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Clinical outcomes of Watchman vs. Amplatzer occluders for left atrial appendage closure (WATCH at LAAC)

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Aims This study compares clinical outcomes of Watchman vs. Amplatzer devices for left atrial appendage closure (LAAC).

Methods and results Of two real-world registries, the Watchman registry Lichtenfels, Germany, and the Amplatzer registry Bern-Zurich, Switzerland, 303 and 333 consecutive patients, respectively, were included. After a 1:1 propensity score matching, 266 vs. 266 patients were compared by use of the predefined primary efficacy endpoint of stroke, systemic embolism and cardiovascular/unexplained death, the primary safety endpoint of major peri-procedural complications and major bleeding events at follow-up, and the combined hazard endpoint, a composite of all above-mentioned hazards. Mean age was 75.3 ± 7.8 (Watchman) vs. 75.1 ± 9.9 (Amplatzer) years, CHA_2DS_2-VASc score 4.5 ± 1.7 vs. 4.5 ± 1.5, and HAS-BLED score 3.2 ± 1.0 vs. 3.2 ± 1.0. At a mean follow-up of 2.4 ± 1.3 vs. 2.5 ± 1.5 years and 1.322 patient-years, the primary endpoints of efficacy [40/646, 6.2% [Watchman] vs. 43/676, 6.4% [Amplatzer]; hazard ratio (HR), 1.02; 95% confidence interval (CI), 0.66–1.58; $P = 0.92$] and safety (33/646, 5.1% vs. 30/676, 4.4%; HR, 0.57; 95% CI, 0.29–1.11; $P = 0.10$), as well as the combined hazard endpoint (69/646, 10.7% vs. 66/676, 9.8%; HR, 0.80; 95% CI, 0.55–1.12; $P = 0.26$) were similar for both groups.

Conclusion This study suggests comparable efficacy and safety of the Watchman and Amplatzer devices.

Keywords Atrial fibrillation • Stroke prevention • Left atrial appendage closure • Watchman • Amplatzer • Anticoagulation

Introduction

Percutaneous left atrial appendage closure (LAAC) has become an alternative to oral anticoagulation (OAC) for stroke prevention in patients with non-valvular atrial fibrillation (AF).[1,2] The most frequently used LAAC occluders are the Amplatzer (Abbott, St Paul, MN, USA), with its 1st generation Amplatzer Cardiac Plug and the 2nd generation Amplatzer Amulet, and the Watchman (Boston Scientific, Marlborough, MA, USA). In contrast to the Watchman, a membrane-capped plug, the Amplatzer occluders feature a two-part plug-and-disc (pacifier) design. Left atrial appendage closure with the US Food and Drug Administration approved Watchman device has set the standard of device-based stroke prevention with randomized controlled trials.[3] The 5-year outcomes of the PROTECT-AF and

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What's new?

- First comparison of long-term clinical outcomes after LAAC with Watchman vs. Amplatzer occluders based on the results of two real-world registries.
- Amplatzer devices may provide similar efficacy and safety as the US Food and Drug Administration approved Watchman, which has set the standard of device-based stroke prevention in randomized trials.

PREVAIL trials showed that LAAC with the Watchman provides similar efficacy in prevention of all-cause stroke as warfarin and reduces cardiovascular mortality and major bleeding events, particularly haemorrhagic stroke.[4] The EWOLUTION and post-approval US experience registries reported high device success rates and low peri-procedural complication rates for all-comers populations.[5,6] For the Amplatzer Cardiac Plug and Amplatzer Amulet devices, favourable outcomes were confirmed in all-comer registries.[7–10] However, a head-to-head comparison of clinical outcomes of Amplatzer and Watchman devices has not been reported yet. Until results of ongoing randomized trials will be available, the present study is supposed to compare clinical efficacy, safety, and net clinical benefit of the Watchman and Amplatzer devices based on the results of two real-world registries.

Methods

Patient population

The Lichtenfels Watchman registry (Watchman, Department of Cardiology, Helmut-G.-Walther-Klinikum, Lichtenfels, Germany) and the Bern-Zurich Amplatzer registry (Amplatzer, Departments of Cardiology of the Bern and Zurich University Hospitals, Switzerland) are observational registries, which prospectively enrolled all patients undergoing LAAC in the respective institutions since 2009. All patients provided written informed consent according to the requirements and approval of the local ethics committees. Between September 2015 and March 2018, clinical follow-up was carried out by patient visits, hospital stays, and surveys. Clinical safety and efficacy events were adjudicated by a clinical event committee of two independent cardiologists and in case of disagreement by a third referee. All analyses were performed according to the intention-to-treat principle.

LAAC procedure and follow-up

Indications for LAAC were based on current guidelines and recommendations.[1,2,11] A wide range of AF patients with high thromboembolic risk with absolute or relative contraindications for OAC were included in both registries. Exclusion criteria were active infection or endocarditis, pregnancy, intra-cardiac thrombus, and reasons for OAC other than AF. Device characteristics and procedural aspects were previously described in detail.[3,7] After LAAC, transoesophageal echocardiography (TEE) was performed at 45 days and 6 months (Watchman) and 4–6 months (Amplatzer) to document sufficient LAAC without device-related thrombus (DRT) or major peri-device leaks (>5 mm).

Anti-thrombotic therapy

In the Watchman group, according to the PROTECT-AF trial, the post-implant anti-thrombotic therapy included 45 days of acetylsalicylic acid and OAC with a vitamin K antagonist or non-vitamin K antagonist, or a combination of low molecular weight heparin, if a contraindication to vitamin K antagonist was present.[3] If TEE at that time showed complete LAAC without relevant peri-device leaks or DRT, the patient was switched to acetylsalicylic acid and clopidogrel for 6 months until the 2nd TEE exam and then to acetylsalicylic acid alone. In the Amplatzer group, the choice and duration of anti-thrombotic treatment following LAAC were left to the discretion of the treating physician for each individual patient accounting for medical history (e.g. recent PCI or other intervention) and typically consisted of dual antiplatelet therapy with acetylsalicylic acid and clopidogrel for 1–6 months.[7]

Definitions and endpoints

Demographic, clinical, and procedural characteristics, as well as adverse events and endpoints, were reported according to the current recommendations of the European Association of Percutaneous Coronary Interventions, the Munich consensus document, the Bleeding Academic Research Consortium, the Valve Academic Research Consortium criteria, and the 2017 Cardiovascular and Stroke Endpoint Definitions for Clinical Trials.[11–15] Device success was defined as correct deployment and implantation of the respective left atrial appendage occluder. At TEE follow-up, a leak >5 mm was considered as major.[12] The primary efficacy endpoint was a composite of all-cause stroke, systemic embolism, and cardiovascular/unexplained death. The primary safety endpoint consisted of major bleeding events and major peri-procedural complications, such as death, ischaemic stroke, cardiac tamponade, major access vessel complication, device embolization, severe kidney injury, need for cardiopulmonary resuscitation, need for urgent surgery, or major bleeding according to the Valve Academic Research Consortium and Bleeding Academic Research Consortium type 3 or higher. The combined hazard endpoint (i.e. the net clinical benefit) was a composite of all above-mentioned hazards.

Statistical analyses

Statistical analyses were performed with the Graph Pad Prism 6 software (GraphPad Inc., La Jolla, CA, USA). Categorical variables are presented as actual numbers and percentages and compared using the χ^2 test. Continuous variables are summarized as mean ± SD and compared using the Mann–Whitney test. The Kaplan–Meier method was used for graphical assessment of time-dependent events. For comparison of event curves, the log-rank (Mantel-Cox) test was used. For determination of hazard ratio, the Mantel–Haenszel method was applied. Findings were considered statistically significant at the 0.05 level.

A propensity score matching was performed using the packages 'MatchIt' and 'cobalt' using the R software.[16] We randomly generated 2000 with ratio 1:1 and calliper 0.35 other new models were randomly generated and the best of those models was chosen. The choice criteria for the best model were a standardized mean difference <0.30 for each variable and minimal mean (0.0554) of all standardized absolute mean differences. As a result, there was no significant difference in the co-variables among the two groups using a univariate logistic regression or unpaired *t*-test.

Table 1 Baseline characteristics

Variable	Watchman ($n = 266$)	Amplatzer ($n = 266$)	*P*-value
Demographics and clinical features			
Age at time of LAAC (years)	75.3 ± 7.8	75.1 ± 9.9	0.82
Body mass index (kg/m^2)	28.4 ± 5.0	27.6 ± 5.4	0.08
Female gender	85 (32.0%)	87 (32.7%)	0.85
Coronary artery disease	131 (49.2%)	134 (50.4%)	0.79
Prior PCI/CABG	114 (42.9%)	122 (45.9%)	0.49
Stroke risk			
CHA_2DS_2-VASc score	4.5 ± 1.7	4.5 ± 1.5	0.98
Prior stroke (all cause)	75 (28.2%)	82 (30.8%)	0.51
Congestive heart failure	76 (28.6%)	71 (26.7%)	0.63
Arterial hypertension	243 (91.4%)	244 (91.7%)	0.88
Age >75 (years)	159 (59.8%)	152 (57.1%)	0.54
Vascular disease	166 (62.4%)	167 (62.8%)	0.93
Diabetes mellitus	82 (30.8%)	74 (27.8%)	0.45
Bleeding risk			
HAS-BLED score	3.2 ± 1.0	3.2 ± 1.0	0.45
Prior bleeding	218 (82.0%)	191 (71.8%)	0.004
Intracranial	26 (9.8%)	42 (15.8%)	0.04
Gastrointestinal	74 (27.8%)	69 (25.9%)	0.62
Other site	45 (16.9%)	50 (18.8%)	0.62
Arterial hypertension >160 mmHg	21 (7.9%)	25 (9.4%)	0.54
Kidney disease	19 (7.1%)	20 (7.5%)	0.87
Liver disease	26 (9.8%)	7 (2.6%)	0.0006
Labile INR (international normalized ratio)	9 (3.4%)	17 (6.4%)	0.11
Drugs with predisposition to bleeding	231 (86.8%)	237 (89.1%)	0.42
Alcohol intake >8 U/week	18 (6.8%)	17 (6.4%)	0.86

Categorical variables are expressed as frequencies (*n*) and percentages (%). Continuous data are reported as means and standard deviation.
CABG, coronary artery bypass grafting; LAAC, left atrial appendage closure; PCI, percutaneous coronary intervention.

Results

Study population

Between February 2009 and March 2017, 303 patients were enrolled in the Watchman registry and 333 patients were entered in the Amplatzer registry. All Watchman occluders were implanted by a single operator (J.Y.), whereas in the Amplatzer group procedures were performed by 13 different operators. After the 1:1 propensity score matching, this analysis includes 266 Watchman and 266 Amplatzer patients. It comprises a total of 1.322 patient-years with a mean follow-up of 2.4 ± 1.3 years (Watchman) and 2.5 ± 1.5 years (Amplatzer; $P = 0.35$). No patient was lost to follow-up.

Baseline characteristics are shown in *Table 1*. All relevant baseline characteristics were similar in both groups, especially stroke and bleeding risk [mean CHA_2DS_2-VASc score 4.5 ± 1.7 (Watchman) vs. 4.5 ± 1.5 (Amplatzer), $P = 0.98$, mean HAS-BLED score 3.2 ± 1.0 vs. 3.2 ± 1.0, $P = 0.45$]. Patients of the Watchman group had a higher body mass index (28.4 ± 5.0 vs. 27.6 ± 5.4, $P = 0.08$) and, prior to LAAC, had suffered more frequently from bleeding (82.0% vs. 71.8%, $P = 0.004$) and liver disease (9.8% vs. 2.6%, $P = 0.0006$) but less frequently from intracranial bleeding (9.8% vs. 15.8%, $P = 0.04$).

Procedural aspects and TEE follow-up

Procedural aspects and TEE follow-up are shown in *Table 2*. Device success was similar for both occluders [96.6% (Watchman) vs. 96.2% (Amplatzer), $P = 0.82$]. The rate of overall major peri-procedural complications did not differ (4.1% vs. 6.0%, respectively, $P = 0.32$). However, there were differences in three single components: The rate of major access vessel complications was higher in the Watchman group (2.3% vs. 0.0%, $P = 0.014$). On the other hand, in the Amplatzer group, a higher rate of device embolizations (0.4% vs. 3.0%, $P = 0.002$), bailout surgery (0.0% vs. 2.6%, $P = 0.008$), and cardio-pulmonary resuscitation (0.0 vs. 2.3%, $P = 0.01$) was documented. In the Amplatzer group, six of eight (75%) embolizations occurred in patients who received the Amplatzer Cardiac Plug. Due to the contemporary usual device-specific anti-thrombotic regimens after LAAC, i.e. at the beginning of the study, more patients of the Watchman group were anticoagulated (96.2% vs. 2.6%, $P < 0.0001$), mostly with low molecular weight heparins (86.5% vs. 0.0%, $P < 0.0001$). Transoesophageal echocardiography at follow-up was available in 255 patients of the Watchman (95.9%) and in 170 (63.9%) in the Amplatzer group ($P < 0.0001$). The rate of DRT was equal (4.1% vs. 4.1%, $P = 1.0$). In the Watchman group, DRT was associated

Table 2 Procedural aspects

Variable	Watchman ($n = 266$)	Amplatzer ($n = 266$)	P-value
Procedural characteristics			
Amplatzer Cardiac Plug		201 (75.6%)	
Amulet		65 (24.4%)	
Device success	257 (96.6%)	256 (96.2%)	0.82
Major peri-procedural complications	11 (4.1%)	16 (6.0%)	0.32
Death	0 (0.0%)	1 (0.4%)	0.32
Stroke (any)	2 (0.8%)	0 (0.0%)	0.16
Pericardial effusion requiring intervention	5 (1.9%)	10 (3.8%)	0.19
Major bleeding (>BARC 3a)	8 (3.0%)	11 (4.1%)	0.48
Major access vessel complication	6 (2.3%)	0 (0.0%)	0.014
Need for bailout surgery	0 (0.0%)	7 (2.6%)	0.008
Device embolization	1 (0.4%)	8 (3.0%)	0.02
VARC-2 severe kidney injury	0 (0.0%)	1 (0.4%)	0.32
Need for cardio-pulmonary resuscitation	0 (0.0%)	6 (2.3%)	0.01
Anti-thrombotic therapy post-LAAC			
Any anticoagulation	256 (96.2%)	7 (2.6%)	<0.0001
Vitamin K antagonists	9 (3.4%)	7 (2.6%)	0.61
Non-vitamin K antagonists	17 (6.4%)	0 (0.0%)	<0.0001
Low molecular weight heparin	230 (86.5%)	0 (0.0%)	<0.0001
Acetylsalicylic acid	250 (94.0%)	248 (93.2%)	0.72
Platelet inhibitors other than acetylsalicylic acid	27 (10.2%)	245 (92.1%)	<0.0001
TEE follow-up			
TEE performed	255 (95.9%)	170 (63.9%)	<0.0001
DRT	11 (4.1%)	11 (4.1%)	1.0
Peri-device leak, ≥5 mm	2 (0.8%)	2 (0.8%)	1.0

Categorical variables are expressed as frequencies (n) and percentages (%). Continuous data are reported as means and standard deviation.
BARC, bleeding academic research consortium; DRT, device-related thrombus; LAAC, left atrial appendage closure; MCD, Munich consensus document; VARC, valve academic research consortium.

with two ischaemic disabling strokes, despite the fact that one patient was still under OAC. In the Amplatzer group, one patient with DRT suffered transient ischaemic attack (TIA), in two other patients a disabling, as well as a non-disabling ischaemic stroke, were documented. Also, the rate of major peri-device leaks (0.8% vs. 0.8%, $P = 1.0$) was equal. In the Watchman group, one patient with a major peri-device leak suffered a TIA despite treatment with a NOAC.

Clinical outcomes

Clinical outcomes are listed in *Table 3*. Kaplan–Meier curves of the primary endpoints and their components are shown in *Figures 1* and *2*. The primary efficacy endpoint was similar in both groups. It was reached in 40/646, 6.2% (Watchman) vs. 43/676, 6.4% (Amplatzer) [hazard ratio (HR), 1.02; 95% confidence interval (CI), 0.66–1.58; $P = 0.92$]. None of the components of the primary efficacy endpoint was significantly different between the two groups. All-cause stroke occurred in 12/646, 1.9% with Watchman vs. 10/676, 1.5% with Amplatzer devices (HR, 0.85; 95% CI, 0.37–2.0, $P = 0.71$). Cardiovascular and unexplained deaths were documented for the Watchman group with 28/646, 4.3% vs. 37/676, 5.5% in the Amplatzer group (HR, 1.29; 95% CI, 0.79–2.1, $P = 0.31$). Also, the primary safety endpoint occurred with a comparable frequency (33/646, 5.1% vs. 30/676, 4.4%; HR, 0.57; 95% CI, 0.29–1.11; $P = 0.10$). A non-significant trend for a higher rate of major bleeding events (23/646, 3.6% vs. 14/676, 2.1%; HR, 0.53; 95% CI, 0.28–1.0, $P = 0.06$) was observed in the Watchman group. Considering all above-mentioned components of the primary efficacy and safety endpoint, the combined hazard endpoint, i.e. the net clinical patient benefit was similar for both devices (69/646, 10.7% vs. 66/676, 9.8%; HR, 0.80; 95% CI, 0.55–1.12; $P = 0.26$).

Discussion

In this direct, propensity matched, comparison, LAAC with Watchman and Amplatzer occluders in 532 patients showed similar efficacy, safety, and net clinical benefit. After a total of 1.322 patient-years during a mean follow-up of 2.4 ± 1.3 years (Watchman) and 2.5 ± 1.5 years (Amplatzer), all components of the primary safety and efficacy endpoints were comparable for the two devices.

The overall rate of major peri-procedural complications of 4.1% in the Watchman and 6.0% in the Amplatzer group reflects the elderly, fragile, and polymorbid patient cohorts of this study and the learning curves of the centres. Differences in access vessel complications, device embolizations, bailout surgery, and cardio-pulmonary resuscitations between the groups may be attributable to the different

Table 3 Clinical outcomes

Variable	Watchman (n = 266)		Amplatzer (n = 266)		P-value
	646 patient-years		676 patient-years		
Age at follow-up (years)	78.2 ± 7.8		78.2 ± 8.8		0.96
Time of follow-up (years)	2.4 ± 1.3		2.5 ± 1.5		0.35
Clinical outcome					
Primary endpoints	Events/patient-years	Observed rate	Events/patient-years	Observed rate	
Primary efficacy endpoint	40/646	6.2 (4.6–8.3)	43/676	6.4 (4.8–8.5)	0.92
Primary safety endpoint	33/646	5.1 (3.7–7.1)	30/676	4.4 (3.1–6.3)	0.10
Combined hazard endpoint	69/646	10.7 (8.5–13.3)	66/676	9.8 (7.7–12.2)	0.26
Death					
30-day mortality (all-cause)	4/266	1.5 (0.6–3.8)	6/266	2.3 (1.0–4.8)	0.52
1-year mortality (all-cause)	18/266	6.8 (4.3–10.4)	28/266	10.5 (7.4–14.8)	0.12
All-cause death	54/646	8.4 (6.5–10.7)	69/676	10.2 (8.1–12.7)	0.27
Cardiovascular/unexplained death	28/646	4.3 (3.0–6.2)	37/676	5.5 (4.0–7.5)	0.31
Non-cardiovascular death	26/646	4.0 (2.8–5.8)	32/676	4.7 (3.4–6.6)	0.88
Stroke					
Stroke and TIA (any)	17/646	2.6 (1.6–4.2)	12/676	1.8 (1.0–3.1)	0.35
Stroke without TIA (any)	12/646	1.9 (1.1–3.2)	10/676	1.5 (0.8–2.7)	0.71
Disabling stroke	8/646	1.2 (0.6–2.4)	7/676	1.0 (0.5–2.1)	0.79
Non-disabling stroke	4/646	0.6 (0.2–1.6)	3/676	0.4 (0.2–1.3)	0.70
Ischemic stroke	10/646	1.5 (0.8–2.8)	9/676	1.3 (0.7–2.5)	0.82
Haemorrhagic stroke	2/646	0.3 (0.1–1.1)	1/676	0.1 (0.0–0.8)	0.56
TIA	5/646	0.8 (0.3–1.8)	2/676	0.3 (0.1–1.1)	0.25
Systemic embolism	1/646	0.2 (0.0–0.9)	1/676	0.1 (0.0–0.8)	1.00
Bleedings					
Any bleeding	40/646	6.2 (4.6–8.3)	32/676	4.7 (3.4–6.6)	0.13
Major bleeding	23/646	3.6 (2.4–5.3)	14/676	2.1 (1.2–3.4)	0.06

Categorical variables are expressed as frequencies (n) and percentages (%). Continuous data are reported as means and standard deviation.
TIA, transient ischaemic attack.

procedural settings of the centres. In the Watchman group, all interventions were performed by a single operator. In contrast, in the Amplatzer group, procedures were performed by 13 operators on different training levels. This may explain the higher rates of device embolizations, bailout surgery, and cardio-pulmonary resuscitations in this group. With regards to device embolizations in the Amplatzer group, a higher number occurred in patients who received the 1st generation Amplatzer Cardiac Plug. Beside the mentioned learning curve of the centres, also device-specific features like a less voluminous lobe and a lower number of hooks compared with the Amulet may be responsible for that. The EWOLUTION[5] and the post-approval US experience[6] trials for the Watchman, as well as multicentre registries for the Amplatzer Cardiac Plug[8] and Amulet[9] reported complication rates of 2.8%, 1.4%, 5.0%, and 3.2%, respectively. However, study populations and definitions of major peri-procedural complications varied between those trials. In the EWOLUTION and US experience, implanting physicians underwent a certification programme in order to ensure an appropriate level of experience. From the results of the PROTECT-AF trial[3] to the EWOLUTION registry,[5] a substantial reduction of peri-procedural complications was observed.

Despite a high-risk patient population, the rate of all-cause stroke and systemic embolism at follow-up was low and similar for both devices. It is comparable with the 5-year ischaemic event rates of the PROTECT-AF (1.7%) and PREVAIL (1.8%) trials[4] for the Watchman, as well as the annual rate of systemic thromboembolism documented in other Amplatzer registries (2.3% for the Amplatzer,[9] 2.9% for the Amulet[9]).

Two (0.75%; Watchman) and three (1.1%; Amplatzer) ischaemic events were associated with DRT. In the Watchman group, one case of TIA was documented in a patient with a major peri-device leak. The rate of DRT and major peri-device leaks was comparable for both devices. In the literature, the incidence of DRT varies (0.3%,[8] 7.2%,[17] and 3.7%[18]). It is associated with an increased rate of ischaemic stroke and systemic embolism. Apart from implantation results and device type, patient-specific factors like older age, permanent AF, vascular disease, history of stroke, low left ventricular ejection fraction, and left atrial appendage size are independent predictors for DRT.[17,18] Transoesophageal echocardiography follow-up of Amplatzer[8] and Amulet[9] multicentre trials, as well as the EWOLUTION[5] registry for the Watchman, revealed DRT peri-device leaks in 1.9%, 1.6%, and 0.7% of the cases. The influence of

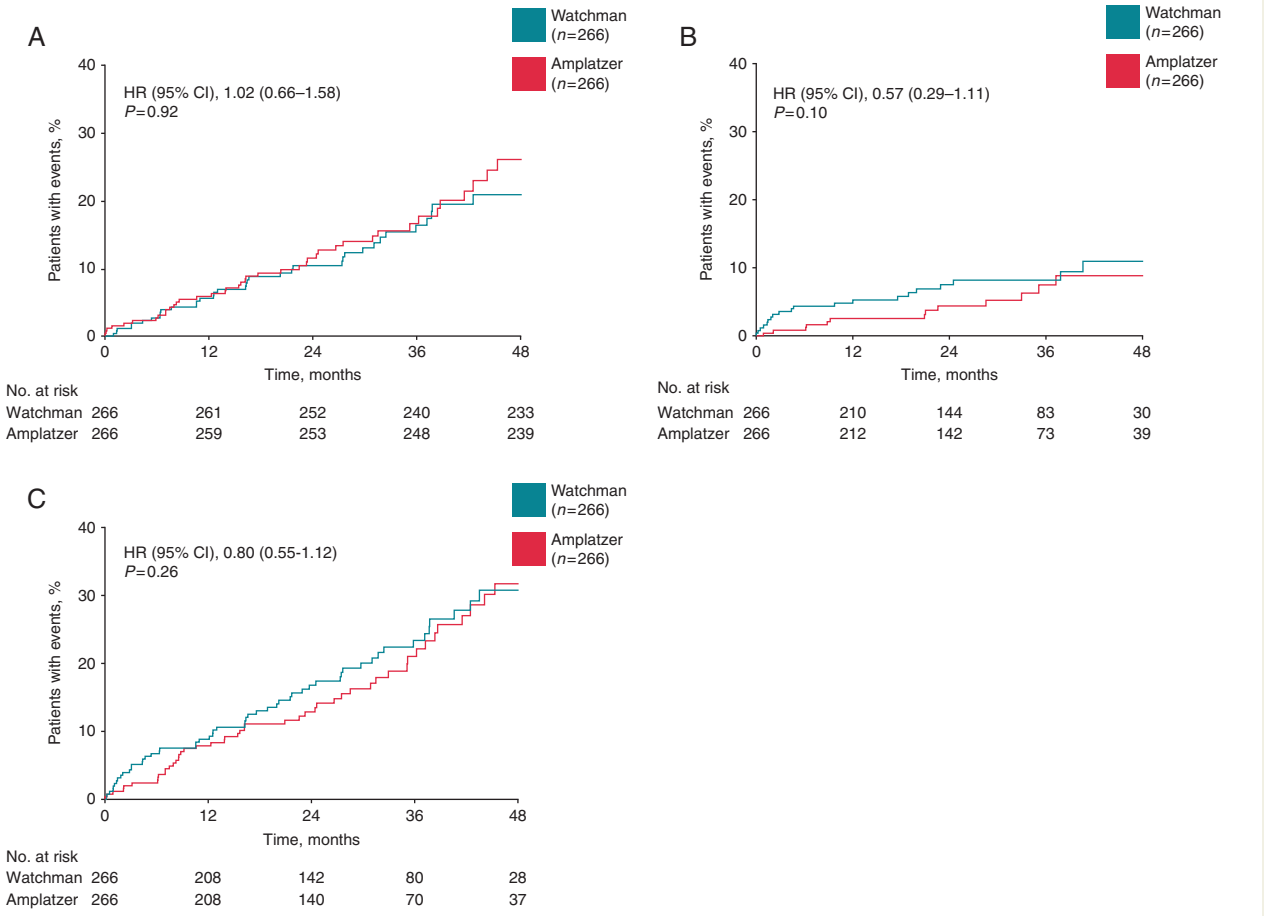

Figure 1 Kaplan–Meier curves of the co-primary endpoints of (*A*) efficacy, (*B*) safety, and (*C*) combined hazard endpoint (net clinical benefit) at 48 months.

peri-device leaks on the occurrence of thromboembolic events still remains unclear. After LAAC with the Amplatzer Cardiac Plug in 339 patients, Saw *et al.*[19] found no association of peri-device leaks and ischaemic events.

In the present study, a numerically higher bleeding rate was observed in the post-procedural period in the Watchman group, although statistical significance was not reached. This group also had a higher rate of major (except intracranial) bleedings prior to LAAC. However, propensity score matching had completely equalized HAS-BLED scores of the Watchman and Amplatzer group. Therefore, the higher bleeding rate during early follow-up in the Watchman group is most likely due to the different post-procedural anti-thrombotic therapy between the groups: In the Watchman cohort, it was a dual anti-thrombotic therapy consisting of anticoagulation and acetylsalicylic acid according to the PROTECT-AF trial.[3] In contrast, patients of the Amplatzer group exclusively received only dual antiplatelet therapy for a limited time. The current Watchman instructions for use recommend an anti-thrombotic regimen tailored to each patient's individual stroke and bleeding risk, allowing either a 3 months dual antiplatelet therapy, or an OAC. Overall, major bleeding events at follow-up are comparable with the results of the Amplatzer Cardiac Plug[8] (2.1% per year) and EWOLUTION[5] (2.6% per year) registries.

Regarding cardiovascular and unexplained death, as well as all-cause mortality, no differences were observed between the Watchman and Amplatzer groups. The 5-year outcomes of the PROTECT-AF and PREVAIL trials observed a 41% decrease in cardiovascular mortality and a 27% decrease in all-cause mortality after LAAC with the Watchman.[4] In this regard, the advantage of LAAC over OAC is explained by a lower rate of haemorrhagic stroke and major bleedings, particularly in elderly, polymorbid, and frail patients. Therefore, LAAC is not only about stroke prevention, but also about reducing bleedings and death.

Limitations

Despite good comparability of the two groups, substantial unmeasured confounders may likely persist. Given the small number of patients, any difference may be type I error. Because of the non-randomized and retrospective study design, definite conclusions about efficacy and safety of Watchman vs. Amplatzer occluders cannot be drawn and need to be confirmed in randomized trials. In the

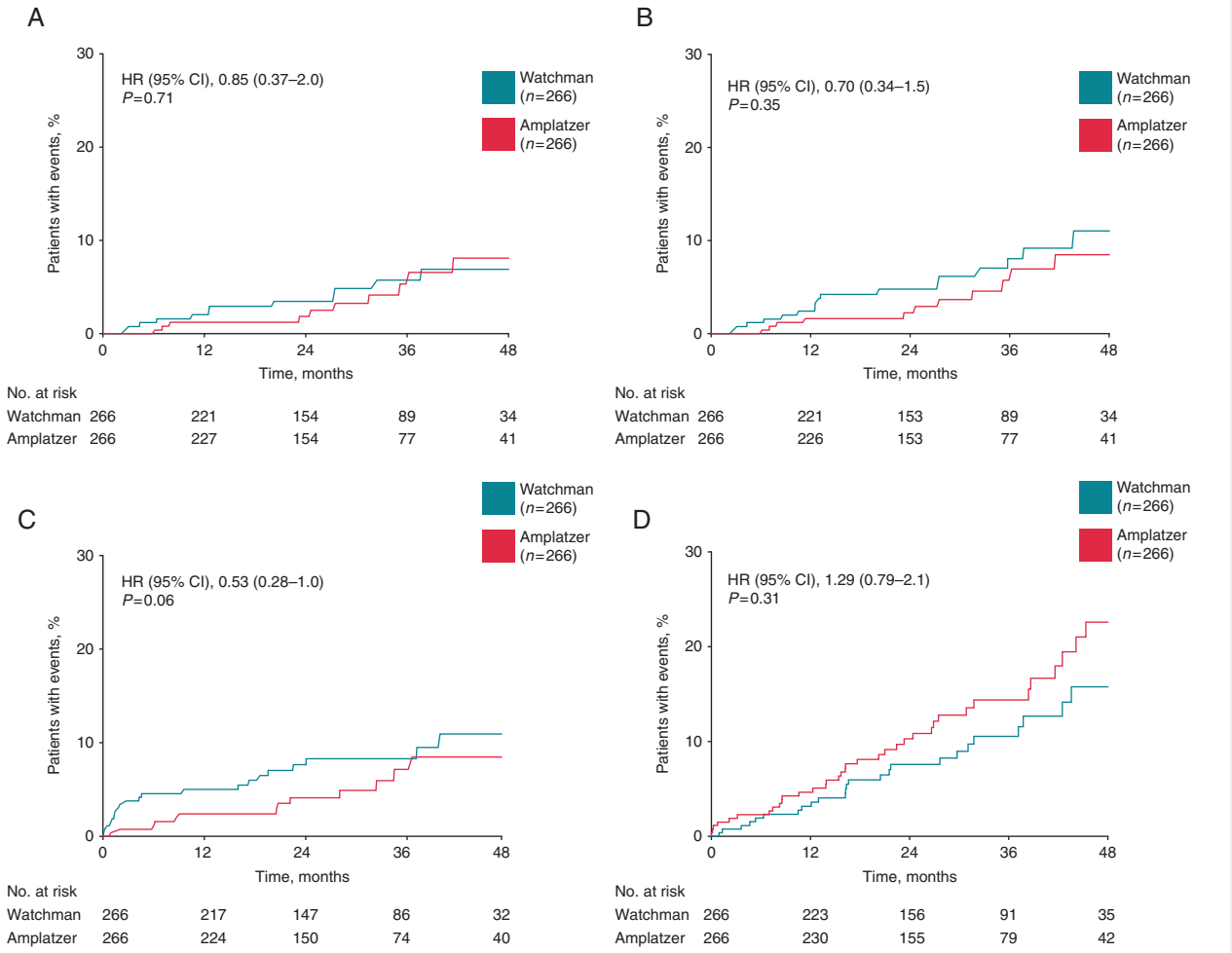

Figure 2 Kaplan–Meier curves of (*A*) all-cause stroke, (*B*) all-cause stroke and TIA, (*C*) major bleedings, and (*D*) cardiovascular/unexplained death at 48 months. TIA, transient ischaemic attack.

Amplatzer group, patient enrolment started in the very early phase of LAAC and 3 years earlier, which may has influenced patient selection, expertise of the procedure and peri-procedural complications. Another confounder may be the difference in the numbers of operators with only one operator in the Watchman and several operators in the Amplatzer group. In the Amplatzer group, TEE at follow-up was performed in only two-thirds of the cases, which may result in over- or under-estimation of device-related thrombi and peri-device leaks. The former post-procedural drug regimen with OAC plus acetylsalicylic acid in the Watchman group resulted in higher number of bleedings events in the post-operative period.

Conclusion

After 1.322 patient-years, percutaneous LAAC with both Watchman and Amplatzer occluders provided similar efficacy, safety, and net clinical benefit. To avoid bleedings in the post-interventional period, dual antiplatelet therapy may be preferred to OAC.

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Declaration of Helsinki

The authors state that the study complies with the Declaration of Helsinki. The locally appointed ethics committee has approved the research protocol. Informed consent has been obtained from the subjects.

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