BMJ Open

# Stand-Alone Left Atrial appendage occlusion for throMboembolism prevention in nonvalvular Atrial fibrillatioN DiseasE Registry (SALAMANDER): protocol for a prospective observational nationwide study

Mariusz Kowalewski ,[1,2,3] Wojciech Wańha,[4] Radoslaw Litwinowicz ,[5] Michalina Kołodziejczak,[6] Michal Pasierski,[1] Rafal Januszek,[7] Łukasz Kuźma,[8] Marek Grygier,[9] Maciej Lesiak,[9] Agnieszka Kapłon-Cieślicka,[10] Krzysztof Reczuch,[11] Robert Gil,[12] Tomasz Pawłowski,[12] Krzysztof Bartuś,[5] Sławomir Dobrzycki,[8] Roberto Lorusso,[3] Stanislaw Bartuś,[7] Marek Andrzej Deja,[13] Grzegorz Smolka,[4] Wojciech Wojakowski,[4] Piotr Suwalski[1]

**To cite:** Kowalewski M, Wańha W, Litwinowicz R, *et al*. Stand-Alone Left Atrial appendage occlusion for throMboembolism prevention in nonvalvular Atrial fibrillatioN DiseasE Registry (SALAMANDER): protocol for a prospective observational nationwide study. *BMJ Open* 2022;**12**:e063990. doi:10.1136/bmjopen-2022-063990

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-063990).

Received 20 April 2022
Accepted 06 September 2022



For numbered affiliations see end of article.

**Correspondence to**
Dr Mariusz Kowalewski; kowalewskimariusz@gazeta.pl

## ABSTRACT

**Introduction** Atrial fibrillation (AF) is a prevalent disease considerably contributing to the worldwide cardiovascular burden. For patients at high thromboembolic risk ($CHA_2DS_2$-VASc ≥3) and not suitable for chronic oral anticoagulation, owing to history of major bleeding or other contraindications, left atrial appendage occlusion (LAAO) is indicated for stroke prevention, as it lowers patient's ischaemic burden without augmentation in their anticoagulation profile.

**Methods and analysis** Stand-Alone Left Atrial appendage occlusion for throMboembolism prevention in nonvalvular Atrial fibrillatioN DiseasE Registry (SALAMANDER) will be conducted in 10 heart surgery and cardiology centres across Poland to assess the outcomes of LAAO performed by fully thoracoscopic-epicardial, percutaneous-endocardial or hybrid endo-epicardial approach. The registry will include patients with nonvalvular AF at a high risk of thromboembolic and bleeding complications (CHA2DS2-VASc Score ≥2 for males, ≥3 for females, HASBLED score ≥2) referred for LAAO. The first primary outcome is composite procedure-related complications, all-cause death or major bleeding at 12 months. The second primary outcome is a composite of ischaemic stroke or systemic embolism at 12 months. The third primary outcome is the device-specific success assessed by an independent core laboratory at 3–6 weeks. The quality of life (QoL) will be assessed as well based on the QoL EQ-5D-5L questionnaire. Medication and drug adherence will be assessed as well.

**Ethics and dissemination** Before enrolment, a detailed explanation is provided by the investigator and patients are given time to make an informed decision. The patient's data will be protected according to the requirements of Polish law, General Data Protection Regulation (GDPR) and hospital Standard Operating Procedures. The study will be conducted in accordance with the Declaration of Helsinki. Ethical approval was granted by the local Bioethics Committee of the Upper-Silesian Medical Centre of the Silesian Medical University in Katowice (decision number KNW/0022/KB/284/19). The results will be published in peer-reviewed journals and presented during national and international conferences.

**Trial registration number** NCT05144958.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Interventions will be performed at highly experienced centres.
⇒ Detailed background patient information will be gathered along with clinically valid efficacy and safety endpoints (including the quality of life post-procedure) of all three currently most common left atrial appendage occlusion technologies.
⇒ Due to a non-randomised nature of the study, the selection bias might influence its results.
⇒ Limited ethnical variety will be present due to predominant Caucasian population in Poland.

## INTRODUCTION

Atrial fibrillation (AF) is the most common clinically relevant arrhythmia, which is strongly associated with increased stroke incidence. The majority of thrombotic material develops within the left atrial appendage (LAA) subsequently leading to

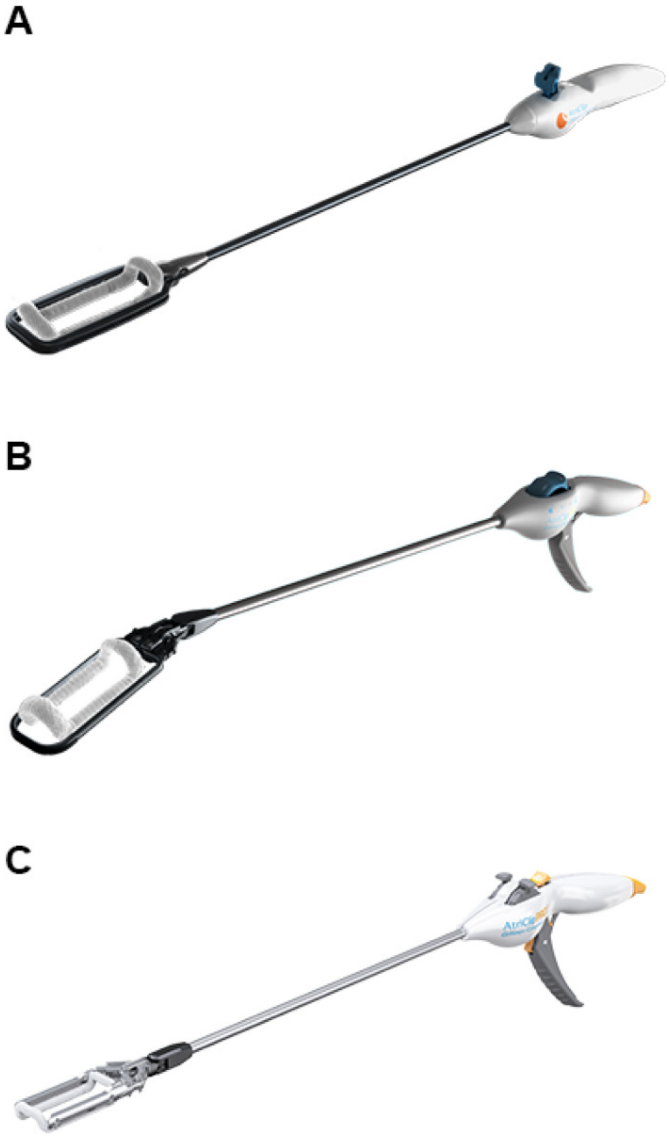


**Figure 1** Fully thoracoscopic-epicardial AtriClip device (AtriCure, Mason, OH, USA).

cerebrovascular ischaemic events.[1] Numerous advancements have been implemented in the AF management over recent years.[2–4] Risk stratification and adequate tailoring of antithrombotic therapies were achieved with the introduction of clinical risk scores (Congestive heart failure, Hypertension, Age ≥75, Diabetes, Stroke, Vascular disease, Age 65–74 and Sex category (female) ($CHA_2DS_2$-VASc) and Hypertension, Abnormal renal/liver function, Stroke, Bleeding history, Labile international normalised ratio, Elderly, Drugs (HASBLED)). Oral anticoagulation (OAC) remains the standard of care of patients with AF and current guidelines recommend such therapy when $CHA_2DS_2$-VASc exceeds 1,[2–6] with recent reports suggesting that approximately 80% of patients with AF in Europe and 55% of patients with AF in North America use oral anticoagulants.[7 8] While non-vitamin K antagonist oral anticoagulants (NOACs) increased safety and efficacy of the antithrombotic therapies, allowing for stable anticoagulation level within therapeutic range, some patients are not feasible for pharmacological management. For patients in whom OAC is not recommended, surgical exclusion of the LAA has been performed by cardiothoracic surgeons for decades, with recent publications indicating that left atrial appendage occlusion (LAAO) might not be inferior to OAC.[9 10] The alternative technique to open epicardial LAAO are fully thoracoscopic-epicardial, percutaneous-endocardial or hybrid endo-epicardial approach. Prospective randomised studies comparing the rate of ischaemic stroke with or without left appendage exclusion are currently lacking or limited.[11] Evidence from randomised controlled trials (RCTs) has shown that less invasive, percutaneous LAAO is a feasible alternative to surgical procedure; however, a residual jet still occurs in 2–8% of patients.[12 13] Stand-Alone Left Atrial appendage occlusion for throMboembolism prevention in nonvalvular Atrial Fibrillation DiseasE Registry (SALAMANDER) aims to assess the durability of LAAO when performed via fully thoracoscopic-epicardial, percutaneous-endocardial or hybrid endo-epicardial access and collect information on efficacy and safety of different procedures.

### Primary and secondary hypotheses

The primary hypothesis assumes that successful LAAO device deployment reduces the risk of stroke (ischaemic, haemorrhagic, total) and its complications. Secondary analyses will test the impact of between-device differences on prespecified clinical endpoints.

## METHODS

The SALAMANDER registry is a prospective, multicentre, observational registry, which will be conducted in 10 high-volume centres (online supplemental material). Patients will be fully informed prior to the study inclusion and informed consent will be obtained. We used the SPIRIT checklist when writing our report.[14] The study conduction is planned from March 2019 until March 2025.

### Intervention

Patients will be prospectively divided into three cohorts: thoracoscopic-epicardial, percutaneous-endocardial or hybrid endo-epicardial. Fully thoracoscopic-epicardial LAAO uses AtriClip of all generations (figure 1) (AtriCure, Mason, OH, USA); endocardial devices include Watchman FLX (Boston Scientific, Natick, MA) (figure 2) or Amulet (Abbott, Plymouth, MN, USA) (figure 3); for hybrid endo-epicardial procedures, LARIAT (SentreHeart, Redwood City, CA, USA) will be used (figure 4).

### Study population

Patients will be enrolled to the study if they meet following inclusion criteria: (1) age ≥18 years; (2) diagnosis of paroxysmal, persistent or permanent nonvalvular AF; (3) high risk of thromboembolic complications—$CHA_2DS_2$-VASc Score ≥2 for males and $CHA_2DS_2$-VASc Score ≥3 for females; (4) HASBLED score of ≥2; (5) contraindications to oral anticoagulation; (6) adherence to the study

**Figure 2** Endocardial Watchman FLX device (Boston Scientific, Natick, MA) (from https://www.bostonscientific.com/en-EU/products/laac-system/watchman-flx.html).

protocol. Patients refusing to participate in the registry will be excluded from the study.

Patients will be consecutively and continuously recruited at each site to ensure a representative inclusion of the population. Enrolment has begun 1 March 2019. Study flow chart is shown in figure 5.

### Device and surgical technique

The device for surgical totally thoracoscopic left atrial appendage occlusion AtriClip Gillinov-Cosgrove (AtriClip, AtriCure, Dayton, OH, USA) consists of an automatically closing clip placed in a deployment loop on a disposable

**Figure 3** Endocardial Amplatzer left atrial appendage occluder amulet (Abbott, Plymouth, MN, USA).

**Figure 4** Hybrid endo-epicardial LARIAT device (SentreHeart, Redwood City, CA, USA) (from http://sentreheart.com/wp-content/uploads/SH_CATALOG_PRM-0006-Rev-E.pdf).

holder with head articulation of 60 degrees side-to-side and up/down (figure 1A–C). The several novel features of the system in comparison with previous ones, such as its length, manoeuvrability and releasing system, enable it to be used in a totally thoracoscopic fashion. The AtriClip PRO (figure 1B–C) has parallel titanium crossbars that equalise the force over the tissue trabeculations of the LAA during deployment, ensuring a sealed line at the base of the LAA orifice, as confirmed in preclinical and clinical studies.[9] The patient is placed in the supine position and intubated under general anaesthesia with a double lumen intratracheal tube. Trans-oesophageal echocardiography (TOE) probe is introduced. Single right lung ventilation is started. Subsequently, three thoracoscopic ports are placed—one through the fourth intercostal space in the anterior axillary line (for the endoscopic camera), and two through the third and sixth intercostal spaces at the midaxillary line into the left pleura (working ports). Working space is created with $CO_2$ insufflation. Pericardiectomy is performed parallel to the phrenic nerve to visualise the LAA. Stay sutures are placed on the lower edge of the pericardium for better access to the LAA. The diameter of the base of the LAA is measured with a dedicated selection guide. The AtriClip device is introduced through the incision in the sixth intercostal space enlarged to 2–3 cm. Under TOE control, AtriClip is deployed at the base of the LAA with special care in order not to leave any residual stump. The possibility of repeated opening of the clip before the final deployment enables correction of its position if the intraoperative echocardiography showed incomplete LAA closure or an LAA remnant. Full LAA exclusion is then confirmed with TOE visualisation. The skin-to-skin procedural time takes

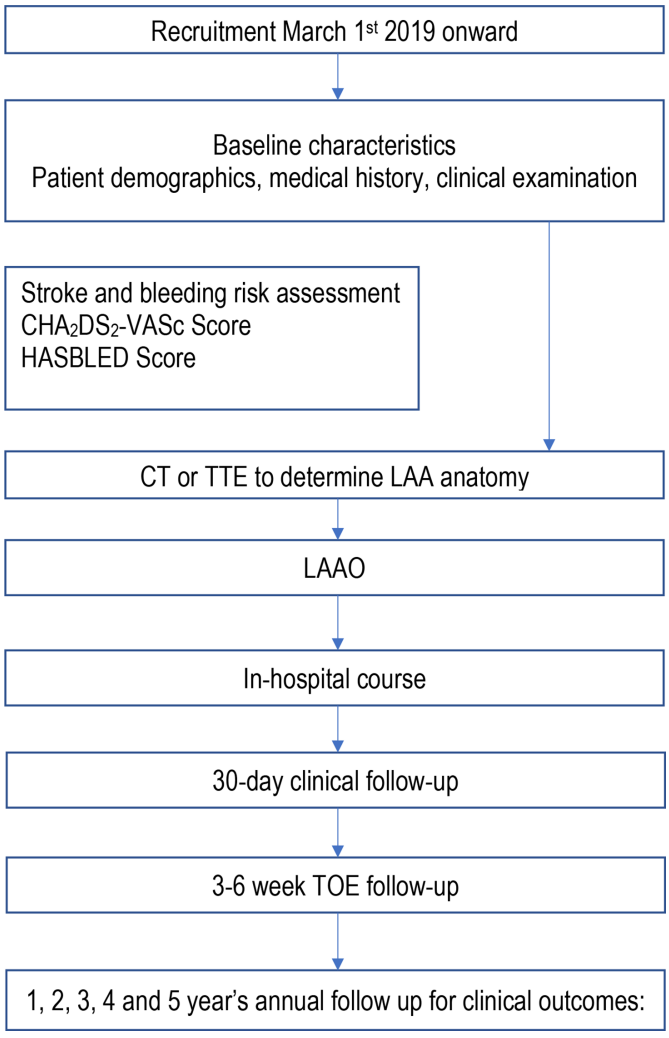


**Figure 5** Study flow chart. CT, computed tomography; LAA, left atrial appendage; LAAO, left atrial appendage occlusion; MACCE, major adverse cardiac and cerebrovascular event; MI, myocardial infarction; TOE, trans-oesophageal echocardiography; TTE, transthoracic echocardiography.

on average 40, minimum 20 min. The operative details and results of a pilot study have been described before.[10]

The Watchman FLX device (figure 2) has a self-expanding nitinol frame structure with fixation anchors and a permeable polyester fabric cover facing the LAA. The Watchman FLX device is available in five sizes (20, 24, 27, 31 and 35 mm) for ostia measuring from 15 mm to 32 mm. The Watchman FLX is preloaded in the delivery system (one size 14 Fr outer diameter access sheath compatible with any FLX device). It comes in two curve configurations—single and double—for different LAA orientation. The device is implanted with use of a catheter-based delivery system via a transseptal approach under fluoroscopy, with positioning in the LAA under the guidance of TOE.

The Amplatzer Amulet device (figure 3) is a self-expanding nitinol device with a distal lobe and a proximal disc. The device comes preloaded in eight different sizes (14–34 mm), the proximal disc is larger (6–7 mm greater than the lobe vs 4–6 mm for Amplatzer Cardiac Plug (ACP)) and the distal lobe is longer (7.5–10 mm). Appropriate sizing is determined by the maximum landing zone at 10 to 12 mm from the ostium, with a general oversizing of 2 to 4 mm. The Amulet device is implanted with use of a catheter-based delivery system through a 12 Fr to 14 Fr double-curved TorqVue 45° × 45° sheath via a transseptal approach under fluoroscopy, with positioning in the LAA under the guidance of TOE.

LARIAT system (figure 4) consists of the following: (1) 0.025-inch endocardial magnet-tipped guidewire, which will be placed inside the left atrial appendage through the introduction of a catheter into the femoral vein; (2) 0.035-inch epicardial magnet-tipped guidewire, which will be placed on the outside of the left atrium through the atrial appendage puncture of the pericardium (each wire has a magnet of opposite polarity enabling end-to-end alignment); (3) a 15 mm compliant occlusion balloon catheter to identify the LAA and allow for a very precise and effective seal of the left atrial appendage; (4) the LARIAT suture delivery device, which will be introduced by earlier puncture of the pericardium in the vicinity of the left atrial appendage. With the LARIAT suture delivery device, the lumen of the left atrial appendage is closed from outside the heart, resulting in the elimination of the thrombus source. The patient is placed in the supine position, intubated under general anaesthesia, and the TOE probe is introduced. The LARIAT procedure is performed with three main components: a compliant occlusion balloon, two magnet-tipped guide wires and a 12 Fr suture delivery device. Following percutaneous pericardial approach, transseptal puncture is performed. The first endocardial magnet-tipped guidewire is placed near the apex of the LAA. Using percutaneous femoral access, the second endocardial magnet-tipped guidewire is placed at the tip of the LAA to establish a stable connection between the wires. The LARIAT snare device is then advanced over the epicardial guidewire to occlude the LAA. After TOE and fluoroscopic confirmation of LAA closure, a pre-tied suture is deployed and tightened to ligate the LAA.[15]

## Anticoagulation regimen

While investigators have no role in defining optimal anticoagulation strategies (antiplatelet and antithrombotic), data on applied treatment regimen will be collected within the registry in an observational manner.

## Evaluations

Table 1 lists patient information and timeframes of follow-up evaluation.

The baseline assessment will record demographic, medical characteristics, and TOE or CT findings as of LAA shape and dimensions. Operatively, the procedural time, technical difficulties (eg, pleural adhesions), LAAO device sizes and immediate results will be evaluated. During intensive care unit stay, any complications connected to surgical intervention will be recorded such as bleeding requiring transfusion or reoperation, phrenic

Table 1 Evaluations at baseline and follow-up visits

| Variable | Baseline | Discharge | 30 days | 3–6 months | 1 year | 2 years | 3 years | 4 years | 5 years |
|---|---|---|---|---|---|---|---|---|---|
| Demographic information | X | | | | | | | | |
| Medical history | X | | | | | | | | |
| Clinical risk factors | X | X | X | X | X | X | X | X | X |
| Risk assessment | X | | | X | | | | | |
| $CHA_2DS_2$-VASc | X | | | X | | | | | |
| HASBLED | X | | | X | | | | | |
| Liver function | X | | | | X | | | | |
| Current medical treatment | X | X | X | X | X | X | X | X | X |
| Physician profile | X | | | X | | | | | |
| TOE | X | | | X | | | | | |
| Clinical events | | | | | | | | | |
| Postoperative complications | | X | X | | | | | | |
| Remote complications | | | | X | X | X | X | X | X |

TOE, trans-oesophageal echocardiography.

nerve palsy, pleural oedema requiring intervention, wound infection or pleural abscess formation, and length of stay. The need for prolonged mechanical ventilation postoperatively, re-intubation and need for vasopressors will be evaluated as well.

## Follow-up and endpoints

Each patient will be followed for 5 years, with follow-up assessments at discharge, 3–6 weeks, 1 year and annually until year 5. The first primary outcome is composite procedure-related complications, all-cause death or major bleeding through 12 months. The second primary outcome is a composite of ischaemic stroke or systemic embolism through 12 months. The third primary outcome is the device-specific success assessed by an independent core laboratory on TOE at the 3–6 weeks' visit. Prespecified secondary end points include a composite of all stroke (ischaemic or haemorrhagic), transient ischaemic attack (TIA), systemic embolism, all-cause death at 12 months and major bleeding at 12 months. The quality of life (QoL) will be assessed as well based on the QoL EQ-5D-5L questionnaire. Medication and drug adherence will be assessed with self-reported questionnaires. Postoperative heart rhythm and, in particular conversion to sinus rhythm, will be assessed as well.

## Outcome definitions

Major bleeding is defined as type 3 or greater, based on the Bleeding Academic Research Consortium definition. Ischaemic stroke is defined as an acute focal neurological deficit presumed to be due to focal ischaemia, with either symptoms persisting 24 hours or greater, or symptoms persisting less than 24 hours associated with MR or CT findings of a new, neuroanatomically relevant, cerebral infarct and does not include TIAs. TIA is defined as an episode of rapid-onset focal neurological dysfunction attributed to focal cerebral ischaemia, with resolution within 24 hours. Systemic embolism is defined as a blood clot that travels through the circulation system and occludes flow in a systemic artery typically with clinical manifestations. Effective device occlusion is defined as a residual jet around the device ≤5 mm, documented by TOE at the 3–6 weeks' visit. This will be assessed by Doppler flow and evaluated by an independent echocardiography core laboratory.

## Data management

All of the site data will be collected locally and forwarded to the central clinical research database. The database will be monitored in real time by a data management centre. Data management for the SALAMANDER registry will be performed independently by Centre for Postgraduate Medical Education (Warsaw, PL). The independent third-party audit will mainly monitor the following points: safety and protection of the subjects' relevant rights, the protocol-based study conduction, the accuracy of collected data, and site staff and facility adherence to the protocol requirements. Proportion of individual devices will be shown in the final report. The patients' data will be anonymised in each centre, combined into one database and statistically analysed as a single cohort.

## Statistical approach

Data will be summarised using mean (SD) and median (range) for continuous data and count (percentages) for categorical data. Continuous variables will be tested for distribution by the Kolmogorov-Smirnov test. Those with a normal distribution will be presented as a mean with SD and analysed by t-test or analysis-of-variance test. Data with a non-normal distribution will be presented as median with IQR and will be analysed by non-parametric methods. The comparison of discrete variables will be performed via the $\chi^2$ test. Registry records with >5% of missing data were not considered; in those with <5%,

missing data were input by artificial neural networks. A Cox proportional hazard model on the outcomes will be performed to test the impact of covariates (patient characteristics, physician characteristics, risk scores and antithrombotic drugs) on assessed survival. The subanalyses will be conducted for risk thresholds groups and age strata, particularly for elderly patients ≥75 years old. All of the statistical analyses will be considered significant at the 5% confidence limit using two-sided tests or two-sided CIs.

Planned analyses include the following:

- Description of patient characteristics and risk factors at baseline, changes in the thromboembolic/bleeding risk profiles and changes in the antithrombotic treatment during follow-up, as well as compliance of antithrombotic therapy related to the risk assessment;
- Evaluation of the 3–6 week durability of LAA occlusion by TOE or angio-CT[16];
- Evaluation of cardiovascular event rates (stroke, systemic thromboembolism, major bleeding and cardiovascular death) in relation to different antithrombotic therapies used for the AF population at 1 year and following time frames (2–5 years)

### Sample size

SALAMANDER is an open registry collecting data on success rates of LAAO and adverse events; sample size required was therefore not determined. At the time of registry design, the enrolment is estimated at 200 patients per year.

## DISCUSSION

Patients receiving oral anticoagulation to counter the increased ischaemic burden related to AF are at risk of developing contradictory complications. The first is a corollary of their underlying disease and an inadequate level of anticoagulation resulting in a suboptimal ischaemic risk reduction. Conversely, patients also face an increased probability of developing bleeding complications that could subsequently result in discontinuation of the anticoagulation therapy, in turn again increasing their risk for thrombotic events. Several reports showed alarming data of complications and discontinuation rate of oral anticoagulation. The study conducted in the UK and Denmark revealed that approximately 30% of patients with nonvalvular AF with ischaemic stroke discontinued OAC prior to their hospitalisation.[17] Moreover, anticoagulants remain profoundly under-prescribed in patients with AF, leading to an excess of stroke events, with almost 45% of patients with AF-related stroke not receiving OAC at the time of the event.[18] The most prevalent reasons for anticoagulation discontinuation are bleeding (13%) and infrequent AF paroxysms (14%).[18] The analysis of 12 129 US patients show that almost half of patients with nonvalvular AF discontinue OACs early after the initiation of the therapy, at the average of 120 days, especially those who experience bleeding complications.[19] Immediate implementation of an alternative strategy, optimising both ischaemic and bleeding risk complications, required to increase the safety profile of AF management.

A number of studies reported an appealing performance of external epicardial occlusion devices, revealing practically no safety issues, nearly absolute rate of LAA closure and stable long-term results.[20–27] The novelty of the technique is represented in reduced invasiveness of the procedure by combination of the epicardial LAAO and thoracoscopic approach. It was initially dedicated for patients not eligible for concomitant ablation due to low chance of success or high fragility status. The presented registry will provide comparable data on the safety and feasibility profile of this approach in a broader profile of patients. Importantly, early data suggest almost absolute acute completeness of LAAO in high-volume centres, which can be associated with simplicity of epicardial clipping and numerous possibilities for repositioning occluder's placement, until achievement of the proper seating. However, a close cooperation between surgeon and echocardiographer is mandatory. The short time of procedure conduction (20–50 min) and its relatively safe profile in experienced centres result in significantly reduced anaesthetic procedures, limited to general anaesthesia and mechanical ventilation without central vein cannulation and invasive blood pressure monitoring.

Transcatheter techniques remain among alternative strategies, characterised by even lower level of invasiveness of procedure, but a debatable feasibility.[28–30] Studies report a noticeable acute complication rate, and suboptimal mid-term and long-term procedural outcomes, including leaking to LAA,[30 31] that result in a need for bridging anticoagulation. Taking into account the structure of implanted device, it seems that epicardial clips as device are resistant to those complications; however, the thoracoscopic intervention itself is burdened with additional, distinctive periprocedural risks (anaesthetic induction and intubation) and contraindications (severely depressed lung function and previous surgery with left pleural cavity opening).

In the previous registry, thoracoscopic LAAO reached the therapeutic goals in certain patients populations, especially those experiencing bleeding events with OACs, where termination of anticoagulation was the primary target of the procedure.[10] Follow-up revealed a significantly lower than expected stroke rate, apparently associated with a very high and stable complete closure rate and no late device-related complication.

A fully thoracoscopic LAA occlusion technique may potentially be considered as an alternative to transcatheter LAAO, with observations suggesting even that surgical approach holds several advantages over transcatheter technique, those two procedures have never been compared in a RCT.

First, thoracoscopic LAAO is a safe technique with an extremely low risk of cardiac tamponade, mandated by visual control of the procedure and need for subsequent surgical interventions. Moreover, the structure of the

occluder does not require LAA tissue puncture, while the anchoring mechanism of transcatheter occluders poses a bleeding risk from LAA and pulmonary artery.[29] Lastly, an incision of pericardial sack during the epicardial access to LAA prevents high intrapericardial pressure formation by allowing communication with left pleural cavity.

Furthermore, because of its specific features, thoracoscopic clipping can be considered as a method of choice in selected groups of patients disqualified from transcatheter technique. First subpopulation requires immediate OAC cessation owing to tremendously high risk of bleeding events and usually presents with intermittent bleeding. As epicardial clipping leaves no intracardiac foreign body, no endothelialisation of the device is required and anticoagulation can be discontinued directly after the procedure with no bridging period (on the contrary to endocardial devices). Second subpopulation consists of individuals with anatomy of LAA not suitable for transcatheter LAAO, as morphological type of LAA has no impact on thoracoscopic procedure effectiveness.[32] In addition, fully thoracoscopic LAAO is performed without use of fluoroscopy, atrial septal puncture (left to right residual shunting) nor intravascular contrast (procedure suitable for patients with renal failure). Growing evidence reports stable position of the Atriclip and LAA closure with no recanalisation over time, diminishing the need for strict imaging follow-up in clinical practice. Finally, surgical epicardial LAAO electrically isolates LAA, providing positive antiarrhythmic effect.[33]

## Limitations

The SALAMANDER registry is an observational, real-world cohort study. The AF population will be recruited across Poland, but as possible limitations common to observational cohort studies, inadequacy of data recording/capture and selection bias may occur. To avoid this as much as possible, site selection was carried out among 2A and 3A Grade reference hospitals in Poland, which would guarantee a similarly high quality of medical services. In addition, the site selection was partly based on the pilot investigation, which will further be confirmed by data monitoring by a third-party contract research organisation through individual site assessment visits.

**Author affiliations**
[1]Department of Cardiac Surgery, Central Clinical Hospital of the Ministry of Interior, Centre of Postgraduate Medical Education, Warsaw, Poland
[2]Thoracic Research Centre, Collegium Medicum, Nicolaus Copernicus University, Innovative Medical Forum, Bydgoszcz, Poland
[3]Cardio-Thoracic Surgery Department, Heart and Vascular Centre, Maastricht University Medical Centre, Maastricht, The Netherlands
[4]Department of Cardiology and Structural Heart Diseases, Medical University of Silesia, Katowice, Poland
[5]Department of Cardiovascular Surgery and Transplantology, Jagiellonian University, John Paul II Hospital, Krakow, Poland
[6]Department of Anaesthesiology and Intensive Care, Ludwik Rydygier Collegium Medicum, Nicolaus Copernicus University, Antoni Jurasz University Hospital No. 1, Bydgoszcz, Poland
[7]Department of Cardiology, Jagiellonian University Medical College, Krakow, Poland
[8]Department of Invasive Cardiology, Medical University of Bialystok, Bialystok, Poland
[9]Department of Cardiology, Poznan University of Medical Sciences, Poznań, Poland
[10]1st Department of Cardiology, Medical University of Warsaw, 02-091 Warsaw, Poland
[11]Centre for Heart Disease, University Hospital Wroclaw Department of Heart Disease, Wroclaw Medical University, Wrocław, Poland
[12]Department of Invasive Cardiology, Center of Postgraduate Medical Education, Central Clinical Hospital of the Ministry of Interior and Administration, Warsaw, Poland
[13]Department of Cardiac Surgery, Medical University of Silesia, Katowice, Poland

**Contributors** MK, WW and RL provided study conception. MK, WW, RL, MKo, MP, RJ, ŁK, MG, ML, GS, KR, KB, SD, RL, SB, MAD, WWo and PS designed methodology. MK, WW, RL, MKo, MG, ML and GS created data collection tools. MK, WW, MP, RL, RG and TP monitored data collection. MK and MKo wrote the statistical analysis plan. MD, WWo and PS initiated and supervised collaborative project. MK, WW, RL and MKo wrote manuscript-first draft. MP, RJ, ŁK, MG, ML, GS, KR, KB, SD, RL, AK-C, SB, MD, WWo and PS revised the first draft. All of the authors have read and approved the final manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants and was approved by Local Bioethics Committee of the Upper-Silesian Medical Centre of the Silesian Medical University in Katowice. Participants gave informed consent to participate in the study before taking part.

**Provenance and peer review** Not commissioned; externally peer reviewed.



**ORCID iDs**
Mariusz Kowalewski http://orcid.org/0000-0002-5478-3245
Radoslaw Litwinowicz http://orcid.org/0000-0003-3736-8987

## REFERENCES

1 Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. *Ann Thorac Surg* 1996;61:755–9.
2 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. *Europace* 2012;2012:1385–413.
3 Heidbuchel H, Verhamme P, Alings M, *et al*. European Heart Rhythm Association practical guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation. *Europace* 2013;15:625–51.
4 Anderson JL, Halperin JL, Albert NM, *et al*. Management of patients with atrial fibrillation (compilation of 2006 ACCF/AHA/ESC and 2011 ACCF/AHA/HRS recommendations): a report of the American College of Cardiology/American Heart Association task force on practice guidelines. *J Am Coll Cardiol* 2013;61:1935–44.

5 January CT, Wann LS, Calkins H, *et al*. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society in collaboration with the Society of Thoracic Surgeons. *Circulation* 2019;140:e125–51.
6 Hindricks G, Potpara T, Dagres N, *et al*. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021;42:373–498.
7 Lip GYH, Laroche C, Dan G-A, *et al*. A prospective survey in European Society of Cardiology member countries of atrial fibrillation management: baseline results of EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. *Europace* 2014;16:308–19.
8 Chan PS, Maddox TM, Tang F, *et al*. Practice-level variation in warfarin use among outpatients with atrial fibrillation (from the NCDR pinnacle program). *Am J Cardiol* 2011;108:1136–40.
9 Salzberg SP, Plass A, Emmert MY, *et al*. Left atrial appendage clip occlusion: early clinical results. *J Thorac Cardiovasc Surg* 2010;139:1269–74.
10 Suwalski P, Witkowska A, Drobiński D, *et al*. Stand-alone totally thoracoscopic left atrial appendage exclusion using a novel clipping system in patients with high risk of stroke—initial experience and literature review. *Kardiochir Torakochirurgia Pol* 2015;12:298–303.
11 Whitlock RP, Belley-Cote EP, Paparella D, *et al*. Left atrial appendage occlusion during cardiac surgery to prevent stroke. *N Engl J Med* 2021;384:2081–91.
12 Holmes DR, Reddy VY, Turi ZG, *et al*. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. *Lancet* 2009;374:534–42.
13 Viles-Gonzalez JF, Kar S, Douglas P, *et al*. The clinical impact of incomplete left atrial appendage closure with the Watchman Device in patients with atrial fibrillation: a PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) substudy. *J Am Coll Cardiol* 2012;59:923–9.
14 Chan A-W, Tetzlaff JM, Gøtzsche PC, *et al*. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
15 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.
16 Kanderian AS, Gillinov AM, Pettersson GB, *et al*. Success of surgical left atrial appendage closure: assessment by transesophageal echocardiography. *J Am Coll Cardiol* 2008;52:924–9.
17 García Rodríguez LA, Cea Soriano L, Munk Hald S, *et al*. Discontinuation of oral anticoagulation in atrial fibrillation and risk of ischaemic stroke. *Heart* 2020;107:542–8.
18 Palomäki A, Mustonen P, Hartikainen JEK, *et al*. Underuse of anticoagulation in stroke patients with atrial fibrillation—the FibStroke study. *Eur J Neurol* 2016;23:133–9.
19 Kachroo S, Hamilton M, Liu X, *et al*. Oral anticoagulant discontinuation in patients with nonvalvular atrial fibrillation. *Am J Manag Care* 2016;22:e1–8.
20 Healey JS, Crystal E, Lamy A, *et al*. Left Atrial Appendage Occlusion Study (LAAOS): results of a randomized controlled pilot study of left atrial appendage occlusion during coronary bypass surgery in patients at risk for stroke. *Am Heart J* 2005;150:288–93.
21 Nagpal AD, Torracca L, Fumero A, *et al*. Concurrent prophylactic left atrial appendage exclusion: results from a randomized controlled trial pilot study. *Eur J Cardiothorac Surg* 2009;36:553–7.
22 Whitlock RP, Vincent J, Blackall MH, *et al*. Left Atrial Appendage Occlusion Study II (LAAOS II). *Can J Cardiol* 2013;29:1443–7.
23 Elbadawi A, Ogunbayo GO, Elgendy IY, *et al*. Impact of left atrial appendage exclusion on cardiovascular outcomes in patients with atrial fibrillation undergoing coronary artery bypass grafting (from the National Inpatient Sample Database). *Am J Cardiol* 2017;120:953–8.
24 Elbadawi A, Olorunfemi O, Ogunbayo GO, *et al*. Cardiovascular outcomes with surgical left atrial appendage exclusion in patients with atrial fibrillation who underwent valvular heart surgery (from the National Inpatient Sample Database). *Am J Cardiol* 2017;119:2056–60.
25 Yao X, Gersh BJ, Holmes DR, *et al*. Association of surgical left atrial appendage occlusion with subsequent stroke and mortality among patients undergoing cardiac surgery. *JAMA* 2018;319:2116–26.
26 Atti V, Anantha-Narayanan M, Turagam MK, *et al*. Surgical left atrial appendage occlusion during cardiac surgery: a systematic review and meta-analysis. *World J Cardiol* 2018;10:242–9.
27 Friedman DJ, Piccini JP, Wang T, *et al*. Association between left atrial appendage occlusion and readmission for thromboembolism among patients with atrial fibrillation undergoing concomitant cardiac surgery. *JAMA* 2018;319:365–74.
28 Schellinger PD, Tsivgoulis G, Steiner T, *et al*. Percutaneous left atrial appendage occlusion for the prevention of stroke in patients with atrial fibrillation: review and critical appraisal. *J Stroke* 2018;20:281–91.
29 Bianchi G, Solinas M, Gasbarri T, *et al*. Pulmonary artery perforation by plug anchoring system after percutaneous closure of left appendage. *Ann Thorac Surg* 2013;96:e3–5.
30 Raphael CE, Friedman PA, Saw J, *et al*. Residual leaks following percutaneous left atrial appendage occlusion: assessment and management implications. *EuroIntervention* 2017;13:1218–25.
31 Reddy VY, Gibson DN, Kar S, *et al*. Post-approval U.S. experience with left atrial appendage closure for stroke prevention in atrial fibrillation. *J Am Coll Cardiol* 2017;69:253–61.
32 Suwalski G, Emery R, Gryszko L, *et al*. Intraoperative assessment of left atrial diverticulum and remnant stump after left atrial appendage epicardial occlusion. *Echocardiography* 2016;33:1368–73.
33 Benussi S, Nascimbene S, Galanti A, *et al*. Complete left atrial ablation with bipolar radiofrequency. *Eur J Cardiothorac Surg* 2008;33:590–5.