

Experience of left atrial appendage occlusion with the WATCHMAN device in Chinese patients

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ABSTRACT

Objective: Little is known about left atrial appendage occlusion (LAAO) with WATCHMAN device in patients with atrial fibrillation (AF) in China. The aim of the present study was to evaluate the acute procedural performance and complication rate of LAAO procedures and patient selection in China.

Methods: A total of 658 consecutive Chinese patients who were referred to receive LAAO procedures with the WATCHMAN device between 2014 and 2017 were retrospectively included in the study. Patients were divided into four groups according to the year of procedures: Group 2014, Group 2015, Group 2016, and Group 2017. The procedural success, complication rates, and characteristics of Chinese patients, as well as the trends of patients' selection and management, were analyzed.

Results: The average age of the patients was 67.7±9.2 years, the CHA₂DS₂-VASc score was 3.7±1.6, and the HAS-BLED score was 2.5±1.1. Both scores of patients in different years show obvious increasing trends (r=0.126, p=0.001 and r=0.145, p<0.001, respectively). Indications for LAAO included increased bleeding risk (45.6%), recent bleeding under oral anticoagulation (OAC) (9.0%), and non-compliance with OAC (51.4%). The implantation was successful in 643 (97.7%) patients, with a procedural complication rate of 0.6%. Approximately 80.1% of the patients received OAC after LAAO.

Conclusion: In China, LAAO with WATCHMAN devices in patients with AF can be performed successfully with a low complication rate. Most of the target population had increased bleeding risk or non-compliance for OAC as indications and received OAC for antithrombotic therapy after the procedure. (*Anatol J Cardiol* 2019; 21: 314-21)

Keywords: stroke, atrial fibrillation, left atrial appendage, WATCHMAN device

Introduction

The burden of atrial fibrillation (AF) in China is huge and increases rapidly, which is estimated to be >8.3 million by 2050, and the stroke rate in Chinese patients is much higher than those in European and American patients (1). As the most serious complication of AF, AF strokes are associated with a higher mortality and morbidity

than non-AF strokes, which make effective stroke prevention more essential in patients with AF (2). Owing to its well-established efficacy, oral anticoagulation (OAC) therapy has been recognized as the cornerstone of stroke prevention (3, 4). However, although an improvement in OAC use was observed in recent years, this treatment is significantly underutilized in China due to poor compliance, contraindications, bleeding risk, and other reasons (5, 6).

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Based on the findings that approximately 90% of thrombi in patients with non-valvular AF originate from the left atrial appendage (LAA) (7), percutaneous left atrial appendage occlusion (LAAO) has the potential to be an alternative to OAC for stroke prevention, and the safety and efficacy of the WATCHMAN device (Boston Scientific, Inc., Natick, MA, USA) has been confirmed in recent years (8-13). This device was approved by the Chinese Food and Drug Administration and has been used in China since 2014, but data about multicenter clinical experiences of LAAO with the WATCHMAN device for Chinese patients with AF are not available.

The aim of the present study was to describe the safety and feasibility of WATCHMAN implantation and to evaluate the patient selection and antithrombotic therapy post-LAAO procedures in the real-world clinical experience of China.

Methods

Study population

A total of 658 patients with AF who received WATCHMAN implantation from May 2014 to December 2017 from a multicenter registry were retrospectively included in the study. The study was approved by the Local Institutional Review Board. Written informed consent was obtained from the patients for LAAO procedure and for research. The baseline characteristics, procedural details, and antithrombotic therapies were collected and analyzed. Additionally, patients were divided into four groups according to the year patients received the LAAO procedures to observe the trends of patient selection and management.

WATCHMAN device and implantation procedure

The WATCHMAN device consists of a self-expanding nitinol frame with fixation bars that fix to the LAA ostium and a permeable polyester fabric membrane cap that covers the atrial-facing surface. The device is available in five sizes: 21 mm, 24 mm, 27 mm, 30 mm, and 33 mm to accommodate a variety of LAA dimensions. After excluding the presence of thrombi through transesophageal echocardiography (TEE), the device is implanted at an optimal position via a catheter-based delivery system.

Implant success and complications

The implant success rate was defined as the confirmation of the device-specified release criteria and the successful implantation of the device among patients. Successful procedural closure of the LAA was defined as a residual flow ≤ 5 mm assessed via periprocedural TEE. Complications were defined as adverse events that occurred during the procedure or within the next 7 days, including pericardial effusion/cardiac tamponade, vascular complications, device embolization, stroke, transient ischemic attack (TIA), systemic embolization, or procedure-related death.

Antithrombotic regimen before and after LAAO procedures

Since there are no recommended regimens or guidelines for antithrombotic treatment prior to and after LAAO, the specific medication given was at the discretion of the physicians. The present study collected and analyzed data about the types of antithrombotic drugs prescribed prior to LAAO procedures and after patients were discharged.

Statistical analysis

All statistical analyses were performed by SPSS software version 23.0 (SPSS Inc., Chicago, IL, USA). Categorical data were expressed as frequencies and percentages. Chi-square or Fisher's exact test was used for comparison of categorical data. One-way analysis of variance was used to analyze normally distributed variables. Normally distributed variables were presented as mean \pm standard deviation. Kruskal-Wallis test was used to analyze non-normally distributed variables. Non-normally distributed variables were expressed in medians with interquartile range. Spearman correlation coefficients (*r*) with *p* value were calculated to correlate the relationships between year and other parameters. A two-tailed *p* value < 0.05 was considered to be statistically significant.

Results

Patient characteristics

Baseline characteristics are presented in Table 1. A total of 658 patients from 27 centers in China were included in the present study, and 91.0% (599/658) of all the procedures evaluated were performed at nine centers and by experienced operators. Among the total population, the number of patients receiving LAAO procedures in 2014, 2015, 2016, and 2017 were 65, 300, 208, and 85, respectively.

The mean age of the population was 67.67 ± 9.19 years, and 62.0% were male. Paroxysmal AF was present in 22.5% of the patients, and persistent AF was present in 77.5%. More than half of the patients had a history of hypertension (68.1%), and approximately 47.9% of all patients had a history of previous stroke or TIA. Approximately 12.5% of all subjects had a history of major bleeding, 16.4% had labile international normalized ratios (INRs), and 15.7% had combination use of antiplatelet or non-steroidal anti-inflammatory drugs. Approximately 92.3% of the patients had a CHA₂DS₂-VASc score ≥ 2 , with a mean score of 3.69 ± 1.61 . In addition, 45.6% of the patients were deemed at high risk for bleeding (HAS-BLED score ≥ 3), and the mean HAS-BLED score of all subjects was 2.5 ± 1.1 . The indications for LAAO mainly included increased bleeding risk (45.6%), recent bleeding under OAC (9.0%), and non-compliance with OAC (51.4%).

The percentage of patients with prior stroke or TIA and the average scores of CHA₂DS₂-VASc and HAS-BLED in different years show obvious increasing trends. The percentage of patients with prior strokes or TIA significantly increased from 22.4% in 2014 to 58.8% in 2017 ($p=0.004$), with a significant positive Spearman

Table 1. Baseline characteristics of patients receiving LAAO with WATCHMAN device

Parameters	All patients	Group 2014	Group 2015	Group 2016	Group 2017	P value
No. of patients	658	65	300	208	85	
Age (year)	67.7±9.2	68.8±7.6	67.5±9.7	67.2±9.2	68.6±8.7	0.482
Female gender	254 (38.6%)	25 (38.5%)	109 (36.3%)	84 (40.4%)	37 (43.5%)	0.598
AF type						<0.001*
PAF	148 (22.5%)	4 (6.2%) ^a	67 (22.3%) ^b	47 (22.6%) ^b	4 (4.7%) ^a	
Persistent AF	510 (77.5%)	61 (93.9%) ^a	233 (77.7%) ^b	161 (77.4%) ^b	81 (95.3%) ^a	
CHA ₂ DS ₂ -VASc score	3.7±1.6	3.3±1.5 ^a	3.6±1.5 ^{a, b}	3.8±1.8 ^{bc}	4.1±1.5 ^{cd}	0.008*
CHF or LV dysfunction	124 (18.8%)	13 (20.0%)	68 (22.7%)	29 (13.9%)	14 (16.5%)	0.09
Hypertension	448 (68.1%)	48 (73.8%)	206 (68.7%)	138 (66.3%)	56 (65.9%)	0.678
Age ≥ 75 years old	160 (39.5%)	16 (24.6%)	75 (25.0%)	44 (21.2%)	25 (29.4%)	0.492
Diabetes mellitus	138 (21.0%)	14 (21.5%)	70 (23.3%)	42 (20.2%)	12 (14.1%)	0.320
Prior stroke or TIA	315 (47.9%)	22 (33.9%) ^a	132 (44.0%) ^{a, b}	111 (53.4%) ^b	50 (58.8%) ^b	0.004*
VASc	226 (34.4%)	6 (9.2%) ^a	94 (31.3%) ^b	89 (42.8%) ^c	37 (43.5%) ^{b, c}	<0.001*
HAS-BLED score	2.5±1.1	2.0±1.0 ^a	2.4±1.1 ^b	2.5±1.2 ^{bc}	2.7±1.1 ^{cd}	0.002*
Abnormal renal function	48 (7.3%)	4 (6.2%)	26 (8.7%)	9 (4.3%)	9 (10.6%)	0.147
Abnormal liver function	8 (1.2%)	0 ^{a, b}	5 (1.7%) ^{a, b}	0 ^b	3 (3.5%) ^a	0.043*
History of major bleeding	80 (12.5%)	2 (3.1%)	34 (11.3%)	30 (14.4%)	14 (16.5%)	0.053
Labile INRs	108 (16.4%)	5 (7.7%)	53 (17.7%)	39 (18.8%)	11 (12.9%)	0.137
Concomitant use of drugs	103 (15.7%)	4 (6.2%) ^a	40 (13.3%) ^{a, b}	45 (21.6%) ^b	14 (16.5%) ^{a, b}	0.010*
Alcohol abuse	61 (9.3%)	2 (3.1%)	31 (10.3%)	17 (8.2%)	11 (12.9%)	0.167
LVEF (%)	57.0 [52.0, 64.0]	54.0 [50.0, 59.5]	59.0 [53.0, 65.0]	57.0 [52.5, 63.0]	59.0 [54.0, 62.5]	0.168
LAD (mm)	46.3±6.4	48.6±5.8 ^a	46.3±6.5 ^b	45.5±6.8 ^{b, c}	45.6±6.2 ^{b, d}	0.009*
LVEDD (mm)	49.0 [45.0, 53.0]	48.0 [45, 52]	49.0 [45, 53.0]	49.0 [45.0, 52.0]	49.0 [45.0, 53.0]	0.133
Indications for LAAO						
Increased bleeding risk	300 (45.6%)	19 (29.2%) ^a	127 (42.3%) ^{a, b}	105 (50.5%) ^b	49 (57.7%) ^b	0.002*
Recent bleeding under OAC	59 (9.0%)	1 (1.5%) ^a	24 (8.0%) ^{a, b}	22 (10.6%) ^{a, b}	12 (14.1%) ^b	0.029*
Non-compliance to OAC	338 (51.4%)	41 (63.1%) ^a	130 (62.5%) ^b	113 (54.3%) ^{a, b}	44 (51.8%) ^{a, b}	0.009*

^{a, b, c, d} - The superscript letters in the table indicate whether the differences between groups are significant: there are no significant differences between values with at least one same superscript letter, and the differences between values with absolutely different superscript letters are significant statistically.

*Statistical significance= $P<0.05$.

Letters indicate the results of post hoc multiple comparison tests.

LAAO - left atrial appendage occlusion; AF, atrial fibrillation; PAF - paroxysmal atrial fibrillation; CHF - congestive heart failure; LV - left ventricular; TIA - transient ischemic attack;

VASc - vascular diseases; INR - international normalized ratio; concomitant use of drugs, combination use of antiplatelet or non-steroidal anti-inflammatory drugs;

LVEF - left ventricular ejection fraction; LAD - left atrial dimension; LVEDD - left ventricular end-diastolic dimension; OAC - oral anticoagulation therapy

correlation coefficient of 0.142 ($p<0.001$). As shown in Figure 1, the mean CHA₂DS₂-VASc score of the patients significantly increased ($p=0.008$) over time from 3.3±1.5 in 2014 to 4.1±1.5 in 2017, and a significant positive linear correlation between year and CHA₂DS₂-VASc score was observed ($r=0.126$, $p=0.001$). The trend was similar in the HAS-BLED score of patients, increasing from 2.0±1.0 in 2014 to 2.7±1.1 in 2017 ($p=0.001$), and there was a significant positive correlation coefficient between year and HAS-BLED score ($r=0.145$, $p<0.001$). Similarly, the percentages of different indications for LAAO in different years showed obvious trends as well. As shown in Figure 2, the increased bleeding risk was 29.2% in 2014 and increased to 57.7% in 2017 ($p=0.002$); the

recent bleeding under OAC increased from 1.5% in 2015 to 14.2% in 2017 ($p=0.029$). The correlations between year and percentage of increase bleeding risk and between year and percentage of recent bleeding under OAC were both positive and significant in statistics ($r=0.149$, $p<0.001$ and $r=0.105$, $p=0.007$, respectively). No obvious trends were observed in the other parameters between the different years.

Implant success and complications

As shown in Table 2, the device was successfully implanted in 643 (97.7%) of 658 subjects, and the difference in implantation success rates in different years was not statistically significant.

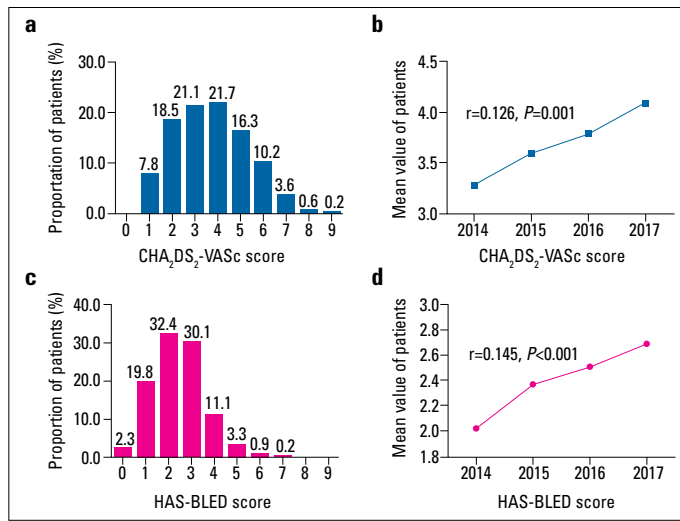


Figure 1. Thromboembolic and bleeding risk of patients at baseline. (a) Distribution of CHA₂DS₂-VASc score in patients. (b) Correlation between year and CHA₂DS₂-VASc score. (c) Distribution of HAS-BLED score in patients. (d) Correlation between year and HAS-BLED score

The complication rate in all subjects was 0.6% (4/658), including two pericardial effusions (0.3%) and one pseudoaneurysm (0.2%) in 2015 and one cardiac tamponade (0.2%) in 2017; the difference between the different years was not significant. Successful procedural closure of the LAA with a complete seal was achieved in 90.5%, approximately 7.9% of the patients had a peri-device

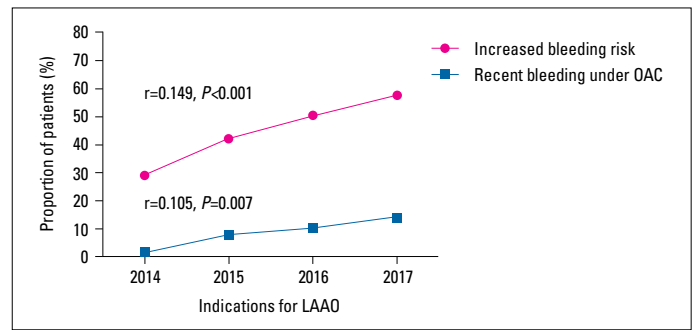


Figure 2. Correlations between year and indications for LAAO with WATCHMAN device in patients
LAAO - left atrial appendage occlusion; OAC - oral anticoagulation

leak ≤3 mm, 1.1% had a peri-device leak of 3–5 mm, and only 0.5% had a peri-device leak >5 mm. The mean LAA maximal diameter was 23.1±4.6 mm, and the mean size of the WATCHMAN device was 28.0±3.5 mm. The mean procedural duration for all years was 97.3±24.0 min, the duration decreased significantly over time from 114.5±19.6 min in 2014 to 70.9±14.1 min in 2017 (p<0.001), and there was a significant negative correlation between year the procedure duration was observed (r=-0.619, p<0.001).

Antithrombotic therapy

As shown in Table 3, prior to LAAO procedures, a total of 327 (49.7%) patients were on anticoagulation therapy. The anti-

Table 2. Procedural results of LAAO with WATCHMAN device

Characteristics	All patients	Group 2014	Group 2015	Group 2016	Group 2017	P value
Success implantation	643 (97.7%)	65 (100.0%)	292 (97.3%)	203 (97.6%)	83 (97.7%)	0.749
LAA maximal diameter	23.1±4.6	21.9±4.7 ^a	22.8±4.6 ^{a, b}	23.3±4.5 ^{b, c}	24.2±4.7 ^{c, d}	0.015*
LAA seal						0.600
Complete seal	582 (90.5%)	61 (93.9%)	264 (90.4%)	186 (91.6%)	71 (85.5%)	
Peri-device leak ≤3 mm	51 (7.9%)	3 (4.6%)	24 (8.2%)	13 (6.4%)	11 (13.3%)	
Peri-device leak 3-5 mm	7 (1.1%)	1 (1.5%)	3 (1.0%)	2 (1.0%)	1 (1.2%)	
Peri-device leak >5 mm	3 (0.5%)	0	1 (0.3%)	2 (1.0%)	0	
Device size						0.238
21 mm	34 (5.3%)	3 (4.6%)	20 (6.9%)	11 (5.4%)	0	
24 mm	128 (19.9%)	15 (23.1%)	54 (18.5%)	41 (20.2%)	18 (21.7%)	
27 mm	204 (31.7%)	21 (32.3%)	93 (31.9%)	63 (31.0%)	27 (32.5%)	
30 mm	148 (23.0%)	15 (23.1%)	74 (25.3%)	43 (21.2%)	16 (19.3%)	
33 mm	130 (20.2%)	11 (16.9%)	51 (17.5%)	45 (22.2%)	23 (27.7%)	
Complications	4 (0.6%)	0	3(1.0%)	0	1 (1.2%)	0.376
Pericardial effusion	2 (0.3%)	0	2 (0.7%)	0	0	
Cardiac tamponade	1 (0.2%)	0	0	0	1 (1.2%)	
Pseudoaneurysm	1 (0.2%)	0	1 (0.3%)	0	0	
Procedure duration (min)	97.23±24.0	114.5±19.6 ^a	106.0±20.6 ^b	81.5±22.6 ^c	70.9±14.1 ^d	<0.001*

^{a, b, c, d} - The superscript letters in the table indicate whether the differences between groups are significant: there are no significant differences between values with at least one same superscript letter, and the differences between values with absolutely different superscript letters are significant statistically.

*Statistical significance=P<0.05.

Letters indicate the results of post hoc multiple comparison tests.

LAAO - left atrial appendage occlusion; LAA - left atrial appendage

Table 3. Anticoagulation therapies of patients post-LAAO when discharge

	All patients	Group 2014	Group 2015	Group 2016	Group 2017	P value
Antithrombotic therapy prior to procedures	327 (49.7%)	12 (26.7%)	150 (50.0%)	117 (56.3%)	48 (56.5%)	<0.001
Single APT	64 (9.7%)	3 (4.6%)	32 (10.7%)	22 (10.6%)	7 (8.2%)	0.456
DAPT	16 (2.4%)	0	9 (3.0%)	5 (2.4%)	2 (2.4%)	0.691
OAC alone	220 (33.4%)	8 (12.3%)	91 (30.3%)	89 (42.8%)	36 (42.4%)	<0.001
OAC plus APT	21 (3.2%)	1 (1.5%)	17 (5.7%)	1 (0.5%)	2 (2.4%)	0.006
Antithrombotic therapy post procedures	653 (99.2%)	65 (100.0%)	296 (98.7%)	207 (99.5%)	85 (100.0%)	0.376
Single APT	25 (3.8%)	2 (3.1%)	14 (4.7%)	6 (2.9%)	3 (3.5%)	0.792
DAPT	56 (8.5%)	5 (7.7%)	18 (6.0%)	23 (11.1%)	10 (11.8%)	0.144
OAC alone	527 (80.1%)	52 (80.0%)	243 (81.0%)	166 (79.8%)	66 (77.7%)	0.922
OAC plus APT	45 (6.8%)	6 (9.2%)	21 (7.0%)	12 (5.8%)	6 (7.1%)	0.895

LAAO - left atrial appendage occlusion; APT - antiplatelet therapy; DAPT - dual antiplatelet therapy; OAC - oral anticoagulation

thrombotic treatment rate of patients prior to LAAO procedures significantly increased ($p<0.001$) from 26.7% in 2014 to 56.3% in 2016 and to 49.4% in 2017, with a positive correlation coefficient of 0.162 ($p<0.001$) and the use of oral coagulants alone increased significantly over time from 12.3% in 2014 to 42.8% in 2016 and to 37.7% in 2017 ($r=0.181$, $p<0.001$).

Of note, almost all patients (99.2%) received antithrombotic therapy after LAAO procedures, and only three patients did not receive any antithrombotic drugs. The majority of these patients (80.1%) were on OAC alone, 3.8% received single antiplatelet therapy (APT), 8.5% were on dual antiplatelet therapy (DAPT), and 6.8% received OAC plus APT. The difference in the antithrombotic regimen in different years was not statistically significant.

Discussion

Major findings

The multicenter data about LAAO with the WATCHMAN device in 658 patients revealed the following: (1) LAAO can be successfully and safely performed in Chinese patients in the real world, with an excellent procedural success of 97.7% and a low complication rate of approximately 0.6%. (2) Compared with previous years, procedural duration in 2017 was significantly decreased year by year, and antithrombotic therapy rates after LAAO discharge were relatively high and were similar in different years. (3) The average CHA_2DS_2 -VASc and HAS-BLED scores of our patients were 3.7 ± 1.6 and 2.5 ± 1.1 , respectively. Approximately 92.2% of the subjects had a CHA_2DS_2 -VASc score ≥ 2 , and approximately 45.6% of the patients had a HAS-BLED score ≥ 3 , indicating a relatively high risk of stroke and bleeding. Additionally, significant positive correlations between year and the two scores were observed ($r=0.126$, $p=0.001$ and $r=0.145$, $p<0.001$, respectively), and patients in 2017 had the highest average CHA_2DS_2 -VASc and HAS-BLED scores (4.1 ± 1.5 and 2.7 ± 1.1 , respectively).

Implantation success and safety of the WATCHMAN device

It is well known that the implant success rate improves significantly as operator experience increases and techniques improve. This rate increased from 88% in the Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation PROTECT AF) trial (11) to 95% in the Prospective Randomized Evaluation of the Watchman Left Atrial Appendage Closure Device in Patients with Atrial Fibrillation in Patients With Atrial Fibrillation Versus Long-Term Warfarin Therapy (PREVAIL) trial (10), 97.2% in the Canadian experience (14), and then improved to 98.5% in the Registry to Evaluate Real-World Clinical Outcomes in Patients With Atrial Fibrillation and High Stroke Risk-Treated With the Watchman Left Atrial Appendage Closure Technology (EWOLUTION) (15). Overall, successful implant placement is achieved in 88%–98.5% of cases. The rate in our study (97.7%) was comparable to the rates of these studies and demonstrated that LAAO with WATCHMAN device could be performed with high success rate in the Chinese population with different ethnic characteristics to the Western population, such as body surface areas. Of note, differences in success rates of different years were not statistically significant in our study, which may be attributed to the unchanged structure of the WATCHMAN device. The most common reasons for implantation failure were unfavorable anatomy or a mismatch between the size of the device and the LAA, indicating that although the continuous improvement in techniques and increased operator experience have increased the implantation success rate significantly in previous years, the presence of an unfavorable anatomy and LAA size might maintain the success rate at a relatively stable level.

A high complication rate was regarded as a major concern for LAAO, but it has been shown that physician-training programs established by societies, institutions, and manufacturers; safer implant strategies; and better patient anatomical selection could be helpful to reduce complications in clinical practice, and a decline

in the complication rate has been observed in previous studies. The procedural complication rates were 8.7% in PROTECT AF (11), 4.2% in PREVAIL (10), 2.7% in EWOLUTION (15), 1.9% in Canadian experience (14), and 1.4% in the Post-FDA Approval Study (16). In our study, we observed a complication rate of 0.6%, which was lower than the rates in previous studies. Additionally, as shown in previous studies, the most significant complications were pericardial effusion/tamponed during device implantation and procedure-related stroke due to inadvertent introduction of air or thrombus into the systemic circulation during device implantation, which was regarded as the major concern for LAAO. The incidence of pericardial effusion requiring intervention was 4.8% in the PROTECT AF trial (11), 1.6% in the PREVAIL trial (10), 2.2% in the Continued Access Protocol (CAP) Registry (17), and 1.3% in the ASA Plavix Feasibility Study with WATCHMAN Left Atrial Appendage Closure Technology (ASAP) Study (18). In the present study, we observed a rate of pericardial effusion (0.5%), which was much lower than reported by the studies above as well. Experienced operators performed the majority of the procedures in our study, which may be the major reason for this obvious decrease in this complication rate since the accumulation of the implant placement experience of operators and their teams could significantly reduce the procedural complication rate of LAAO in the real world. Additionally, the conditions of our population were better than those of population in other studies, with less comorbidity, such as previous bleeding and stroke. Differences in baseline characteristics between our population and population in other studies may be one of the reasons. Third, owing to the retrospective design of this registry, it was not required to perform routine transthoracic echocardiography on day 1 after the procedure, the second TEE examination before discharge except for presenting symptoms, asymptomatic effusion, and device-related thromboembolization may be misdiagnosed, and the true rate of complication in our population was underestimated. Additionally, the lack of expert committee to define and identify the complications strictly during and after procedures may lead to the missing reports of complications. Nevertheless, our complication rate was approximately 3-fold lower than the closest values in the Canadian experience and the Post-FDA Approval Study (14, 16), and the rate of pericardial effusion was also nearly 3-fold lower than the rate in the CAP Registry and the ASAP Registry (17, 18), which needs to be confirmed in a prospective study performed in Chinese patients to determine the skills or reasons for the low complication rate the present study have not revealed.

Patient selection for LAAO in China

As we all know, the target population of the first two randomized trials of LAAO, the PROTECT AF and the PREVAIL (10, 11), was patients with AF eligible for OACs, and both of the trials had not paid enough attention on patients with high risk of bleeding or previous bleeding events because a contraindication to warfarin was an exclusion criterion. However, the patient profile has changed substantially in recent years. The series of studies after PROTECT AF and PREVAIL included more patients with bleeding

events or increased bleeding risk who were deemed to be ineligible for OACs (10, 11). Two-thirds of the patients in the EWOLUTION study were unsuitable for OACs and even 100% in the ASAP Study (15, 18). The proportion of patients who experienced previous hemorrhagic/bleeding events or tendencies in the Canadian experience, ASAP Study, and French Nationwide Observational LAA Closure (FLAAC) Registry was as high as 90%, 93%, and 90%, respectively (14, 18, 19). All of these studies demonstrate that it is reasonable to perform LAAO in patients with AF with no other options for thromboembolic risk reduction.

The background of LAAO in China is significantly different from Western countries. There are three main serious problems of AF management in China. First, antithrombotic therapy is significantly underused in China, especially anticoagulation (5, 20, 21). Although it has been improved in recent years, the antithrombotic rate of approximately 50% in our study was still much lower than that in the EWOLUTION study (63%) and in the Canadian experience (87%) (14, 15). Additionally, the proportion of INR values between 2.0 and 3.0 in Chinese patients was only 36% as reported by the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) registry (5) and was lower than the rates in Western countries as well. Another outstanding and serious problem is the high incidence of non-persistence of warfarin therapy. As reported by Wang et al. (22) in 2016, as high as 58% of the patients discontinued warfarin during a follow-up of 2 years because of the fear of bleeding, the inconvenience of INR monitoring, and other causes. In this background, the application of LAAO in China has specific characteristics. Our study population is highly representative of the types of Chinese patients who underwent LAAO in the past 4 years, and the results indicated that patient selection for LAAO with WATCHMAN device in China still remains in the initial stage when compared with the studies above. In the present study, the mean HAS-BLED score of our study (2.5 ± 1.1) was comparable to the values of the EWOLUTION (2.3 ± 1.2) (15), Canadian experience (3.0 ± 1.2) (14), and FLAAC Registry (3.1 ± 0.1) (19). However, the percentage of patients who had increased bleeding risk in our population was only 46%, and only 12.5% of the whole population had a history of major bleeding, which was significantly lower than the proportions of major bleeding or bleeding events in the EWOLUTION (31%) (15), Canadian experience (91%) (14), ASAP Study (93%) (18), and FLAAC Registry (90.4%) (19). The low rate of patients who had a history of major bleeding may be partly attributed to the underuse of OAC therapy before LAAO procedures and the difference in patient selection in the present study. Additionally, although the rate of recent bleeding events was only 9% in the whole population, only approximately 37% of our patients received OAC therapy before the procedure, and approximately 25% had experienced bleeding.

Furthermore, in addition to increased bleeding risk (46%), approximately one-half of our patients received LAAO due to the non-compliance to OAC therapy due to the fear of bleeding, inconvenience of INR monitoring, other limitations of warfarin, and high price of novel OACs, which was so different from other studies. The ASAP Study showed that LAAO for patients with previ-

ous bleeding events and ineligible for OACs is safe and effective, and the Canadian experience, FLAAC Registry, and EWOLUTION have also demonstrated a similar conclusion that LAAO plays a more significant role for specific patients with a contraindication to chronic OAC use, but not as an alternative for OACs (14, 15, 19). Therefore, Chinese physicians should re-examine their clinical practice about LAAO and select patients for LAAO more strictly and following the scientific evidence of these studies. For patients who are suitable for long-term OAC therapy, physicians should consider the standardized OAC therapy as the first choice to prevent stroke and improve the compliance of the patients. For those who are ineligible for OACs, LAAO can be used very carefully. Of note, the correlation between year and percentage of increasing bleeding risk and the correlation between year and percentage of recent bleeding under OAC therapy were both positive significantly, thereby indicating that LAAO practice in China has been developing in a good direction.

Antithrombotic therapy after LAAO in China

The patient selection for LAAO in our study is different from the studies we discussed above, which is associated with the antithrombotic therapy strategy post-LAAO procedures as well. The post-LAAO antithrombotic rate in our study was approximately 99%, which was similar to the rates of the EWOLUTION (94%), Canadian experience (97%), ASAP Study (100%), and FLAAC Registry (97%) (14, 15, 18, 19). However, since the majority of our patients were eligible for short-term OAC therapy, the antithrombotic regimen post-LAAO procedures often followed the strategy of the PROTECT AF and PREVAIL (10, 11), which has been demonstrated to be safe and effective to prevent device-related thrombus. The short-term OAC therapy rate after LAAO at discharge in our study was as high as 87%, and DAPT was used only in approximately 9% of our population. However, this antithrombotic strategy was substantially different when compared with strategies in other studies that enrolled more patients unsuitable for OAC therapy. The proportions of patients who received OAC therapy in the EWOLUTION study (27%), Canadian experience (20%), and FLAAC Registry (24%) were significantly lower, but the use of DAPT was more frequent (14, 15, 19). DAPT was prescribed in 59% of the patients in the EWOLUTION study, 46% in the FLAAC Registry, 74% in the Canadian experience, and 100% in the ASAP Study and has been demonstrated to be safe and effective for patients who were ineligible for OAC therapy (14, 15, 18, 19). Since more scientific evidence on LAAO including patient selection and antithrombotic strategy post-procedures has been provided in recent years, DAPT can be used to prevent device-related thrombus with satisfactory safety and efficacy. Chinese physicians should consider changing their antithrombotic strategy after LAAO and improving individualization in the future.

Study limitations

The present study, which focused on the implantation success and safety of LAAO with the WATCHMAN device and patient se-

lection in real-world China, has several limitations. The major limitation of our study was the lack of follow-up data after discharge. Therefore, we were unable to evaluate the long-term efficacy and safety of LAAO with the WATCHMAN device in the Chinese population and the changes of the antithrombotic agents and patients' compliance after discharge. Second, although the present study described the LAAO experience with WATCHMAN device in China, the absence of comparison between WATCHMAN device and antithrombotic therapy, such as warfarin, was one of the major limitations. Studies aimed at analyzing the long-term follow-up data of stroke, device-related or not related embolism, and bleeding events in LAAO patients and randomized controlled clinical trials to compare the efficacy of LAAO with OAC in China are urgently needed. Third, limited by the observational design, some procedural details of LAAO were excluded in the present study, such as the number of devices per patient and the depth of LAAO. Additionally, although more physician-training programs can be helpful to improve the success rate of LAAO procedures and avoid possible underreporting of complications, what is in more urgent need for Chinese physicians is to self-criticize their previous clinical experience of patient selection, to learn from the new findings of clinical research more proactively, and to control the LAAO indications and antithrombotic therapy more strictly.

Conclusion

In conclusion, LAAO with the WATCHMAN device has been performed successfully and safely in Chinese patients with AF in previous years. Additionally, more Chinese patients received LAAO with increased bleeding risk or non-compliance for OAC as indications, but less previous bleeding events on OAC, and received OAC for antithrombotic therapy after LAAO, which was different from indications in other countries and resulted in differences in the antithrombotic regimen after LAAO.

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