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Left atrial appendage closure–indications, techniques, and outcomes: results of the European Heart Rhythm Association Survey

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The purpose of this EP Wire was to assess the indications, techniques, and outcomes of left atrial appendage occlusion (LAAO) in Europe. Thirty-three European centres, all members of the European Heart Rhythm Association electrophysiology (EP) research network, responded to this survey by completing the questionnaire. The major indication for LAAO (94%) was the prevention of stroke in patients at high thrombo-embolic risk (CHA_2DS_2-VASc ≥ 2) and contraindications to oral anticoagulants (OACs). Twenty-one (64%) of the responding centres perform LAAO in their own institution and 80% implanted 30 or less LAAO devices in 2014. Two-dimensional transoesophageal echocardiography was the preferred imaging technique to visualize LAA before, during, and after LAAO in 79, 58, and 62% of the participating centres, respectively. Following LAAO, 49% of the centres prescribe vitamin K antagonists or novel OACs. Twenty-five per cent of the centres combine LAAO with pulmonary vein isolation. The periprocedural complications included death (range, 0–3%), ischaemic or haemorrhagic stroke (0–25%), tamponade (0–25%), and device embolization (0–20%). In conclusion, this EP Wire has demonstrated that LAAO is most commonly employed in patients at high thrombo-embolic risk in whom OAC is contraindicated. The technique is not yet very widespread and the complication rates remain significant.

Keywords Atrial fibrillation • Stroke • Anticoagulation • Left atrial appendage • Occluder • Outcome • EHRA survey • EP wire

Introduction

Ninety per cent of thrombi leading to stroke in patients with atrial fibrillation (AF) are formed in the left atrial appendage (LAA).[1,2] Warfarin and new oral anticoagulants (NOACs) reduce significantly the thrombo-embolic risk associated with AF. However, some patients at high thrombo-embolic risk cannot be treated with oral anticoagulants (OACs) due to major contraindications or intolerance. In order to reduce the risk for stroke in these patients, endovascular LAA occlusion (LAAO) using the percutaneous approach has been developed. The goal of this European Heart Rhythm Association (EHRA) survey was to assess indications, techniques, and outcomes of LAA closure among the European centres.

Methods and results

Participating centres

Thirty-three European centres, all members of the EHRA electrophysiology (EP) research network, responded to this survey by completing the dedicated questionnaire. Of these, 24 (73%) were university hospitals, 6 (18%) were private hospitals, and 3 (9%) other types of hospital. Four (12%) of the responding centres performed 400 or more catheter ablations for AF in 2014, 12 (36%) performed 200–399 procedures, 6 (18%) performed 100–199 procedures, 8 (24%) performed 1–99 procedures, and 3 (9%) of the centres did not perform catheter ablation for AF. Ten (42%) of 24

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responding centres reported participating in a trial or registry on LAAO.

Indications, facilities, and funding

The majority (31, or 94%) of the responding centres consider LAAO in patients at high thrombo-embolic risk (CHA_2DS_2-VASc ≥ 2) with contraindications to OACs, e.g. due to a history of significant bleeding (*Figure 1*). Eighteen (55%) of the centres consider LAAO in patients at high thrombo-embolic risk (CHA_2DS_2-VASc ≥ 2) and increased risk of bleeding (HAS-BLED ≥ 3) as well as in patients with thrombo-embolic events despite adequate OAC after other plausible causes (e.g. carotid disease) have been excluded. Patients at high thrombo-embolic risk (CHA_2DS_2-VASc ≥ 2), increased risk of bleeding, and end-stage renal dysfunction (creatinine clearance $<15-30$ mL/min) were deemed to be candidates for LAAO in 10 (30%) centres. Eight (24%) of the centres offer implanting LAAO in patients at high thrombo-embolic risk and the concomitant need for a prolonged period of triple anticoagulant and antiplatelet therapy as a result of severe coronary artery disease treated with stents. Five (15%) centres stated that LAAO should be considered in patients with AF and high thrombo-embolic risk (CHA_2DS_2-VASc ≥ 2) who do not wish to continue on OACs after pulmonary vein isolation (PVI). Only one centre would consider LAAO as an alternative to OACs in patients who are eligible for OACs and in whom there is no increased risk for bleeding. One centre considers LAAO in patients <60 years of age in whom the potential side effects and complications of long-term OAC therapy are thought to be more serious than LAAO.

In 21 (64%) of the responding centres, LAAO is performed in their own institution: 50 LAAO procedures in 2 (10%) of 21 centres, 31–40 procedures in 2 (10%), 21–30 procedures in 3 (14%), 16–20 procedures in 2 (10%), 11–15 procedures in 4 (18%), 6–10 procedures in 2 (10%), and 1–5 procedures in 6 (28%) of the centres in 2014.

The remaining 12 (36%) of the centres outsource this procedure to other hospitals: in 5 (42%) of the centres because of lack of reimbursement, in 3 (25%) due to the difficulty finding suitable patients, in 1 (8%) because of the fact that too many complications have been reported for LAAO, and in 1 (8%) due to the perceived lack of scientific evidence supporting this procedure. Two (17%) centres responded that they were not performing LAAO at the time of this EP Wire survey, but intended to do so in the near future. Of these 12 outsourcing centres, 3 (25%) referred 5 patients to another centre for LAAO in 2014, 1 (8%) referred 4 patients, and 2 (17%) referred 2 patients, whereas 6 (50%) of the centres made no referrals.

In 11 (46%) of 24 centres, LAAO implantation is performed by both interventional cardiologists and electrophysiologists, in 5 (21%) only by interventional cardiologists, in 5 (21%) only by electrophysiologists, and in 3 (12%) by other physicians. All centres replied to the question whether the LAAO device was funded in their country when performed as a stand-alone procedure: in 15 (62%) it is funded, and in 9 (38%) the device is not funded when LAAO is performed as a stand-alone procedure.

Selection of the type of the left atrial appendage occluder

The question regarding which LAAO device type is used has been answered by 24 centres: 7 (29%) of the centres use exclusively the Watchman device (Boston Scientific, Maple Grove, MN, USA), 8 (33%) use only the Amplatzer Cardiac Plug (St Jude Medical, Minneapolis, MN, USA), and 9 (38%) use both. No other type of LAAO device is used by the responding centres.

The EP Wire questionnaire also included the question regarding the criteria applied in implanting centres when choosing a particular type of device. This question was answered by 24 centres: 13 (54%)

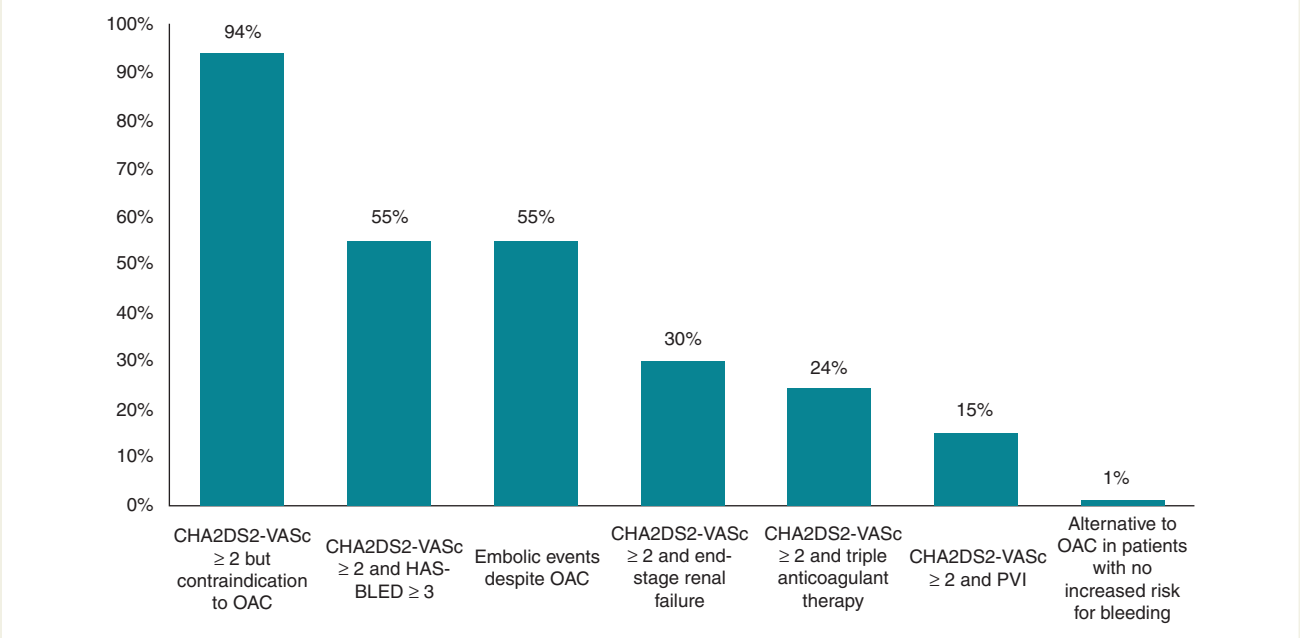

Figure 1 Indications for LAA closure in the 33 responding centres. OAC, oral anticoagulant; PVI, pulmonary vein isolation.

choose a particular type of LAAO device based on superior scientific evidence in terms of the efficacy and outcome, 11 (46%) based their choice on better educational support, 3 (12%) relied on the pre-existing relationship with a particular company, 2 (8%) based their decision on the ease using the device during implantation, and 2 (8%) centres based their decision on lower price.

Thirteen (54%) of 24 centres perform LAAO under the general anaesthesia with intubation, 9 (37%) with conscious sedation, and 2 (8%) with local anaesthesia only.

In 18 (75%) of 24 responding centres, LAAO is never performed in combination with PVI. Six (25%) centres performed LAAO in combination with PVI: one centre performed LAAO in 0.2% of their PVI procedures, one centre performed 5% of their LAAO procedures in combination with PVI, two centres reported performing combined LAAO and PVI in 10%, one centre in 80%, and one centre in 90%.

Left atrial appendage imaging

The question regarding what LAA imaging is performed before LAAO was answered by 24 centres: 19 (79%) perform transoesophageal echocardiography (TEE), 12 (50%) transthoracic echocardiography, 8 (33%) computed tomography (CT), and 1 (4%) cardiac magnetic resonance imaging.

During LAAO, 14 (58%) of the responding centres use fluoroscopy guidance together with 2D TEE, 9 (37%) used fluoroscopy guidance together with 3D TEE, and 1 (4%) used fluoroscopy guidance together with intracardiac echocardiography (ICE).

These 24 centres gave also insight regarding the type of imaging that was performed during follow-up after LAAO: in 15 (62%) this is done using 2D TEE, in 9 (37%) 3D TEE, whereas 2 (8%) of the centres employ CT in combination with 2D or 3D TEE.

Anticoagulation following left atrial appendage occlude implantation

Following LAAO, 9 (37%) of the centres prescribe vitamin K antagonists, 9 (37%) do not use OACs at all, 3 (12%) administer subcutaneous heparin, and 3 (12%) prescribe NOACs. Eighteen (75%) centres would consider stopping aspirin in patients with complete LAAO in the absence of other indications for aspirin (e.g. coronary artery disease) to minimize the risk of gastrointestinal bleeding, whereas 6 (25%) of the centres would continue aspirin.

Incomplete occlusion and complications

The question regarding the percentage of incomplete LAAO (defined as a peri-device flow with a jet $\geq$5 mm width during TEE) was answered by 21 centres: 0% of the procedures in 5 (24%) of the centres, 1–5% of the procedures in 8 (38%), 6–10% of the procedures in 6 (28%), 30% of the procedures in 1 (5%) centre, and 50% of the procedures in 1 (5%) centre.

Twenty-one responding centres disclosed the periprocedural complications associated with LAAO in their institution in 2014. Death occurred in 1 patient (range: 0–3% of LAAO procedures in the responding centres). Ischaemic or haemorrhagic stroke occurred in one patient (range: 0–25%), pericardial effusion with tamponade occurred in five patients (range: 0–25%), and device embolization occurred in two patients (range: 0–20%) of LAAO procedures in the responding centres. Major bleeding occurred in five patients (range: 0–20% of LAAO procedures in responding centres). One (5%) centre reported one case of thrombus formation outside the LAAO device.

Discussion

According to the current European Society of Cardiology (ESC) Guidelines, patients at risk of stroke should be treated with antithrombotic therapy based on the risk factors for stroke and bleeding as evaluated by the CHA_2DS_2-VASc score and the HAS-BLED score, respectively.[3] Patients at risk of stroke but with contraindications to OAC or who must interrupt OAC treatment due to major bleeding can be considered for endovascular LAAO. Current ESC Guidelines state that percutaneous LAAO 'may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation' with a Class IIb recommendation.

Indications

The majority (64%) of the responding centres performs LAAO in their own institution and most of them performed 30 or less procedures in 2014. For the centres not performing LAAO themselves, the most important reason not to do so was lack of reimbursement of the device in their centre. However, according to one budget impact model, the majority of LAAO costs is endured in the first year after implant, in contrast to costs for pharmacological OAC which continue to accrue over years, suggesting that LAAO may be cost-saving in the long term.[4] Only a minority of centres (25%) performed LAAO in combination with PVI in 2014.

According to the EHRA/European Association of Percutaneous Cardiovascular Interventions expert consensus statement on catheter-based LAAO, there are five patient categories in whom risks and benefits of LAAO should be considered.[5] From the clinical point of view, the most widely recognized indication for LAAO is stroke prevention patients at high thrombo-embolic risk (CHA_2DS_2-VASc $\geq$ 2) and contraindications to OACs due to history of significant bleeding (e.g. intracranial or life-threatening bleeding).[6] However, this indication is based on the extrapolation of the results of the PROTECT AF trial since no data regarding this specific patient populations can be drawn from the randomized trials.[7,8] Among the responding European centres, this was the most common indication for considering LAAO (94%).

The second potential indication is preventing stroke in patients at high thrombo-embolic risk (CHA_2DS_2-VASc $\geq$ 2) and increased bleeding risk associated with systemic OACs: (i) patients with HAS-BLED score $\geq$3, (ii) patients requiring the prolonged period of triple anticoagulant and antiplatelet therapy for severe coronary artery disease treated with stents, and (iii) patients with end-stage renal dysfunction (creatinine clearance $<$15–30 mL/min). Nevertheless, in these three patient groups, the decision to implant LAAO is determined by the individual risk–benefit evaluation emphasizing the fact that the use of OACs (NOACs) remains the strategy of choice.[5] Fifty-five per cent of the responding centres consider LAAO in patients at high thrombo-embolic risk (CHA_2DS_2-VASc $\geq$ 2) and increased risk of bleeding (HAS-BLED $\geq$ 3), but only 33% of the participating European centres considered the latter two patient categories for LAAO.

The third potential indication for LAAO is using the device as an alternative to OAC in patients who are eligible for OACs in whom there is no increased risk of bleeding. This group represents only a small minority of current LAAO procedures, but is actually the only indication based on the randomized controlled data.[9] This was also reflected in the results of this EP Wire with only 3% of the responding centres considering LAAO for this patient category.

The second-to-last possible indication for LAAO is in patients with embolic events despite adequate OAC after other plausible causes (e.g. carotid disease) have been excluded. Although this indication is considered by 55% of responding centres, there are no robust data demonstrating the beneficial effect in this setting, and ESC Guidelines recommend increasing the target international normalized ratio in patients on warfarin or switching from vitamin K antagonists to NOAC.

The fifth potential indication for LAAO is in patients at high thrombo-embolic risk (CHA_2DS_2-VASc ≥ 2) undergoing PVI who wish to discontinue OAC after AF ablation. This indication would be considered by 15% of the responding centres. However, since there are currently no randomized data available to prove a significant reduction in thrombo-embolic events after successful AF ablation, it seems reasonable to restrict AF ablation combined with LAAO to patients with CHA_2DS_2-VASc ≥ 2 undergoing AF catheter ablation who have a contraindication to OAC.

Imaging

Transoesophageal echocardiography remains the reference technique to exclude the presence of LAA thrombi prior to LAAO and to assess LAA dimensions and morphology. This was also the case among the responding centres as almost 80% of them perform TEE before LAAO. The preferred procedural imaging technique to guide LAAO among the responding centres was 2D TEE in combination with fluoroscopy guidance in 58%, whereas 37% preferred 3D TEE and fluoroscopy. Although one study has shown that 3D TEE is superior compared with 2D TEE for the assessment of LAA dimensions and orifice size, future trials are necessary to define the advantages of 3D TEE during LAAO.[10,11] Only one centre reported using fluoroscopy guidance together with ICE.

Since 54% of centres perform this procedure with patients in general anaesthesia and intubation, the use of ICE during LAAO makes it possible to perform this procedure with local anaesthesia.[12] Post-procedural follow-up imaging should make it possible to assess the device position, peri-device residual flow in LAA, and thrombus formation outside the device. Sixty-two per cent of the centres rely on 2D TEE for this purpose.

Incomplete LAAO has been reported in 10% or less of the procedures in 90% of the responding centres. In the PROTECT AF study, this was observed in 41% of patients during TEE at 45 days but the majority of patients had flow jets widths of 3 mm or less.[13] Although peri-device residual flow in LAA could potentially result in thrombo-embolic events, this was not the case in PROTECT AF patients with peri-device flow who stopped warfarin.

Anticoagulation

The post-procedural anticoagulation regimen including antithrombotics and antiplatelets, should be dictated by risk of bleeding in each individual patient and the device-related anticoagulation protocols. For the Watchman device, this includes OACs for 6 weeks, dual antiplatelet therapy for 6 months, and aspirin for life according to the PROTECT AF trial protocol. In patients at high bleeding risk, OAC therapy is withheld and dual antiplatelet therapy is prescribed for at least 1 month or until 6-month TEE follow-up ensures adequate LAA occlusion after which only aspirin is continued indefinitely. For the Amplatzer Cardiac Plug, dual antiplatelet is recommended for 1–6 months without OACs and after that aspirin is given indefinitely.[14]

Regardless of the device type, 49% of the responding centres prescribe OACs after LAAO, whereas 37% do not use anticoagulants at all. Interestingly, 75% of the centres would consider stopping aspirin in LAAO patients with complete LAAO in the absence of other indications for aspirin (e.g. coronary artery disease) to minimize the risk of gastrointestinal bleeding. Indeed, the rationale for prescribing aspirin indefinitely beyond the post-procedural period is the prevention of device-related thrombo-embolic events, but this practice does not have good evidence base.[5] It is also important to recognize that so far there is no scientific data comparing NOACs to LAAO available.

Complications

The results of this EP Wire highlight fairly high periprocedural complication rates among the responding centres compared with published data.[9,14–16] One (5%) centre reported 3% death associated with LAAO. The occurrence of ischaemic or haemorrhagic stroke varied from 1 to 25% in two centres (10%). Pericardial effusion with tamponade was reported by seven (33%) centres and in the majority of them the occurrence was 6% or less. Device embolization occurred in two (10%) centres and in one of them in 20% of their procedures. This EP Wire cannot explain the reasons behind these figures. However, the Continued Access Protocol registry suggests that the operator experience results in improving complications rates associated with LAAO.[15] One could speculate that the learning curve at some centres has not yet reached its plateau as the majority of centres implanted a limited number of devices in 2014.

Conclusions

This EP Wire has shown that the major indication for LAAO is prevention of stroke in patients at high thrombo-embolic risk (CHA_2DS_2-VASc ≥ 2) and contraindications to oral OAC. The number of procedures per centre per year remains limited. Two-dimensional TEE plays a key role for visualizing the LAA before, during, and after LAAO. Incomplete LAAO has been reported in 10% or less of the procedures in 90% of the responding centres. Almost half the responding centres prescribe OAC after LAAO. Complication rates of this procedure remain significant.

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