Causes of death and morbidity in patients with atrial fibrillation after left atrial appendage occlusion

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KEY WORDS
atrial fibrillation, left atrial appendage, left atrial appendage occlusion, stroke

ABSTRACT

BACKGROUND Left atrial appendage occlusion (LAAO) is a safe and effective alternative for stroke prevention in patients with atrial fibrillation (AF). However, there is little literature on the exact causes of death and adverse events during follow-up after LAAO.

AIMS The primary aim of this study was to evaluate survival free of any serious adverse events and of any-cause death in midterm follow-up. The secondary aims were to analyze causes of mortality and further hospitalization as well as adverse events, thromboembolism, and bleeding risk reduction during follow-up.

METHODS A retrospective, single-center study was performed in 84 consecutive patients with AF who underwent LAAO with endocardial occluders. The mean (SD) $CHADS_2$ score was 3.5 (1.1), CHA_2DS_2-VASc score, 5.0 (1.5), and HAS-BLED score, 4.4 (0.9). After LAAO, dual 6-month antiplatelet therapy and then lifelong aspirin monotherapy was recommended. Mean (SD) follow-up was 25.3 (13.2) months with an accumulated total follow-up of 174.6 patient-years.

RESULTS The annual mortality rate was 12.02%. More than half of deaths (57%) were due to noncardiovascular causes with leading malignancy. Survival at the end of the periprocedural period was 98.8%, at 3 months, 97.6%, at 6 months, 95.2%, at 12 months, 86.5%, at 18 months, 85.1%, and at 24 months, 80.6%. The average annual thromboembolic event rate was 2.87%. The most common adverse event was severe bleeding with an annual rate of 6.3% (3 cases while receiving dual antiplatelet therapy and 6 cases while receiving aspirin).

CONCLUSIONS The majority of deaths were not related to stroke in patients with AF after LAAO. Mortality in first 2 years following the procedure was predominantly from noncardiovascular causes.

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INTRODUCTION

More than 10 years after the first-in-man case, left atrial appendage occlusion (LAAO) continues to revolutionize the management of stroke prevention in patients with nonvalvular atrial fibrillation (AF) and has become, over time, a routinely performed procedure worldwide.[1-4] In 2012, the European Society of Cardiology guidelines recommended LAAO for patients with AF in whom oral anticoagulation (OAC) is contraindicated (indication IIb, level of evidence B).[5] Recently, the indication for LAAO in some European countries was expanded to include patients in whom OAC therapy is ineffective. Consequently, the number of LAAO procedures performed is steadily increasing each year.[3]

Various studies show that LAAO is associated with good short- and midterm results, even in high-risk patients.[1,2,6-8] However, these studies mainly focus on stroke risk reduction and mortality. There are no recent analyses of the causes of death and clinical outcomes of patients undergoing LAAO.

The primary aim of this study was to evaluate survival free of any serious adverse events and of any-cause death in midterm (>2 years)

WHAT'S NEW?

Previous studies on left atrial appendage occlusion (LAAO) were mainly focused on stroke risk reduction and mortality. There are no recent analyses of the causes of death and clinical outcomes of patients undergoing LAAO. Therefore, we evaluated survival free of any serious adverse events and of any-cause death in midterm follow-up after LAAO. More than half of deaths (57%) were not related to stroke but were due to noncardiovascular causes with leading malignancy. The most common adverse event was severe bleeding with an annual rate of 6.3%.

follow-up. The secondary aims were to analyze causes of mortality, further hospitalizations, adverse events, thromboembolism, and bleeding risk reduction during follow-up.

METHODS

A retrospective, single-center study was performed in 84 consecutive patients with nonvalvular AF who underwent LAAO with the AMPLATZER Amulet (Abbott, St. Paul, Minnesota, United States) or The LAmbre (Lifetech Scientific Corp., Shenzhen, China) endocardial left atrial appendage (LAA) occluders between March 2015 and December 2018. All procedures were performed by 2 operators who underwent training using a simulation model that allowed the operator understand and practice the various steps of procedure using both types of occluders (AMPLATZER and LAmbre). Inclusion and exclusion criteria for the Amulet and the LAmbre LAAO procedures have been described previously.[1,2,9] We collected data on patient demographics, medical history, stroke risk ($CHADS_2$ score and CHA_2DS_2-VAS score), and bleeding risk (HAS-BLED score).

Implantation procedure All patients underwent transesophageal echocardiography (TEE) 24 hours before the procedure in order to exclude the presence of thrombus in the left atrial appendage. The patients were hydrated in order to optimize atrial filling. The procedure was performed under general anesthesia and antibiotic protection (2nd generation cephalosporin) using echocardiographic-fluoroscopic fusion system, EchoNavigator (Philips Inc., Amsterdam, Netherlands). Heparin was administered in 2 doses of 100 U/kg bw: first, after the introduction of the catheter into the lumen of the superior vena cava; second, after transseptal puncture and the introduction of the catheter into the lumen of the left atrium. Mean left atrial pressure was measured, and 10 mm Hg was assumed as the value allowing for continuation of the procedure. Using contrast fluoroscopy, the left atrial appendage was visualized selectively in order to evaluate the anatomy. Angiography was performed using RAO 20°, caudal 20° and RAO 30°, cranial 10° projections. Simultaneously, the performed actions were constantly monitored using 2-dimensional and 3-dimensional TEE. During the first stage of the procedure, this examination was particularly useful for determining the optimal site of transseptal puncture. During the subsequent stages, TEE was used to establish the dimensions of the left atrial appendage, control the implantation process, and provide ultimate confirmation that the occluder system is in the proper position. Once the implant was placed in the LAA, angiography and echocardiography were performed to check device positioning, LAA sealing and impingement on surrounding structures. A gentle tug test was performed to ensure device stability.[1,2]

Postprocedure anticoagulation After device implantation, it was recommended to administer dual antiplatelet therapy (DAPT) for 6 months (75-mg aspirin once daily and 75-mg clopidogrel once daily) and after that lifelong aspirin monotherapy (75-mg once daily).

Follow-up Hospital follow-up visits were performed at 3 months and 6 months after the procedure. To evaluate the presence of postprocedure leak, TEE was performed in each patient. Telephone follow-up calls and analysis of hospital records were performed at 12, 24, 36, and 42 months after LAAO. Data collection and adverse event reporting were completed by the physician who performed the procedure.

Adverse events, serious adverse events, and mortality The study variables were included in a dedicated database. Adverse events were reported during follow-up visits based on the Munich LAA consensus document.[10] We recorded mortality (cardiovascular, noncardiovascular, procedural, immediate procedural), thromboembolic events (stroke, transient ischemic attack [TIA], systemic embolism), and life-threatening, disabling, or major bleeding. For this study, we classified heavy bleeding as life threatening, or disabling, or major bleeding (Bleeding Academic Research Consortium type 3a bleeding). Additionally, each patient's hospitalization and cause of admission were reported as adverse events. Researchers had access to the medical records from each patient's hospitalization.

Mortality definitions were based on those included in the Valve Academic Research Consortium-2 consensus document.[11] All deaths were reported with timing relative to the index procedure as well as the underlying causes. Mortality was classified into 3 categories: cardiovascular, noncardiovascular, and procedural. Procedural mortality was defined as mortality between implantation and hospital discharge or between implantation and day 30 of follow-up.[10]

TABLE 1 Baseline patient characteristics (continued on the next page)

Variable		Patients (n = 84)
Age, y	Mean (SD)	72 (8.4)
	Median (Q_1; Q_3)	73 (67; 78)
	Range	46–87
Sex, female, n (%)		36 (42.9)
$CHADS_2$ score	Mean (SD)	3.5 (1.14)
	Median (Q_1; Q_3)	3 (3; 4)
CHA_2DS_2-VASc score	Mean (SD)	5.0 (1.5)
	Median (Q_1; Q_3)	5 (4; 6)
HAS-BLED	Mean (SD)	4.4 (0.9)
	Median (Q_1; Q_3)	4 (4; 5)
Successful LAAO, n (%)		83 (98.8)
Comorbidities, n (%)		
Congestive heart failure		34 (40.5)
Hypertension		84 (100)
Type 2 diabetes mellitus		35 (41.7)
Previous stroke		33 (39.2)
Vascular disease		54 (64.3)
Alcoholism		2 (2.4)
Indication for LAAO procedure, n (%)		
Gastrointestinal bleeding		68 (57.1)
CNS bleeding		6 (7.1)
Respiratory tract bleeding		1 (1.2)
Urinary tract bleeding		2 (2.4)
Thrombus in LAA despite OAC		5 (6)
Stroke/TIA despite OAC		21 (25)
Preprocedure medications, n (%)		
Vitamin K antagonists	Total	38 (45.2)
	Acenocumarol	3 (3.6)
	Acenocumarol + ASA	1 (1.2)
	Acenocumarol + ASA + clopidogrel	1 (1.2)
	Warfarin	17 (20.2)
	Warfarin + ASA	13 (15.5)
	Warfarin + ASA + clopidogrel	3 (3.6)
DOACs	Total	43 (51.2)
	Dabigatran	18 (21.4)
	Dabigatran + ASA	2 (2.4)
	Dabigatran + ASA+ clopidogrel	2 (2.4)
	Rivaroxaban	13 (15.5)
	Rivaroxaban + ASA	6 (7.1)
	Rivaroxaban + clopidogrel	2 (2.4)
Antiplatelet agents	Total	2 (2.4)
	ASA	2 (2.4)
LMWH		1 (1.2)

Thromboembolism and bleeding reduction calculation As in our previous study,[7,8] the efficacy of the procedure in the prevention of thromboembolic events (stroke, TIA, systemic embolism, intraventricular thrombus) was calculated by comparing the actual event rate to the event rate predicted by CHA_2DS_2-VASc score.[5,12,13] Individual patient's annual risk was recorded and the average annual risk for the entire study population was calculated. Thromboembolism reduction was calculated as follows: (estimated percent of event rate – actual percent of event rate)/estimated percent of event rate.[6]

Bleeding reduction was assessed with the same method as stroke reduction. The total number of major bleeding events per year was compared with the number of events predicted by the HAS-BLED score[14]: (estimated percent of event rate – actual percent of event rate)/estimated percent of event rate.[6]

Statistical analysis Continuous variables were analyzed for normal distribution using the Shapiro–Wilk test. Data were expressed as mean (SD). Categorical variables were expressed as counts and percentages. The Kaplan–Meier analysis was performed to estimate survival over time. Statistical analysis was performed with STATISTICA 12.0 (StatSoft, Tulsa, Oklahoma, United States). A 2-tailed *P* value of less than 0.05 was considered significant.

RESULTS

Patient characteristics The LAAO procedure was performed in 84 patients with a mean (SD) age of 72 (8.4) years. Patients' baseline characteristics are summarized in TABLE 1. The mean (SD) $CHADS_2$ score was 3.5 (1.1), mean (SD) CHA_2DS_2-VAS score was 5.0 (1.5), and mean (SD) HAS-BLED score was 4.4 (0.9). Until the procedure, 45.2% of patients were taking vitamin K antagonists, 51.2% were taking direct oral anticoagulant, 2.4% an antiplatelet agent, and 1.2% received low-molecular-weight heparin. The most common indication for LAAO was gastrointestinal bleeding which was present in 57.1% of patients.

Procedure In 71.4% of patients (60 cases), the AMPLATZER Amulet occluder was used, and in 28.6% patients (24 cases) the LAmbre occluder was selected. The procedure was successful in 98.8% of cases. Procedural or device-related adverse events were noted in 5 of cases (5.9%). In 1 patient with unsuccessful Amulet device implantation, iatrogenic aortic damage with tamponade occurred and was resolved with surgical intervention using a left minithoracotomy approach. During surgical intervention, the LAA was closed with an epicardial AtriClip device (AtriCure, Mason, Ohio, United States). Two patients developed tamponade 2 days after the procedure: first due to damage to the pulmonary

TABLE 1 Baseline patient characteristics (continued from the previous page)

Variable	Patients (n = 84)
Device selected, n (%)	
AMPLATZER Amulet	60 (71.4)
LAmbre	24 (28.6)
LAA leak, n (%)	
Total	11 (13.1)
Residual flow <1 mm	4 (4.7)
Residual flow 1–3 mm	6 (7.1)
Residual flow >3 mm	1 (1.2)

Abbreviations: ASA, aspirin; $CHADS_2$, congestive heart failure, hypertension, diabetes mellitus, age ≥75 years, history of stroke or transient ischemic attack; CHA_2DS_2-VASc, congestive heart failure, hypertension, age years, diabetes mellitus, history of stroke or thromboembolism, vascular disease, age 65 to 74 years, female sex; CNS, central nervous system; DOAC, direct oral anticoagulant; HAS-BLED, hypertension, abnormal liver function, history of stroke or thromboembolism, history of bleeding, age >65 years, use of nonsteroidal anti-inflammatory drugs, and alcohol abuse; LAA, left atrial appendage; LAAO, left atrial appendage occlusion; LMWH, low-molecular-weight heparin; OAC, oral anticoagulation; TIA, transient ischemic attack

vein and second due to damage to the pericardial sac. Both cases were resolved by surgical intervention by left minithoracotomy without further consequences. There was one sudden cardiac death on day 4. There was one case of gastrointestinal bleeding on day 11. Additionally, there were 4 minor bleeding and vascular complications at the femoral access site on days 1, 2, 4, and 10 which resolved with no further complications.

Mortality and midterm survival All patients were included in the follow-up analysis. Mean (SD) follow-up was 25.3 (13.2) months with an accumulated total follow-up of 174.6 patient-years.

The time trend in mortality during follow-up and causes of death are listed in TABLE 2. A total of 21 patients (overall mortality, 21.4%) died during the follow-up period: 1 patient (1.2%) during the procedural mortality period, 11 (12.4%) due to noncardiovascular causes, and 9 patients (9.5%) due to cardiovascular causes. The annual mortality rate was 12.02%.

Survival at the end of the periprocedural period was 98.8%, at 3 months, 97.6%, at 6 months, 95.2%, at 12 months, 86.5%, at 18 months, 85.1%, and at 24 months, 80.6%. Survival estimated by the Kaplan–Meier analysis for all-cause mortality is presented in FIGURE 1.

The time trend in adverse events (including deaths) during follow-up and causes are listed in TABLE 3. The most common adverse event was gastrointestinal bleeding, reported in 9 patients (10.7%). Thromboembolic events were reported in 3 patients (3.6%). Survival estimated by the Kaplan–Meier analysis for all-cause adverse events is presented in FIGURE 2.

Thromboembolism and bleeding risk reduction During the study period, the average annual thromboembolic event rate was 2.87%. There was 1 episode of ischemic stroke (while receiving DAPT, control TEE showed no evidence

TABLE 2 Descriptive analysis of causes of death during the procedure and at various stages of follow-up

	Procedural mortality	Follow-up, months						All
		1–3	4–6	7–12	13–18	19–24	>24	
All-cause mortality								
Deaths, n (%)	1 (1.2)	1 (1.2)	2 (2.4)	7 (8.3)	1 (1.2)	3 (3.5)	6 (7.1)	21 (21.4)
Noncardiovascular mortality								
Deaths, n (%)	0	1	0	4	1	2	4	12 (14.2)
Cause (age at death, y)	–	Gastrointestinal bleeding (74)	–	Breast cancer (69); pancreatic cancer (70); colon cancer (77); prostate cancer (52)	Middle cerebral artery aneurysm (neurosurgery complications) (65)	Liver cancer (66); gastrointestinal bleeding (78)	Intestinal obstruction (65); kidney cancer (72); transport accident commission (68); lymphoma (68)	
Cardiovascular mortality								
Deaths, n (%)	1	0	2	3	0	1	2	9 (10.7%)
Cause (age at death, y)	SCD (86)	–	Heart failure (78); AMI (68)	Heart failure (76); heart failure (80); SCD (PCI complications) (74)	–	SCD (81)	SCD (67) SCD (79)	

Abbreviations: AMI, acute myocardial infraction; PCI, percutaneous coronary intervention; SCD, sudden cardiac death

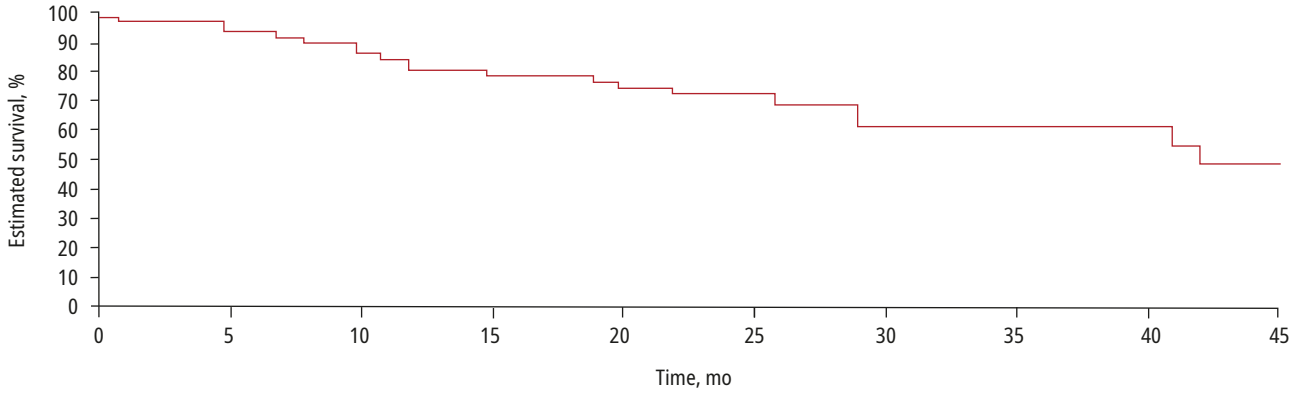

FIGURE 1 Kaplan–Meier curve for all-cause mortality in patients with atrial fibrillation after left atrial appendage occlusion

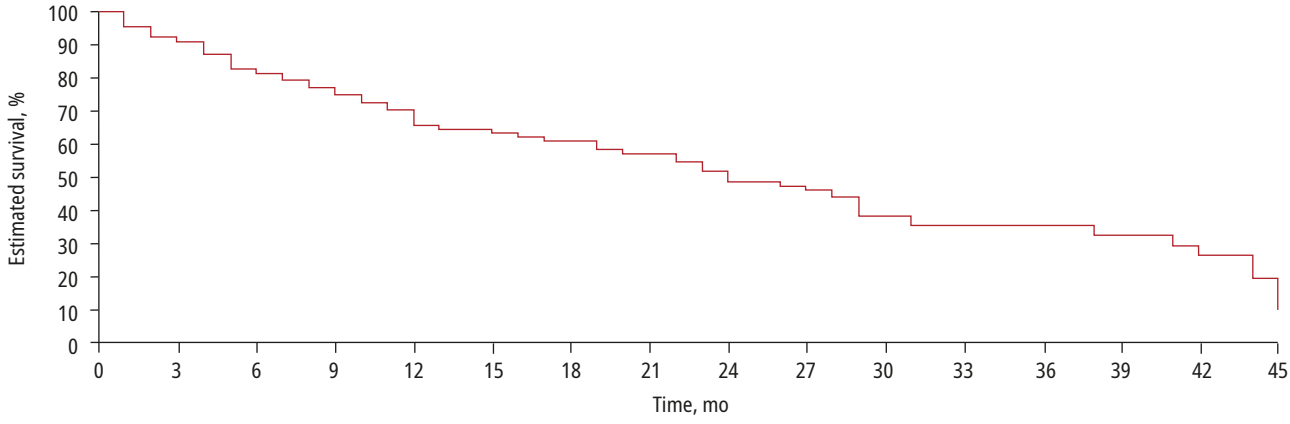

FIGURE 2 Kaplan–Meier curve for all-cause adverse events in patients with atrial fibrillation after left atrial appendage occlusion

TABLE 3 **Descriptive analysis of serious adverse events, including mortality, and thromboembolic events during the procedure and at various stages of follow-up**

	Procedural mortality	Follow-up, months					
		1–3	4–6	7–12	13–18	19–24	>24
Cases, n (%)	2 (2.4)	8 (9.5)	9 (10.7)	14 (16.6)	9 (10.7)	10 (11.9)	12 (14.3)
Serious adverse events[a]	Death; gastrointestinal bleeding	Death; ICD implantation; gastrointestinal bleeding; epileptic seizure (2); urosepsis; CNS vascular malformation; thrombs on the occluder device	Death (2); gastrointestinal bleeding; dizziness; suicide attempt; varicose vein bleeding; cardioversion; thrombus on the occluder device	Death (7); gastrointestinal bleeding (3); hypertensive crisis; pancreatitis; cardioversion; hip surgery	Death; gastrointestinal bleeding; epileptic seizure; cardioversion	Death (3); gastrointestinal bleeding; compression fracture of the vertebrae; penile cancer; urosepsis; myocardial infraction; alcoholic intoxication	Death (6); gastrointestinal bleeding; gangrenous appendicitis; urinary tract infection; bladder cancer; sepsis
Thromboembolic events	–	–	Ischemic stroke	–	–	TIA	Pulmonary embolism

a Numbers in brackets represent the number of cases with a given adverse event.

Abbreviations: ICD, implantable cardioverter-defibrillator; others, see TABLE 1

of device thrombus, postprocedure anticoagulation was changed from DAPT to 75-mg aspirin once daily and dabigatran 150-mg twice daily), 1 episode of TIA (while receiving aspirin, control TEE showed mobile interatrial septum with no evidence of device thrombus), 1 episode of pulmonary embolism (while receiving aspirin). Additionally, there were 2 episodes of thrombus formation on the Amplatzer Amulet device (1 case while receiving DAPT and 1 case

without DAPT) and there was no thrombus on the LAmbre device. The annual rate of severe bleeding complications was 6.3%. There were 2 cases of fatal gastrointestinal bleeding and 9 serious gastrointestinal bleeding episodes requiring hospitalization. Out of those, 6 episodes were observed in patients with gastrointestinal bleeding history on anticoagulation treatment. Estimated thromboembolic risk reduction and estimated bleeding risk reduction are presented in FIGURE 3. Surgical interventions were required in 16.6% of patients: 4.7% in perioperative period because of bleeding and vascular complications at the femoral access, 10.7% in patients with gastrointestinal bleeding treated with endoscopic management, and 1.2% was the temporary surgical supply of varicose vein bleeding. A total of 33.3% of bleeding episodes were observed in the first 6 months after LAAO.

DISCUSSION The results of our study suggest that most of the deaths after LAAO are not caused by ischemic stroke or TIA but by a noncardiovascular cause. Secondly, most hospitalization and adverse events after LAAO are not caused by thromboembolic events but due to severe bleeding. To the best of our knowledge, we present the first detailed analysis of causes of death and morbidity after LAAO.

Worldwide, AF is the most common cardiac arrhythmia with low rates of successful long-term treatment.[8,15] Atrial fibrillation is independently associated with a 1.5- to 2-fold increased risk of all-cause mortality and morbidity.[5] Oral anticoagulation significantly reduces the risk of death and stroke but may be associated with severe or life-threating complications.[16] Despite OAC, there is still a significant risk of death (approximately 5% per year), with stroke being the cause of almost 10% of all deaths.[17] In clinical trials with 2 years of follow-up, death was also the most frequent adverse event in anticoagulated patients.[17-19]

Patients with contraindications to OAC would seem to be the most likely candidates to benefit from LAAO, but may have a higher comorbidity profile and higher mortality rate that may temper the long-term benefits of LAAO.[20] In clinical registries of LAAO, the reported mortality rate was 8.4% for the Amulet device [21] and 9.8% for the Watchman device.[20] In clinical trials with long-term data, all-cause mortality has been reported as 10.9% for endocardial devices and 5.5% for epicardial devices.[8,22] In our study, 1-year mortality was 13.1%, which may be perceived as high, with overall mortality of 21.4% at 2 years of follow-up. However, higher observed mortality was associated with several clinical factors. First of all, our patients had multiple comorbidities as evidenced by a higher CHA_2DS_2-VAS score (mean, 5.0) and higher HAS-BLED score (mean, 4.4) compared with other LAAO clinical trials.[7,8,20-23] In our study, most of the patients were older, with a mean age of 72 years, 69% had a history of severe bleeding, of whom 7.8% had central nervous system bleeding, 39% had a history of previous ischemic stroke, 40% had heart failure, 64% had evidence of vascular disease, 41% had diabetes mellitus, 100% had hypertension, and 2.4% were addicted to alcohol. Additionally, in our study, more than half of deaths (57%) were due to noncardiovascular causes with malignancy being the leading cause of death. Other LAAO clinical registries reported rates of noncardiovascular causes of death from 39%[21] to 60%.[20] Interestingly, our results are in contrast to a study of anticoagulated patients with AF, in which more than half of the patients died from cardiovascular causes.[17-19]

In our study, there were no deaths caused by ischemic stroke or TIA. To the best of our knowledge, there are no studies in the literature that report ischemic stroke or TIA mortality after LAAO. Based on our study results, in patients with AF after LAAO, as in anticoagulated patients, the majority of deaths are not related to stroke. In clinical registries of anticoagulated patients with AF, ischemic stroke is the cause of death in 5% to 10% of patients[17-19] and stroke mortality is similar in patients treated with either vitamin K antagonists or direct oral anticoagulants.[18] It should be added that the PREVAIL (Prospective Randomized Evaluation of the Watchman Left Atrial Appendage Closure Device in Patients With Atrial Fibrillation Versus Long-Term Warfarin Therapy) trial reported that rates of ischemic or hemorrhagic stroke or cardiovascular or unexplained death were similar following LAAO compared with warfarin therapy.[24] The RE-LY (Randomized Evaluation of Long-Term Anticoagulation

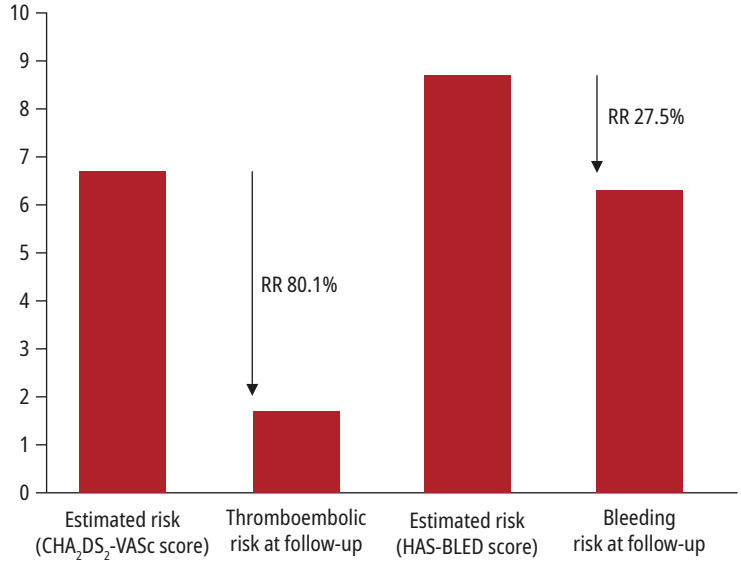

FIGURE 3 Effectiveness in reducing stroke risk and bleeding (/100 patient-years) during follow-up

Therapy)[25] and ROCKET AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation)[26] trials reported that a history of stroke, heart failure, and older age were strong predictors of stroke-related death. In our study, patients were older, with high CHA_2DS_2-VASc scores and previous heart failure. A history of previous stroke was observed in almost 40% of our patients. Therefore, our cohort had a high risk of death caused by stroke. Additionally, during follow-up, there were 3 cases of thromboembolic events. This translates into an 80.1% thromboembolism risk reduction, as compared with the calculated stroke rate of 6.7% without the use of anticoagulation in patients with similar CHA_2DS_2-VASc scores. Our results are comparable to other LAAO studies, including those employing endocardial and epicardial devices.[6-8,20,21]

The most common adverse event was severe bleeding (including 2 fatal bleeding episodes) with an annual major bleeding rate of 6.3%. The observed bleeding risk reduction was 27.5%. Although the bleeding rate reported in our study is higher than in the EWOLUTION registry (2.3%)[20] or Amplatzer study (2.3%),[21] comparisons must be made cautiously. In our study, the mean (SD) HAS-BLED score of 4.4 (0.9) was significantly higher than reported in EWOLUTION and Amplatzer trials (2.3 [1.2] and 3.3 [1.1], respectively).[20,21] Secondly, our study population consisted of 69% of patients with a history of major bleeding and contraindications to OAC, a higher prevalence than reported in other LAAO trials.[6-8,20,21,27] In patients with a high risk of bleeding, there is no safe pharmacological treatment to reduce the risk of thromboembolic events in the first 6 months after a procedure because of endocardial device epithelization. In our study, nearly 40% of severe bleeding, including 1 fatal bleeding episode, was observed within the first 6 months, when patients were on DAPT as recommended by the device protocol. The rate of major bleeding over the next 18 months of follow-up was acceptable in a population with a history of high bleeding risk. This observation may be confirmed by a study in patients at high risk for major bleeding (mean [SD] HAS-BLED, 3.5 [1.0]) where major bleeding events following LAAO were not related to the device or procedure. Interestingly, in clinical registry data for a larger group of patients, higher major bleeding rates were observed in patients discharged on aspirin alone or no antithrombotic medications as compared with those on OAC.[21]

Limitations This was a nonrandomized, retrospective, observational single-center study. The major limitations in estimating the overall value of LAAO are the lack of a control group and the use of only a calculated stroke or bleeding risk score for analysis. The analyzed group is small. We only assessed patients after LAAO in which the endocardial devices were employed and our results cannot be easily extrapolated to patients in whom epicardial devices were employed.

Conclusion The majority of deaths are not related to stroke in patients with AF after LAAO. Mortality in the first 2 years following the procedure was predominantly from noncardiovascular causes, with 57% of deaths caused by malignancy. The most common adverse event was severe bleeding with an annual rate of 6.3%. However, in our study the numbers of patients with a high bleeding risk (mean [SD], HAS-BLED score 4.4 [0.9]) or history of severe bleeding were relatively high. Importantly, stroke risk reduction and bleeding risk reduction after LAAO were comparable with other studies.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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REFERENCES

1 Lam YY. A new left atrial appendage occluder (Lifetech LAmbre Device) for stroke prevention in atrial fibrillation. Cardiovasc Revasc Med. 2013; 14: 134-136.

2 Tzikas A, Gafoor S, Meerkin D, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: an expert consensus step-by-step approach. EuroIntervention. 2016; 11: 1512-1521.

3 Grygier M, Wojakowski W, Smolka G, et al. Left atrial appendage occlusion: consensus document of Association of Cardiovascular Interventions and Heart Rhythm Section of Polish Cardiac Society [in Polish]. Kardiol Pol. 2018; 76: 677-697.

4 Litwinowicz R, Bartus M, Burysz M, et al. Long term outcomes after left atrial appendage closure with the LARIAT device - stroke risk reduction over five years follow-up. PLoS One. 2018; 13: e0208710.

5 Camm AJ, Lip GY, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J. 2012; 33: 2719-2747.

6 Freixa X, Gafoor S, Regueiro A, et al. Comparison of efficacy and safety of left atrial appendage occlusion in patients aged <75 to >/= 75 years. Am J Cardiol. 2016; 117: 84-90.

7 Litwinowicz R, Bartus M, Ceranowicz P, et al. Left atrial appendage occlusion for stroke prevention in diabetes mellitus patients with atrial fibrillation: long-term results. J Diabetes. 2019; 11: 75-82.

8 Litwinowicz R, Bartus M, Ceranowicz P, et al. Stroke risk reduction after LAA occlusion in elderly patients with atrial fibrillation: long-term results. Pol Arch Intern Med. 2018; 128: 327-329.

9 Burysz M, Litwinowicz R, Bryndza M, et al. Percutaneous left atrial appendage closure using the LAmbre device. First clinical results in Poland. Postepy Kardiol Interwencyjnej. 2019; 15: 251-254.

10 Tzikas A, Holmes DR Jr, Gafoor S, et al. Percutaneous left atrial appendage occlusion: the Munich consensus document on definitions, endpoints, and data collection requirements for clinical studies. Europace. 2017; 19: 4-15.

11 Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. Eur Heart J. 2012; 33: 2403-2418.

12 January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation. 2014; 130: 2071-2104.

13 Melgaard L, Gorst-Rasmussen A, Lane DA, et al. Assessment of the CHA2DS2-VASc score in predicting ischemic stroke, thromboembolism, and death in patients with heart failure with and without atrial fibrillation. JAMA. 2015; 314: 1030-1038.

14 Lip GY, Frison L, Halperin JL, et al. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. J Am Coll Cardiol. 2011; 57: 173-180.

15 Bryndza M, Litwinowicz R, Kapelak B, et al. Recurrence of atrial fibrillation ten years after thoracoscopic transdiaphragmatic radiofrequency epicardial ablation. Kardiol Pol. 2018; 76: 1733-1735.

16 Litwinowicz R, Konstanty-Kalandyk J, Goralczyk T, et al. Dabigatran level monitoring prior to idarucizumab administration in patients requiring emergent cardiac surgery. J Thromb Thrombolysis. 2018; 45: 9-12.

17 Gomez-Outes A, Suarez-Gea ML, Garcia-Pinilla JM. Causes of death in atrial fibrillation: challenges and opportunities. Trends Cardiovasc Med. 2017; 27: 494-503.

18 Gomez-Outes A, Lagunar-Ruiz J, Terleira-Fernandez AI, et al. Causes of death in anticoagulated patients with atrial fibrillation. J Am Coll Cardiol. 2016; 68: 2508-2521.

19 Bassand JP, Accetta G, Camm AJ, et al. Two-year outcomes of patients with newly diagnosed atrial fibrillation: results from GARFIELD-AF. Eur Heart J. 2016; 37: 2882-2889.

20 Boersma LV, Ince H, Kische S, et al. EWOLUTION Investigators. Efficacy and safety of left atrial appendage closure with WATCHMAN in patients with or without contraindication to oral anticoagulation: 1-year follow-up outcome data of the EWOLUTION trial. Heart Rhythm. 2017; 14: 1302-1308.

21 Landmesser U, Tondo C, Camm J, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: one-year follow-up from the prospective global Amulet observational registry. EuroIntervention. 2018; 14: e590-e597.

22 Block PC, Burstein S, Casale PN, et al. Percutaneous left atrial appendage occlusion for patients in atrial fibrillation suboptimal for warfarin therapy: 5-year results of the PLAATO (Percutaneous Left Atrial Appendage Transcatheter Occlusion) Study. JACC Cardiovasc Interv. 2009; 2: 594-600.

23 Litwinowicz R, Bartus M, Malec-Litwinowicz M, et al. Left atrial appendage occlusion for secondary stroke prevention in patients with atrial fibrillation: long-term results. Cerebrovasc Dis. 2019; 47: 188-195.

24 Holmes DR Jr, Kar S, Price MJ, et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol. 2014; 64: 1-12.

25 Marijon E, Le Heuzey JY, Connolly S, et al. Causes of death and influencing factors in patients with atrial fibrillation: a competing-risk analysis from the randomized evaluation of long-term anticoagulant therapy study. Circulation. 2013; 128: 2192-2201.

26 Hart RG, Diener HC, Yang S, et al. Intracranial hemorrhage in atrial fibrillation patients during anticoagulation with warfarin or dabigatran: the RE-LY trial. Stroke. 2012; 43: 1511-1517.

27 Litwinowicz R, Bartus M, Kapelak B, et al. Reduction in risk of stroke and bleeding after left atrial appendage closure with LARIAT device in patients with increased risk of stroke and bleeding: long term results. Catheter Cardiovasc Interv. 2019; 94: 837-842.