



Left Atrial Appendage Occlusion in Non-Valvular Atrial Fibrillation in a Korean Multi-Center Registry

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Background: The aim of this study was to evaluate clinical outcome after left atrial appendage (LAA) occlusion in real clinical practice and compare between Amplatzer cardiac plug (ACP) and Watchman.

Methods and Results: From October 2010 to February 2015, 96 successful LAA occlusion procedures were performed using either ACP (n=50) or Watchman device (n=46) in non-valvular atrial fibrillation (AF) patients (59 male; age, 65.1±9.4 years; CHADS₂, 2.5±1.2; CHA₂DS₂-VASc, 3.9±1.6; HAS-BLED, 2.7±1.3). The procedure success rate was 96.8%. There were serious complications in 4 patients (4.1%; 2 cardiac tamponade, 1 device embolization, and 1 major bleed). The anticoagulation cessation rate after 6 weeks was 92.7%. During mean 21.9-month follow-up, the incidence of death, stroke, systemic embolization and major bleeding was 5.2%, 4.2%, 0% and 1.0%, respectively. On transesophageal echocardiography of 93 patients within 6 months after the procedure, 24 residual leaks were observed (25.8%; 2 mild, 18 moderate, and 4 major). Clinical outcome was similar for the 2 devices, but peridevice leakage was more frequent with the Watchman than the ACP.

Conclusions: LAA occlusion was feasible in non-valvular AF patients with high risk of stroke and hemorrhage. The ACP and Watchman devices were similar in terms of procedural and clinical outcomes. (*Circ J* 2016; **80**: 1123–1130)

Key Words: Atrial fibrillation; Left atrial appendage occlusion; Stroke

Atrial fibrillation (AF) is the most common and significant arrhythmia in the clinical field of cardiology, and it increases the risk for thromboembolic stroke.^{1,2} It is not easy, however, to maintain chronic anticoagulation with warfarin without complications in real clinical situations, although stroke prevention with anticoagulation is essential and is considered standard therapy in the management of AF.^{3,4} Warfarin has a narrow therapeutic range, requires regular monitoring, and carries considerable risk of complications, such as cerebral or gastrointestinal bleeding, especially in old patients with medication or comorbidity.^{5–7} According to a previous review of 23 separate studies, the majority (91%) of thrombi were localized in or originated from the left atrial appendage (LAA) in patients with non-valvular AF.⁸ Based on

these prior observations, LAA occlusion was introduced as an alternative to anticoagulation treatment in non-valvular AF. Two kinds of closing devices are currently available in clinical practice: the Watchman (Boston Scientific, Natick, MA, USA) and the Amplatzer cardiac plug (ACP; St. Jude Medical, St. Paul, MN, USA).⁹ Recently, the WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation (PROTECT-AF) trial reported long-term (mean follow-up period, 3.8 years) data that the Watchman device was superior compared with warfarin treatment for preventing the combined outcome of stroke, systemic embolism, and cardiovascular death in non-valvular AF patients without contraindication to anticoagulation.¹⁰ Additionally, the non-randomized aspirin and plavix (ASAP) trial reported

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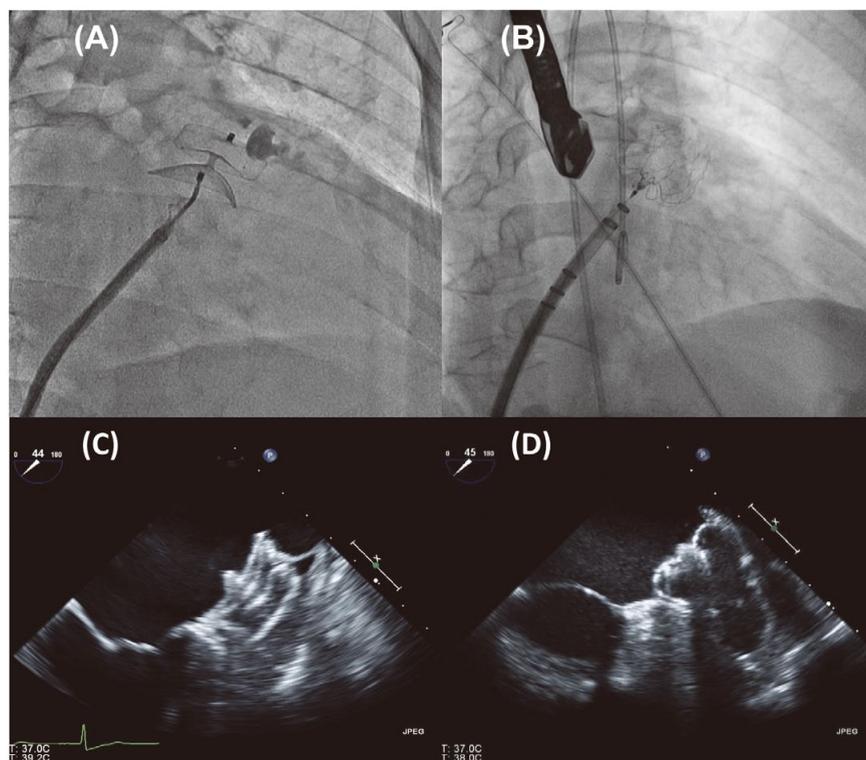


Figure 1. Representative intra-procedural fluoroscopy (right anterior oblique 30°/cranial 20°) and transesophageal echocardiography during left atrial appendage occlusion. (A,C) Amplatzer cardiac plug; (B,D) Watchman.

the safety and efficacy of the Watchman device with antiplatelet agent in non-valvular AF patients with contraindication to anticoagulation.¹¹ With respect to ACP, many registry studies on LAA closure using ACP reported that LAA occlusion is feasible in non-valvular AF patients.^{12–18} Thus, the aim of the present study was to compare the results of LAA occlusion using the 2 devices in unrestricted non-valvular AF patients with a high risk for bleeding or contraindication to anticoagulation and a high risk for stroke.

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Methods

Subjects

In a Korean multi-center registry involving 5 hospitals (Yonsei University Severance Hospital, Korea University Anam Hospital, Sejong General Hospital, Gachon University Gil Hospital, and Ulsan University Hospital), a total of 99 LAA occlusions were attempted between October 2010 and February 2015 at each institution after informed consent. Implantation was not done in 3 patients (large size of landing zone, 2 ACP; insufficient depth, 1 Watchman), therefore the procedure was successful in 96 patients with non-valvular AF (ACP, n=50; Watchman, n=46). Indications for the procedure were non-valvular AF (paroxysmal, persistent, or permanent) with CHADS₂ score ≥ 1 or CHADS₂VASc score ≥ 2 and high risk of bleeding or contraindication to anticoagulation. High risk of bleeding or contraindication to warfarin were defined as follows: (1) major or recurrent minor bleeding event during

anticoagulation; (2) high risk of bleeding according to HAS-BLED score ≥ 3 ; or (3) stroke during anticoagulation.

Procedure and Clinical Follow-up

All procedures were performed with fluoroscopy and transesophageal echocardiography (TEE) guidance under general anesthesia. Heparin (150 IU/kg) was used as an anticoagulant after atrial septal puncture to achieve activated clotting time 300–350 s. The size of the implanted device size was determined after LAA angiography. Implanted devices were approximately 10–20% larger in size than estimated in order to minimize device embolization and peridevice leakage (Figure 1). After positioning the devices into the LAA, we meticulously evaluated the stability of the device and intra- or peridevice leakage on angiography and TEE before deployment. After the procedure, all patients were followed on clinical visits at 2 weeks, 6–8 weeks, 3 months, and 6 months after the procedure, and then every 6 months. Clinical follow-up data, including on thromboembolic events such as stroke, transient ischemic attack (TIA), and systemic thromboembolism were collected during each physician visit. Anticoagulation after the procedure was continued for 6 weeks in 61 patients (Watchman, n=46; ACP, n=15), and dual antiplatelet agent (aspirin+clopidogrel) was prescribed in 35 patients with ACP immediately after LAA occlusion. In the early period of the registry, 15 patients with ACP were treated using the same anticoagulation strategy as that used with the Watchman device. Anticoagulation cessation and switch to antiplatelet agent was determined based on physician discretion after the confirmation of successful LAA occlusion on TEE within 6 weeks after

Table 1. Clinical Subject Characteristics				
Variable	All (n=96)	ACP (n=50)	Watchman (n=46)	P-value
Male	59 (61.5)	32 (64.0)	27 (58.7)	0.60
Age (years)	65.1±9.4	64.7±10.0	65.6±8.8	0.64
Height (cm)	163±9	165±9	162±9	0.19
Weight (kg)	67.7±12.1	70.0±13.9	66.2±9.9	0.24
AF pattern				
Paroxysmal	22 (22.9)	13 (26.0)	9 (19.6)	
Persistent	49 (51.0)	23 (46.0)	26 (56.5)	
Permanent	25 (26.0)	14 (28.0)	11 (23.9)	
Underlying disease				
Previous stroke	42 (43.8)	22 (44.0)	20 (43.5)	0.96
Heart failure	68 (70.8)	15 (30.0)	24 (52.2)	0.03
CAD	37 (38.5)	19 (38.0)	18 (39.1)	0.91
Hypertension	68 (70.8)	33 (66.0)	35 (76.1)	0.28
Diabetes mellitus	37 (38.5)	20 (40.0)	17 (37.0)	0.76
Dyslipidemia	48 (50.0)	24 (48.0)	24 (52.2)	0.68
CHADS₂ score	2.5±1.2	2.4±1.2	2.7±1.3	0.27
CHA₂DS₂-VASc score	3.9±1.6	3.6±1.6	4.1±1.7	0.18
HAS-BLED score	2.7±1.3	2.7±1.3	2.8±1.2	0.75
Medication at discharge				
Aspirin	65 (67.7)	37 (74.0)	28 (60.9)	0.09
Clopidogrel	46 (47.9)	31 (68.9)	13 (28.3)	<0.001
NOAC	14 (14.6)	5 (10.0)	9 (19.6)	0.16
Warfarin	47 (49.0)	13 (26.0)	34 (73.9)	<0.001
ACEi/ARB	52 (54.2)	24 (48.0)	28 (60.9)	0.21
β-blocker	39 (40.6)	23 (46.0)	16 (34.8)	0.26
Lipid-lowering agents	53 (55.2)	26 (52.0)	27 (58.7)	0.51

Data given as n (%) or mean±SD. ACEi, angiotensin converting enzyme inhibitor; ACP, Amplatzer cardiac plug; AF, atrial fibrillation; ARB, angiotensin receptor blocker; CAD, coronary artery disease; NOAC, novel oral anticoagulant.

procedure in all Watchman patients and in 15 ACP patients (35% of ACP patients).

TEE

TEE was performed in all patients before the procedure to assess LAA size, morphology, and intracardiac thrombi. LAA ostial size measurements were performed at 0°, 45°, 90°, and 135°. Maximum diameter was usually used for device size determination. Follow-up TEE was recommended at 6–8 weeks after the procedure to evaluate device positioning, intra- or peridevice leakage, and device-related thrombi.

Definition and Outcomes

The expected annual risks of stroke and bleeding were calculated for all of the patients at the time of the procedure according to previously described methods (ie, CHA₂DS₂-VASc¹⁹ and HAS-BLED⁵ scoring systems), and then the average annual risk for whole subject group was calculated. Successful LAA occlusion was defined as stability of device positioning in the LAA without intra- or peridevice leakage ≥5 mm. Grade of intra-procedural and follow-up device leakage was classified as minor (<1 mm), moderate (1–3 mm), or major (>3 mm) according to color jet width on Doppler echocardiography as previously described.²⁰ Intra- or peridevice leakage ≥5 mm at follow-up was defined as device failure. Death, ischemic stroke, systemic embolization, and major bleeding during follow-up were assessed as clinical outcomes.²¹

Statistical Analysis

Statistical analysis was performed using SPSS v20.0 (SPSS, Chicago, IL, USA). Continuous variables are expressed as mean±SD or median (IQR), and categorical variables as number and percentage. Student's t-test and paired T-test were used to compare continuous variables. Mann-Whitney U-test was used for skewed distributions. Categorical variables are expressed as both number and percentage and were compared using the chi-squared test or Fisher's exact-test. Occurrence of follow-up events is expressed as the number of events per 100 patient-years. Event-free survival was analyzed on Kaplan-Meier survival curves, and the differences between event-free survival curves were compared with log-rank test. Additionally, we also described the characteristics of patients with adverse events during follow-up. P<0.05 was defined as statistically significant.

Results

Clinical and Echocardiographic Characteristics

Subject baseline characteristics are listed in Table 1. Mean CHADS₂, CHA₂DS₂-VASc, and HAS-BLED scores were 2.5±1.2, 3.9±1.6, and 2.7±1.3, respectively. In regards to thromboembolic history, 42 patients (43.8%) had a history of previous stroke or TIA. In terms of bleeding risk, 23 patients (23.9%) had HAS-BLED score ≥4 points. Of them, 4 patients (17.3%) had major bleeding events on warfarin, consisting of 1 gastrointestinal hemorrhage and 3 intracranial hemorrhages.

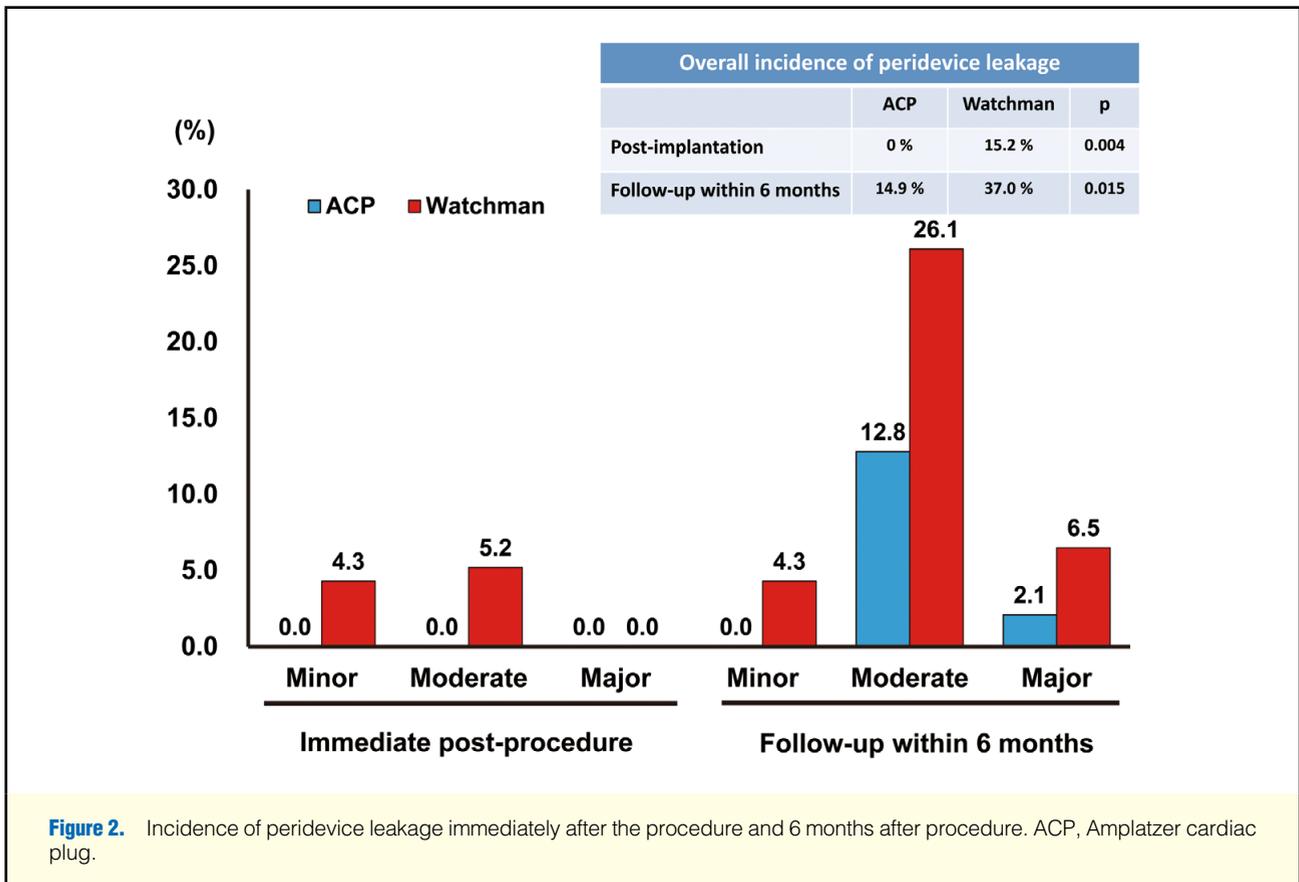


Table 2. Echocardiographic and Procedural Findings				
	All (n=96)	ACP (n=50)	Watchman (n=46)	P-value
Echocardiographic parameters				
LVEF (%)	58.5±10.1	58.1±10.4	58.9±9.9	0.94
LA diameter (mm)	50.1±8.9	51.1±10.2	49.1±7.1	0.40
LA volume index (ml/m ²)	48.1±24.9	50.0±28.6	46.4±21.1	0.30
LAA size				
45°	19.7±4.7	19.2±5.8	20.4±3.0	0.19
90°	20.6±3.8	20.6±4.0	20.6±3.6	0.94
135°	21.5±4.3	21.1±4.5	21.8±4.1	0.42
SEC				
Mild	25 (26.0)	10 (20.0)	15 (32.6)	0.47
Moderate	7 (7.3)	3 (6.0)	4 (8.7)	
Severe	5 (5.2)	3 (6.0)	2 (4.3)	
Device				
Device size (mm)	27.0±3.3	26.8±3.2	27.4±3.5	0.40
Any leakage	7 (7.3)	0 (0.0)	7 (15.2)	0.004
Leakage size (mm)			1.85±0.75	
Complication†				
Pericardial effusion	8 (8.3)	3 (6.0)	5 (10.9)	0.47
Cardiac tamponade	2 (2.1)	1 (2.0)	1 (2.2)	1.00
Device embolization	1 (1.3)	1 (2.0)	0 (0.0)	1.00
Major bleeding	1 (1.3)	1 (2.0)	0 (0.0)	1.00
FAP	0 (0.0)	0 (0.0)	0 (0.0)	—

Data given as n (%) or mean±SD. †Defined according to the Valve Academic Research Consortium criteria.¹⁸ FAP, femoral artery pseudoaneurysm; LA, left atrium; LAA, left atrial appendage; LVEF, left ventricular ejection fraction; SEC, spontaneous echo contrast. Other abbreviations as in Table 1.

Patient ID no.	Age (years)	Sex	CHA ₂ DS ₂ -VASc	Device	Follow-up duration (months)	Cause of death
1	62	M	5	Watchman	37	ARDS
2	79	M	3	Watchman	21	Septic shock
3	78	F	6	Watchman	8	COPD exacerbation
4	74	M	6	ACP	2	Septic shock
5	54	F	5	ACP	1	Cardiac tamponade

ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease. Other abbreviations as in Table 1.

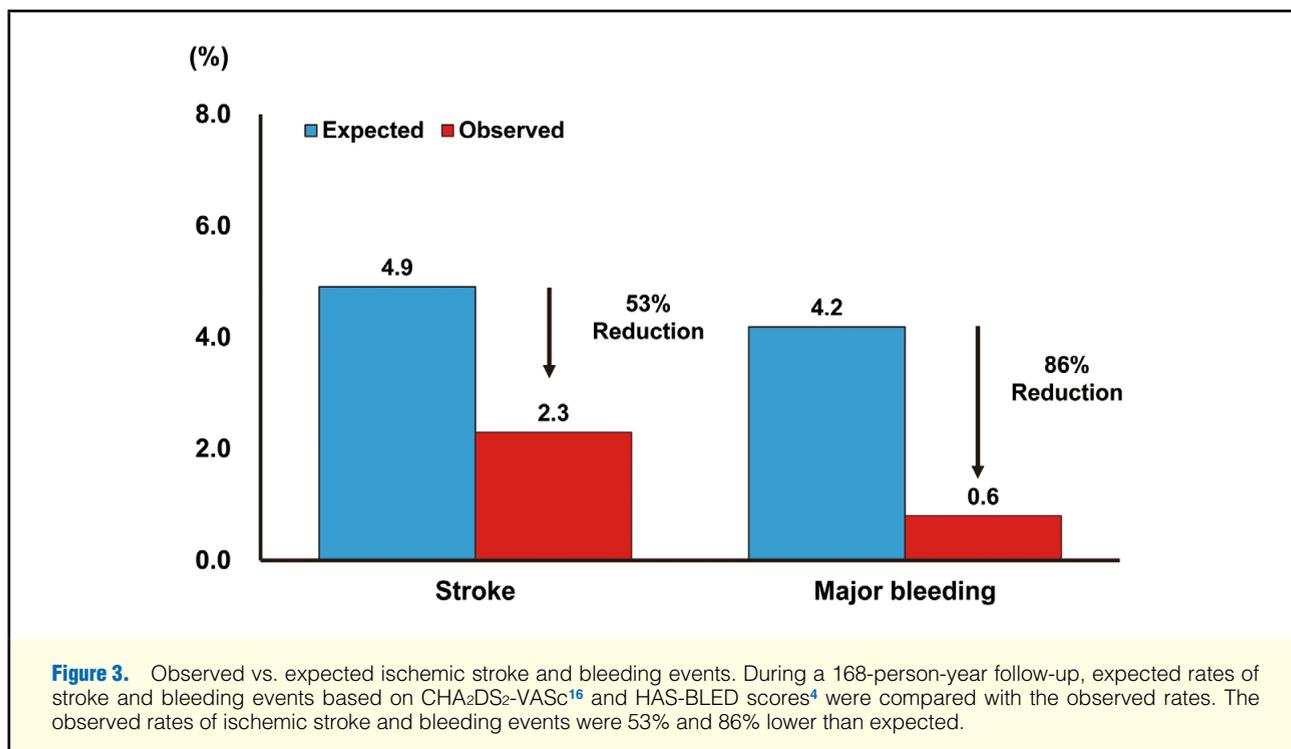


Figure 3. Observed vs. expected ischemic stroke and bleeding events. During a 168-person-year follow-up, expected rates of stroke and bleeding events based on CHA₂DS₂-VASc¹⁶ and HAS-BLED scores⁴ were compared with the observed rates. The observed rates of ischemic stroke and bleeding events were 53% and 86% lower than expected.

LAA ostium diameter at 45°, 90°, and 135° on TEE was 17.8±7.0, 18.6±6.9, and 19.3±7.5 mm, respectively. Severe spontaneous echo contrast (SEC) was detected on pre-procedure TEE in 5 patients (5.2%), and also on follow-up TEE.

Procedural and In-Hospital Outcome

Devices were successfully implanted in 96/99 patients (96.9%); 3 patients had LAA not optimal for device implantation (2 patients with LAA too large for an ACP, and 1 patient with LAA too shallow for a Watchman). During the periprocedural period, there was 1 device embolization (1.0%), 2 cardiac tamponades (2.0%), and 1 groin hematoma requiring transfusion (1.0%). There were 8 cases of self-limited mild pericardial effusion after the procedure. There were no thromboembolic events, although suspected organized thrombi localized in the LAA occluded the ACP device in 2 patients. There was 1 cardiac death due to cardiac tamponade 2 days after the procedure.

Mean size of the ACP and Watchman devices was 26.8±3.2 mm and 27.4±3.5 mm, respectively (P=0.40). One patient had respiratory arrest 1 day after the procedure, and significant peridevice leakage occurred after cardiac compression, although

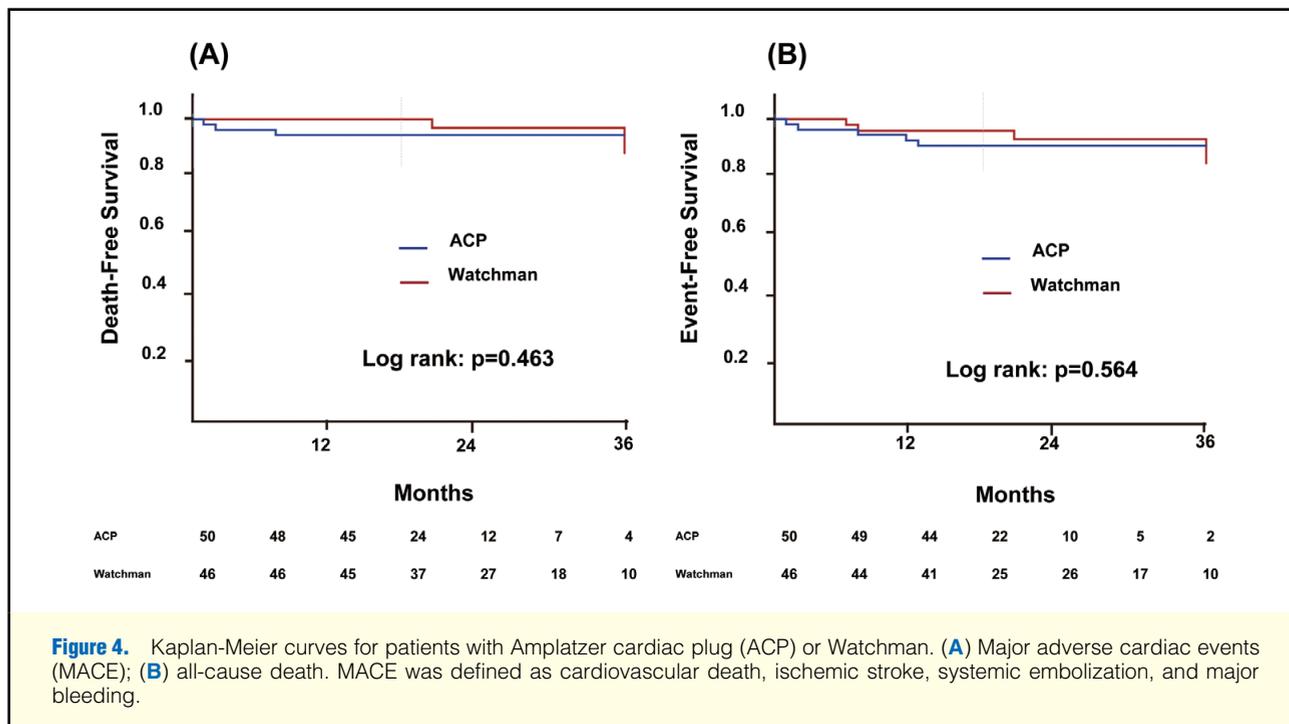
the device was implanted successfully without any leakage. This patient was therefore excluded from analysis at follow-up.

Peridevice Leakage on TEE

There were 7 (2 minor and 5 moderate, 7.3%) residual peridevice leakages noted immediately after deployment on intra-procedural TEE. Follow-up TEE was performed in 93 patients within 6 months of the procedure, and 24 residual leakages (25.8%), including 2 minor, 18 moderate, and 4 major, were observed (Figure 2). All 5 major residual leakages developed in 1 ACP and 4 Watchman patients, in whom no leakages were observed immediately after deployment. With regard to comparison of peridevice leakage between the ACP and Watchman devices, overall peridevice leakage was more frequently observed on post-procedural follow-up TEE: 0% vs. 15.2% (P=0.004) after implantation and 14.9% vs. 37.0% (P=0.015) at follow-up, but no significant leakage was noted during use.

Clinical Outcome at Follow-up

Follow-up outcome is summarized in Table 2. Total follow-



Patient ID no.	Event	Onset (months)	Age (years)	Sex	CHA ₂ DS ₂ -VASC	HAS-BLED score	Device type	Device size (mm)	Peridevice leakage	Carotid stenosis	Severe SEC	Anti-thrombotic therapy
1	TIA	6	81	M	5	4	Watchman	33	Major	Y	N	Aspirin+clopidogrel
2	Minor stroke	15	54	M	4	6	ACP	28	No	N	Y	Aspirin+warfarin
3	Minor stroke	15	54	M	2	4	ACP	30	No	N	Y	Aspirin+clopidogrel
4	Minor stroke	7	69	M	2	3	Watchman	27	No	N	N	Aspirin+clopidogrel

TIA, transient ischemic attack. Other abbreviations as in Tables 1,2.

up duration was 175.1 patient-years. Mean follow-up duration was 21.9 months (median, 20.5 months). Rate of anticoagulation cessation at 6 weeks after the procedure was 93.6%. Five patients (5.2%) died during follow-up; 1 death was caused by cardiac tamponade and 4 were not related to the device (Table 3). Three minor strokes and 1 TIA occurred during the follow-up period (2.3 events/100 patient-years); the strokes were completely resolved without any sequelae. Annual rate of ischemic stroke and major bleeding was 2.3% (4/168 patient-years) and 0.6 (1/168 patient-years), a 53% and 86% risk reduction, respectively (Figure 3). All 4 patients who had TIA or stroke underwent magnetic resonance imaging (MRI) to evaluate the brain and vascular status. Significant left carotid artery stenosis was found in 1 patient, but the remaining 3 patients had no significant stenosis in the intracranial or internal carotid artery on MRI.

Distal embolization and major bleeding were not observed 7 days after the procedure. When comparing the ACP and Watchman devices, there were no significant differences between the 2 devices in terms of major adverse cardiac events, including cardiovascular death, ischemic stroke, distal embolization, and major bleeding or overall death (Figure 4).

Additionally, 3 device thrombi (ACP, n=1; Watchman, n=2) were found incidentally, but all device thrombi were completely dissolved with anticoagulation without any adverse events. After verifying via TEE the dissolution of the thrombus after 2–3 months of anticoagulation, anticoagulation was continued in 1 patient thereafter, while the remaining 2 patients discontinued anticoagulation after confirmation of the complete dissolution around the device, and were maintained on only aspirin without any embolic event.

The clinical characteristics of individuals with stroke events are listed in Table 4.

Discussion

Percutaneous LAA occlusion was safely performed in most patients and had a high procedure success rate in the present multicenter registry. In terms of procedure-related complications, there were 4 serious adverse events (4.1%) and 8 self-limited pericardial effusions that did not require additional procedures. The present stroke rate was slightly higher than in

previous reports after percutaneous LAA occlusion but was acceptable.^{11,13,18,22} This difference may be due to the unrestricted inclusion of patients with a higher risk of stroke due to significant carotid stenosis, severe SEC, and lower ejection fraction. Therefore, careful patient selection and pre-procedural evaluation for extracardiac thromboembolic sources may be needed before performing this procedure.

Procedural and In-Hospital Outcome

In previous studies of percutaneous LAA occlusion, there were safety concerns with regards to high periprocedural complication rates, including serious pericardial effusion and procedure-related stroke.^{14,22} Cardiac tamponade developed in 2 cases (2.0%), which might have been related to injury of the LA or LAA from the delivery sheath, stiff wire, or the device during the procedure because the cardiac tamponade was detected after device implantation. The registry data, however, showed improved periprocedural complication rates, which were explained as a learning curve effect.²³ Other studies reported high procedure success rates with acceptable procedure-related complication rates, which is consistent with the present results.^{11,13,15,24} Another interesting finding from the present study was that there were no procedure-related thromboembolic events, although organized LAA thrombi were suspected on TEE in 2 cases. The prevalence of intracardiac thrombi is generally considered a contraindication to intracardiac device manipulation due to concern regarding thromboembolism.^{11,15,22} We previously reported a successful LAA occlusion with ACP in a patient with suspected organized thrombi localized in the LAA.²¹ Additionally, we prefer ACP for LAA occlusion rather than the Watchman device in patients with LAA thrombi, because of the ACP shape (short length) and because the ACP device allows for minimal manipulation of LAA thrombi.²⁵ Percutaneous LAA occlusion, however, is generally not recommended in patients with intracardiac thrombi.

Peridevice Leakage

In the present study, the prevalence of peridevice leakage on follow-up TEE was similar to that of previous reports (ACP, 0–11.5% immediately after procedure and 11.6–16.2% at 6 months; Watchman, 13% immediately after procedure, 40.9% at 45 days, 33.8% at 6 months, and 21.1% at 12 months).^{12,22,24} When comparing the ACP and Watchman devices, immediate post-procedural and follow-up peridevice leakage were more commonly observed for the Watchman device. This may be related to the double disc structure of the ACP, which contributes to better sealing.¹² Significant leakage (≥ 5 mm), however, was not detected and the incidence of clinical events was similar for both devices. Interestingly, all major leakages (3–5 mm) developed in patients in whom no peridevice leakage was detected immediately after the procedure. Furthermore, peridevice leakage observed during the post-procedure period either remained the same or improved during follow-up, but 70% of leaks detected on follow-up were newly developed. Based on the current study, serial follow-up may be necessary to check the status of LAA occlusion. Several possible explanations include incomplete device endothelialization, anatomical remodeling of LAA ostium over time, use of an undersized device without periprocedural residual leak due to LAA contraction immediately after implantation, and low left ventricular ejection fraction, which might increase the LA dimensions.¹² In general, the presence of peridevice leakage (< 5 mm) was not clinically relevant, indicating that anticoagulation can be discontinued at the discretion of physicians. Significant leakage (≥ 5 mm) and the progressive increase of

leakage may necessitate the continuation of anticoagulation and additional intervention with another device implantation, or surgical ligation and removal of the device.^{22,26}

Follow-up Outcome

In terms of follow-up outcome, anticoagulation was stopped and switched to antiplatelet agent in 93.6% of patients 6–8 weeks after the procedure. Novel oral anticoagulant (NOAC) was prescribed in 14 of 61 patients (23.0%) on anticoagulation, and had an efficacy and safety similar to warfarin, but data to assess the efficacy of NOAC after LAA occlusion were lacking. Recently, Bösch et al reported that NOAC may be safe and effective during a 45-day period after Watchman implantation.²⁷ The efficacy and safety of NOAC, however, after LAA occlusion, should be compared with warfarin in a future clinical study. In the present study only one major bleeding event occurred after the procedure due to a groin hematoma that required a blood transfusion, but no further bleeding events were reported during follow-up. Considering that the expected rate of major bleeding event was approximately 8.9% according to high HAS-BLED score (2.7 ± 1.3) in the present patients, LAA occlusion could be considered effective in reducing major bleeding events (81% risk reduction).⁵ In contrast, 3 minor stroke and 1 TIA (2.3 events/100 patient-year) were observed during follow-up. This was a relatively higher thromboembolic event rate than expected, and might be related to differences in patient population between the present study and other studies. Previous prospective studies excluded patients with severe SEC, carotid stenosis, severe heart failure, and repeated radiofrequency catheter ablation of AF.^{11,22} In contrast, the present study had no definite exclusion criteria other than exclusion of optimal candidates for anticoagulation. In the present study (Table 3), 2 patients with stroke would have been excluded from other studies. SEC is a well-known risk factor for stroke or other embolic events and is observed in 12% of non-valvular AF patients per year.²⁸ In the present study, 2 patients had stroke but they completely recovered, which suggests that LAA occlusion may lessen thrombus burden in patients with AF. Based on the present results, LAA occlusion is a good alternative to anticoagulation to prevent ischemic thromboembolic events in carefully selected patients. LAA occlusion, however, might be an option to reduce the thrombus burden in the LA to prevent stroke and even improve prognosis after stroke.

Study Limitations

The major limitation of the present study was the relatively small number of patients used to assess the efficacy and safety of the devices. The LAA occlusion devices were not randomly assigned in this study, and the comparison of 2 different LAA occlusion devices requires consideration of confounding factors for accurate interpretation of the data. Therefore, the present findings should be confirmed on prospective randomized trial. Follow-up TEE was not performed in all of the patients and the follow-up period varied for some of the patients. Finally, the annual stroke and bleeding risks were estimated based on previous observations. We acknowledge, however, that ethnic differences might have existed, because there are no published data for real stroke and bleeding rates according to CHA₂DS₂-VASc and HAS-BLED scores in a Korean population.

Conclusions

Percutaneous LAA occlusion was a relatively safe and feasi-

ble procedure as an alternative to anticoagulation in patients at high risk for bleeding or contraindication to anticoagulation, or in whom anticoagulation failed to prevent stroke. The ACP and Watchman devices were similar in terms of reducing ischemic stroke, although peridevice leakage was more frequently observed with the Watchman device. Careful patient selection and pre-procedural evaluation for extracardiac thromboembolic source are needed before performing this procedure.

Acknowledgments

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Conflicts of Interest

J.-W.P. is a consultant for Amplatzer cardiac plug, St. Jude Medical, St. Paul, MN, USA and Occlutech, Jena, Germany. S.K. is a consultant for Watchman, Boston Scientific, Natick, MA, USA.

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