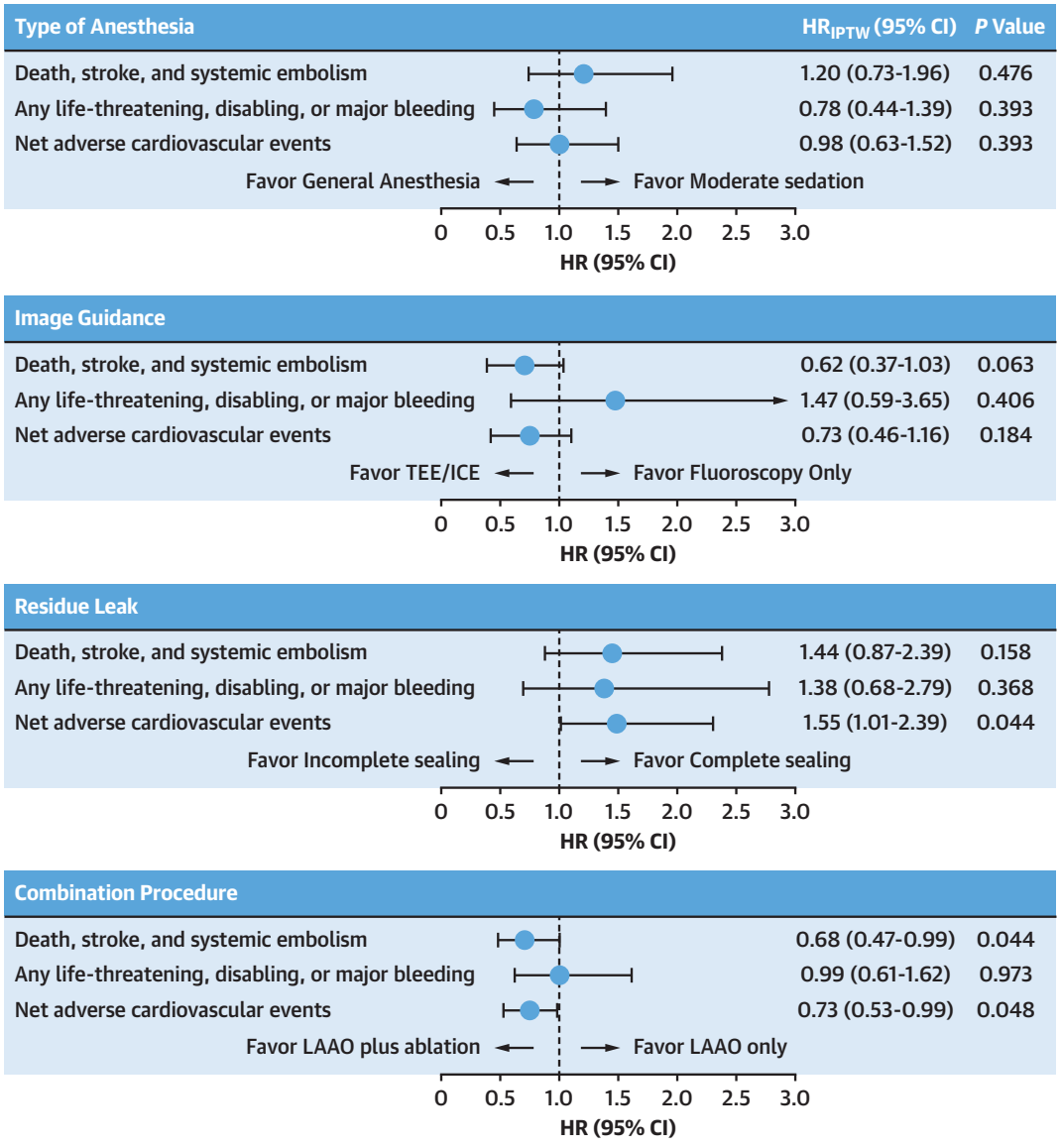
CENTRAL ILLUSTRATION Continued

C



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limited. To the best of our knowledge, our study represents the largest real-world cohort to date investigating the impact of implantation configurations and post-LAAO medication regimens. The main findings of our study can be summarized as follows:

- At 1 year, the rate of the composite endpoint of death, stroke, and SE was 4.51%, and the rate any life-threatening, disabling, or major bleeding was 2.36% in Chinese AF patients after implanting the percutaneous LAA closure device.
- There was no significant association between the type of anesthesia (general anesthesia vs moderate sedation) or the modality of image guidance (TEE, ICE, or fluoroscopy) regarding the ischemic or bleeding events.

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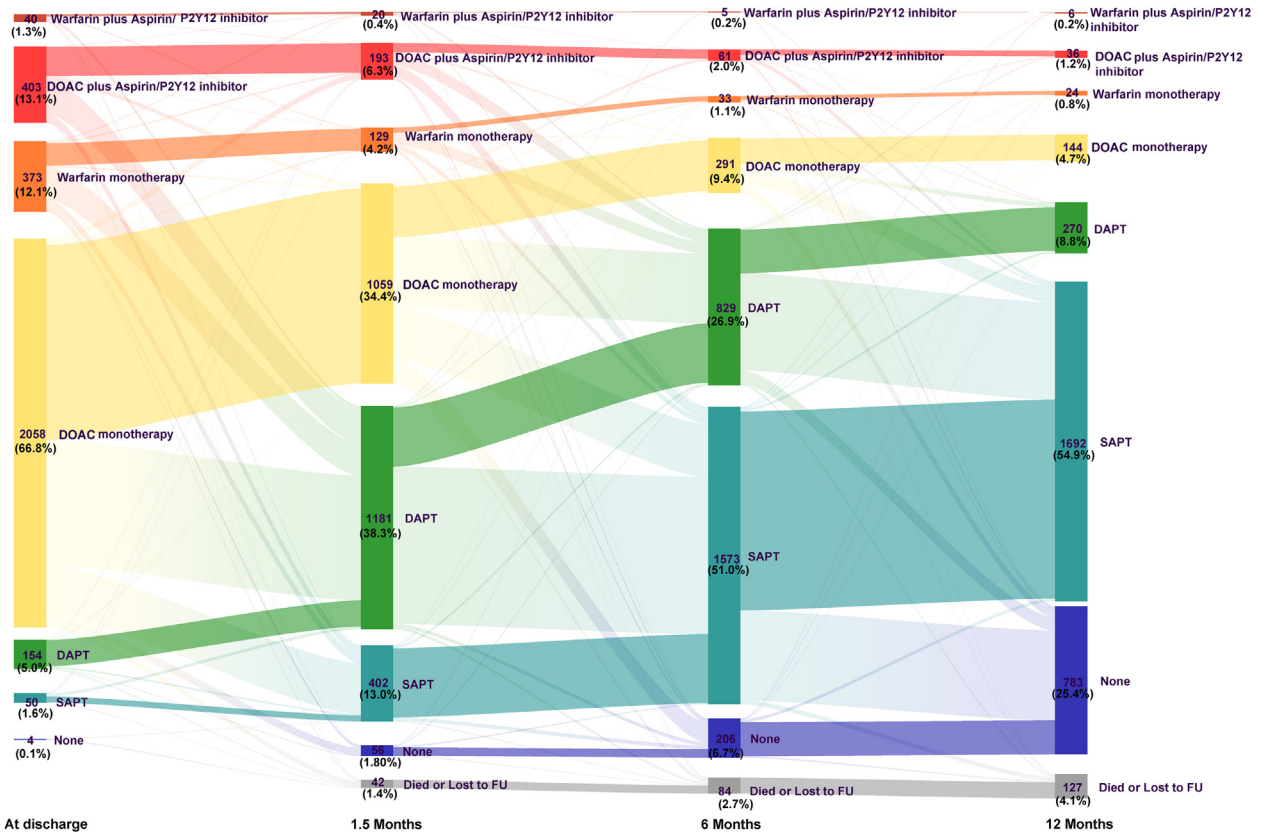
FIGURE 2 Medication Strategies From the Index LAAO Procedure to 1-Year Follow-Up



Sankey diagram showing the post-LAAO medication strategies. DAPT = dual-antiplatelet therapy; DOAC = direct oral anticoagulation; FU = follow-up; LAAO = left atrial appendage occlusion; SAPT = single-antiplatelet therapy.

- The 1-stage combination procedure of LAAO and CA was associated with a significantly lower rate of death, stroke, or SE compared with LAAO only.
- The antithrombotic medication regimens post-LAAO deviated substantially from guideline recommendations. The strategy of OAC | APT | APT was applied in 38.1% of participants and was associated with the numerically lowest rate of death; stroke; SE; or life-threatening, disabling, or major bleeding.

Patient characteristics and clinical outcomes between the current and previous studies[3,4,6-11] are tabulated in Supplemental Table 8. Notably, nearly all these pivotal studies supporting the use of LAAO were conducted primarily with White populations, with other ethnic groups, including Black, Asian, Hispanic, and so on, being less represented. Compared with other ethnic groups, East Asian individuals have a unique risk-benefit tradeoff in managing stroke prevention in AF. East Asians experience reduced anti-ischemic benefits and increased bleeding risk with antithrombotic therapies, particularly intracranial bleeding, known as the "East Asian paradox."[22] Additionally, adherence to OAC is commonly suboptimal in this population.[23] Consequently, East Asians with nonvalvular AF might have a greater propensity to benefit from non-pharmacologic strategies for stroke prevention, such as the use of LAA closure devices.

RECORD is the first large-scale, real-world registry documenting the safety and efficacy profiles of the LAA closure device among the East Asian population. Compared with the other studies, RECORD's rate of all-cause death was numerically the lowest, and the rates of stroke and major bleeding were similar. The average younger age of patients enrolled in RECORD might be related to the lower death rate. Nevertheless, these findings suggest that patients at high risk of stroke (mean CHA_2DS_2-VASc score of 4.0) and

TABLE 4 The 1-Year Clinical Outcomes According to Post-LAAO Medications (Mutually Exclusive Categories)

	OAC | APT | APT (n = 1,176; 38.1%)								
	OAC | DAPT | DAPT (n = 191; 6.2%)	OAC | SAPT | SAPT (n = 352; 11.4%)	OAC | DAPT | SAPT (n = 633; 20.5%)	Total	OAC | OAC | APT (n = 832; 27.0%)	OAC + APT | APT | APT (n = 202; 6.6%)	OAC | OAC | OAC (n = 348; 11.3%)	APT | APT | APT (n = 150; 4.9%)	Others (n = 374; 12.1%)
CHA2DS2-VASc score	3.73 ± 1.81	3.76 ± 1.80	3.87 ± 1.75	3.81 ± 1.78	3.92 ± 1.77	4.16 ± 1.94	4.27 ± 1.82	4.29 ± 1.80	4.07 ± 1.81
HAS-BLED score	2.24 ± 1.18	2.26 ± 1.12	2.27 ± 1.14	2.26 ± 1.14	2.31 ± 1.13	2.56 ± 1.28	2.51 ± 1.11	2.82 ± 1.19	2.67 ± 1.14
ATRIA score	5.73 ± 3.01	5.98 ± 2.98	6.04 ± 3.03	5.97 ± 3.01	6.24 ± 2.97	6.10 ± 2.90	6.72 ± 2.82	7.02 ± 2.69	6.23 ± 2.85
Total									
Death, stroke, systemic embolism	6/191 (3.2)	13/352 (3.9)	14/633 (2.3)	33/1,176 (2.9)	23/832 (3.0)	6/202 (3.0)	35/348 (10.8)	12/150 (8.3)	24/374 (6.6)
Life-threatening, disabling, or major bleeding	2/191 (1.0)	7/352 (2.0)	5/633 (0.8)	14/1,176 (1.2)	20/832 (2.5)	5/202 (2.5)	12/348 (3.8)	8/150 (5.4)	12/374 (3.3)
Death; stroke; systemic embolism; and any life-threatening, disabling, or major bleeding	7/191 (3.7)	16/352 (4.8)	17/633 (2.7)	40/1,176 (3.5)	40/832 (5.0)	9/202 (4.5)	39/348 (12.0)	18/150 (12.3)	31/374 (8.5)
HAS-BLED score <3									
Death, stroke, systemic embolism	3/119 (2.6)	6/208 (2.9)	3/377 (0.8)	12/704 (1.7)	8/481 (1.8)	3/97 (3.1)	12/181 (7.2)	0/60 (0.0)	5/168 (3.2)
Life-threatening, disabling, or major bleeding	1/119 (0.8)	4/208 (1.9)	4/377 (1.1)	9/704 (1.3)	11/481 (2.4	0/97 (0.0)	3/181 (1.7)	4/60 (6.7)	3/168 (1.8)
Death; stroke; systemic embolism; and any life-threatening, disabling, or major bleeding	4/119 (3.4)	7/208 (3.4)	6/377 (1.6)	17/704 (2.4)	18/481 (3.9)	3/97 (3.1)	13/181 (7.7)	4/60 (6.7)	8/168 (5.0)
HAS-BLED score ≥3									
Death, stroke, systemic embolism	3/72 (4.3)	7/144 (5.3)	11/256 (4.4)	21/472 (4.7)	15/351 (4.5)	3/105 (2.9)	23/167 (14.8)	12/90 (13.7)	19/206 (9.4)
Life-threatening, disabling, or major bleeding	1/72 (1.4)	3/144 (2.1)	1/256 (0.4)	5/472 (1.1)	9/351 (2.6)	5/105 (4.8)	9/167 (6.0)	4/90 (4.6)	9/206 (4.5)
Death; stroke; systemic embolism; and any life-threatening, disabling, or major bleeding	3/72 (4.2)	9/144 (6.6)	11/256 (4.4)	23/472 (5.1)	22/351 (6.5)	6/105 (5.8)	26/167 (16.6)	14/90 (16.0)	23/206 (11.3)

Values are mean ± SD or n/N (%).

APT = antiplatelet therapy; DAPT = dual-antiplatelet therapy; LAAO = left atrial appendage occlusion; OAC = oral anticoagulant; SAPT = single-antiplatelet therapy.

moderate to high risk of bleeding (mean HAS-BLED score of 2.4) who underwent implantation of an LAA closure device in the East Asian population experienced relatively low rates of ischemic and bleeding events.

Expert consensus documents[13] recommend intraprocedural imaging using either TEE or ICE to guide LAAO, with fluoroscopy guidance alone reserved for exceptional circumstances and performed only by experts. To reduce medical expenses, avoid the discomfort and risk of TEE, and obviate the need for general anesthesia, an increasing number of operators have applied LAAO procedures by fluoroscopy alone. However, little evidence exists regarding the long-term safety and efficacy of LAAO performed by fluoroscopy guidance alone. The Bern registry,[14] which enrolled 811 participants and followed them for 5 months, showed that procedures guided by TEE had a significantly lower rate of device-related complications compared with fluoroscopy. On the other hand, other small-scale studies[24,25] showed no significant differences in outcomes between TEE and fluoroscopy guidance.

In RECORD, because the number of ICE-guided LAAOs was small and previous meta-analyses have suggested that ICE guidance is as effective as TEE,[26] we combined ICE and TEE guidance into 1 group and compared it with fluoroscopy guidance. After adjusting for confounding factors, we found that the rates of ischemic and bleeding endpoints were similar between the TEE/ICE group and the fluoroscopy alone group at 1 year. However, this result could also be explained by the fact that most fluoroscopy-guided LAAO procedures were conducted by expert operators, as demonstrated in our previous report.[12] More careful studies of the use of fluoroscopy-guided LAAO are warranted.

In cases of symptomatic atrial fibrillation, physicians typically offer ablation for symptom relief. For patients in this category who either have a contraindication to long-term OAC or are at a high risk of major bleeding and prefer a treatment option free from anticoagulation, LAAO has emerged as a viable alternative.[27] However, most studies of LAAO, such as the PROTECT-AF,[3] PREVAIL,[4] and PRAGUE-17,[5] have excluded participants who

underwent a combined procedure of LAAO with CA to focus solely on the impact of LAAO. Some small-scale registries[28-31] have suggested that the rate of adverse events in a combined procedure of LAAO and CA is low. However, the long-term impact of LAAO in combination with CA remains unclear. In RECORD, 1-stage LAAO combination with CA was performed in 42.0% of cases, likely because of the fact that 80.5% of operators were electrophysiologists.

Previously, we showed that these combined procedures were not associated with increased periprocedural adverse event rates.[12] In the current report, we found that at 1 year, the composite rate of death, stroke, and SE was significantly lower in the combined procedure group compared with the LAAO only group. The Kaplan-Meier curves of the 2 groups started to diverge at 6 months, coinciding with the timepoint when most patients stopped (D)OAC or DAPT and switched to single-antiplatelet therapy (**Figure 2**).

We also found that patients with AF of ≤1 year who underwent LAAO and CA benefitted the most compared with those who underwent LAAO only or LAAO plus CA in patients with AF of >1 year. However, with currently available evidence, we cannot support the routine use of LAAO plus CA, and further dedicated randomized studies are necessary before making any recommendations. The ongoing OPTION trial (NCT03795298), which compares the effectiveness of LAAO to OAC in postablation patients with AF, will partially provide the medical community with more evidence on this issue.

Only 1 of 20 patients received the post-LAAO medication treatment in concordance with the European Society of Cardiology AF guideline.[2] The most significant deviation was that (D)OAC monotherapy (78.9%) was prescribed instead of (D)OAC plus aspirin between discharge and 45 days post-LAAO. Previous analyses of the LAAO Registry of the National Cardiovascular Data Registry database[10] have also shown that (D)OAC monotherapy was applied in 57.7% of U.S. patients and was associated with a lower risk of major adverse outcomes compared with aspirin plus (D)OAC. Similarly, our study demonstrated that an increased risk of bleeding was associated with adding aspirin to anticoagulation at discharge post-LAAO, particularly in patients with a HAS-BLED score of >3. As such, an RCT that removes aspirin from the list of recommended post-LAAO treatments may be warranted.

Incomplete endothelialization after LAAO may lead to device-related thrombosis and ischemic events.[32] Studies have shown that complete endothelial coverage might require more than 45 days.[32,33] In the EWOLUTION study, nearly 8% of LAAO patients continued OAC at the 6-month visit.[8] The latest and ongoing CHAMPION-AF trial, which compares DOAC to closure, has also stipulated the use of DOAC plus aspirin or DAPT until the 3-month visit. However, such prolongation raised concerns about the safety of (D)OAC agents in a patient population at a higher risk for bleeding. Our analyses showed that extending (D)OAC to 6 months post-LAAO was not associated with a lower risk of thrombotic events; however, it significantly increased the risk of major bleeding. Balancing the risk of thrombotic events and bleeding remains a challenge. A recent study suggested that using a prolonged half-dose DOAC might be an alternative option.[34]

STUDY LIMITATIONS. First, imbalances exist among the subgroups. Although statistical adjustments were made to try to estimate the true differences among groups, the inability to eliminate the impact of unmeasurable confounders produces bias that cannot be adjusted. Second, RECORD enrolled only Chinese patients; therefore, extrapolation of these results to the other ethnic groups requires cautious interpretation.

Third, because of the limited resources available, imaging follow-up was not provided free of charge. As a result, patients who underwent optimal implantation may have been reluctant to undergo routine CTA/TEE imaging follow-up. Additionally, the timing of the follow-up overlaps with the COVID-19 pandemic, which may have further contributed to patients' reluctance to undergo the examination. As a result, only 60% of patients had TEE/CTA examinations during follow-up. The rate of DRT or incomplete sealing might be underestimated; however, with a follow-up rate of 97.8%, the vital status and serious adverse events such as stroke, SE, or major bleeding were collected robustly.

Fourth, it is worth noting that the COVID-19 pandemic may have led to an increase in mortality. However, the recent Global Burden of Disease Study 2021[35] revealed that in East Asia, COVID-19 accounted for only 0.4% of deaths. Finally, the device used in the current study was the generation 2.5 LAA closure device instead of the next-generation LAA closure device, which was not commercially available at the time of the study. However, the difference in adverse events between the 2 devices was believed to be mainly confined to periprocedural and in-hospital events.[11,36,37]

CONCLUSIONS

In Chinese centers, patients with an LAA device experienced low rates of ischemic and bleeding events at 1 year. There was no significant association between the type of anesthesia or the modality of imaging guidance with respect to ischemic or bleeding events at 1 year. The 1-stage combination procedure of LAAO and CA was associated with a significantly lower rate of ischemic events compared with performing LAAO only; however, these results should be considered exploratory and for hypothesis generation only.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE: Among East Asian patients with AF at elevated risk of stroke and bleeding, percutaneous LAAO is associated with low rates of ischemic and bleeding events.

TRANSLATIONAL OUTLOOK: The implantation configurations and antithrombotic strategies adopted after LAAO are diverse. Although the type of anesthesia and modality of imaging guidance have limited impact on adverse events, we found that LAAO with catheter ablation, compared with LAAO only, might be associated with better outcomes. However, further randomized controlled trials are needed to verify this application.

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KEY WORDS 1-year outcomes, antithrombotic strategies, left atrial appendage occlusion, procedural configurations

APPENDIX For supplemental tables and figures as well as an expanded Methods section, please see the online version of this paper.

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