

Case report. Thrombus formation on left atrial appendage clip: surgical exclusion and anticoagulation do not obviate transesophageal echocardiography prior to cardioversion

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Background

The cornerstone treatment for atrial fibrillation (Afib) is based on the prevention of cardioembolism with the use oral anticoagulants, which inherently increase the risk of bleeding. An alternative for these patients corresponds to left atrial appendage (LAA) exclusion/closure techniques such as *Atriclip*.

Cases summary

Patient 1: Seventy-two-year-old female who presented with decompensated heart failure, non ST elevation myocardial infarct, and paroxysmal Afib. She underwent coronary artery bypass graft, MAZE procedure, mitral valve repair, and *Atriclip* (40 mm). Recurrence of Afib postoperatively led to a precardioversion transesophageal echocardiogram (TEE) which demonstrated a LAA pouch thrombus. **Patient 2:** Sixty-seven-year-old male who underwent electively mitral and tricuspid valve repairs, MAZE procedure, and *Atriclip* (35 mm). He had recurrent atrial flutter/Afib postoperatively. He received apixaban in addition to rate control medications, and he was readmitted for precardioversion TEE which also demonstrated a LAA pouch thrombus.

Discussion

Atriclip is a stapler exclusion device via epicardial approach which has shown excellent exclusion rates in contemporary data. One of the pitfalls of this technique is the possibility of leaving a LAA remnant stump or pouch that is highly thrombogenic. The optimal timing for stopping anticoagulation and the need for precardioversion echocardiography remain uncertain.

Keywords

Atriclip • Appendage pouch thrombus • Anticoagulation • Precardioversion transesophageal echocardiogram • Case report

ESC Curriculum 5.3 Atrial fibrillation • 7.5 Cardiac surgery • 2.1 Imaging modalities • 2.2 Echocardiography

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Learning points

- Despite the excellent exclusion rates of stapling closure devices via epicardial approach in contemporary data, there is a potential risk of leaving a sizable pouch with increased thrombogenicity.
- The safety of stopping anticoagulation after *Atriclip* and the need for transesophageal echocardiogram (TEE) precardioversion are equi-poise. However, long-term anticoagulation is recommended after surgical exclusion based on the patient's thromboembolic risk.
- Left atrial appendage (LAA) surgical exclusion concomitant with oral anticoagulation reduces further the risk of stroke.
- TEE precardioversion in patients not receiving anticoagulation and in those with residual > 1 cm LAA pouch could be considered for risk mitigation.

Introduction

Atrial fibrillation (Afib) is an independent risk factor for stroke, portending near five-fold increase in risk.¹ The latest iteration of the European Society of Cardiology (ESC) guidelines for management of Afib recommends oral anticoagulation (OAC) in men with CHA₂DS₂-Vasc scores ≥ 2 and women ≥ 3 , while this therapy can be considered in patients with lower scores under specific settings.² Although clearly demonstrated to reduced cardioembolic risk, this strategy does have several limitations, such as: incorrect dosing, need for temporary interruptions during surgical procedures, poor compliance with prescribed doses, fluctuations of therapeutic levels, and overall clinical scenarios where the bleeding risk precludes the use of OAC.^{3,4} It is also important to consider that at best, only 60% of patients treated with warfarin, achieved consistent therapeutic international normalized ratio levels.⁵ Direct oral anticoagulants (DOAC) have emerged as an alternative to overcome some of these limitations associated with warfarin. This group of medications tested in four large randomized clinical trials have shown to be at least non-inferior to warfarin in mitigating cardioembolic risk while causing less bleeding.³ In a recent meta-analysis, DOACs were found to be superior to warfarin in decreasing intracranial bleeding, but without a real incremental benefit in attenuating the risk of bleeding elsewhere.⁶

All of these limitations, in addition to the need for stroke risk mitigation in patients not eligible for OAC therapy, have promoted the development of novel catheter-based procedures and the improvement of surgical techniques, with overall favourable results.² These interventions aim for themechanical exclusion of the left atrial appendage (LAA), known to harbor around 90% of thrombus found in patient with non-valvular Afib related strokes.⁷

Atriclip is a surgical stapling closure device implanted via an epicardial approach, with reported excellent exclusions rates.⁸ Despite its technical success, the safety of discontinuing OAC after surgery remains uncertain.³ Herein, we report two cases of thrombus formation in patients after *Atriclip* and while receiving anticoagulation.

Timeline Patient 1

Date	Event
5 January 2021	Onset of symptoms
7 January 2021	Hospital admission

Continued

Continued

Date	Event
8 January 2021	Diagnostic coronary angiogram revealing multi-vessel CAD
13 January 2021	Transesophageal echocardiogram (TEE)-guided direct current cardioversion (DCCV) without complications
19 January 2021	IMPELLA-assisted three-vessel coronary artery bypass graft (CABG), mitral valve repair, MAZE procedure, and left atrial appendage (LAA) exclusion with <i>Atriclip</i> device (40 mm)
1 February 2021	Saphenous vein harvest site haematoma surgical drainage
2 February 2021	TEE-guided DCCV without complications and IMPELLA removal
3 February 2021	Posterior stroke
19 February 2021	Heparin drip initiated
22 February 2021	Repeat precardioversion TEE demonstrated a LAA pouch thrombus, procedure abandoned (partial thromboplastin time 74, reference 23–34 s). Bridged to warfarin with bivalirudin
11 March 2021	Transferred to hospice care due deteriorated clinical status
13 March 2021	Patient expired

Timeline Patient 2

Date	Event
18 January 2021	Admitted for elective mitral and tricuspid valve repairs, MAZE procedure and LAA exclusion with <i>AtriClip</i> (35 mm)
19 January 2021	Recurrent atrial Flutter/Afib
20 January 2021	Acute inferior and anterolateral STEMI due to 95% focal stenosis of the mid left circumflex artery and 90% focal stenosis of the proximal left PDA status post one-vessel CABG (SVG to L-PDA)
30 January 2021	Discharged from the hospital on rate control and apixaban

Continued

Continued

Date	Event
23 February 2021	Precardioversion TEE demonstrated LAA pouch thrombus, procedure abandoned. Apixaban dose increased and plan for repeat TEE in 6 weeks.

Patient #1

Seventy-two-year-old female with history of hypertension, dyslipidemia, and chronic kidney disease presented with decompensated heart failure, non ST elevation myocardial infarct, and paroxysmal Afib with rapid ventricular response (RVR). She was diagnosed with new onset ischaemic cardiomyopathy and severely impaired left ventricular systolic function (ejection fraction 15%). A diagnostic coronary angiogram demonstrated severe multi-vessel coronary artery disease. The patient received medical treatment while on preparation for coronary artery bypass graft (CABG). A transesophageal echocardiogram (TEE)-guided direct current cardioversion (DCCV) was performed without complications (Figure 1A). After medical optimization, the patient underwent right axillary Artery 5.5 IMPELLA-assisted three-vessel CABG, mitral valve repair (27 mm Duran band annuloplasty), MAZE procedure, and LAA exclusion with *AtriClip* device (40 mm). The procedure was complicated by acute upper left limb ischaemia due to a thromboembolism requiring left brachial artery thromboembolism. Her postoperative course was complicated by Afib with RVR treated with TEE-guided DCCV; and the development of a haematoma at the saphenous vein harvest site requiring surgical drainage. Unfortunately, the following day after the IMPELLA was removed, the patient developed a right posterior cerebral artery stroke presumably from an IMPELLA-related embolus. Due to high risk for haemorrhagic conversion, the decision was made to temporarily hold anticoagulation for the following 2 weeks. Her Afib recurred, though it was managed with rate-controlled medications alone, until she was cleared for anticoagulation. A repeat precardioversion TEE while on therapeutic levels of heparin (Figure 1B) demonstrated this time the presence of a soft thrombus in the LAA stump, after which DCCV was abandoned. In light of the development of thrombocytopenia and positive platelet factor 4 antibodies, the concern for heparin induced thrombocytopenia (HIT) was raised [haemoglobin nadir 7.6 g/dL (normal range 13–17 g/dL); platelets nadir 63 (normal range 150–400 k/uL)], and the patient was switched to bivalirudin. Confirmatory tests heparin induced platelet antibody/serotonin release assay resulted indeterminate, and the patient was bridged to warfarin. Ultimately, her clinical status deteriorated due to progressive multi-organ failure. Honoring her family wishes, the patient was transitioned to hospice care and ultimately expired.

Patient #2

Sixty-seven-year-old male with history of severe mitral and tricuspid regurgitation, long-standing persistent Afib not receiving OAC due to

poor compliance, who was admitted for elective mitral and tricuspid valve repairs (Duran band 31 mm and MC3 32 mm respectively), MAZE procedure, and LAA exclusion with *AtriClip* device (35 mm) (Figure 2A). His early postoperative period was complicated by biventricular dysfunction and inferior-anterolateral STEMI due to kinking of the mid left circumflex and left posterior descending artery requiring an emergency one-vessel CABG [saphenous vein graft (SVG) to left-posterior descending artery (L-PDA)]. The patient had recurrent atrial flutter/Afib postoperatively, treated conservatively with beta blockers for rate control and 2.5 mg bid of apixaban for anticoagulation due to the presence of mild anaemia and thrombocytopenia postoperatively [haemoglobin nadir 9 g/dL (normal range 13–17 g/dL); platelets nadir 130 (normal range 150–400 k/uL)] and residual mild to moderate localized pericardial effusion. His liver and renal function remain stable postoperatively and the patient was discharged home with plan for elective TEE-guided cardioversion as outpatient. One week later, a repeat precardioversion TEE demonstrated severely impaired left ventricular systolic function (ejection fraction 25%) and the presence of a soft thrombus in the LAA stump, after which the procedure was abandoned (Figure 2B). After this finding, the patient was maintained on a rate-control strategy, and the dose of apixaban was increased to 5 mg bid. A follow-up TEE was ultimately recommended.

Discussion

LAA exclusion is performed to eliminate the major source of cardioembolism in patients with Afib.⁷ Although the first intervention to exclude the LAA was in 1949, it was not until 2003 when García-Fernández *et al.* described the therapeutic role of LAA exclusion, and the paradoxical increase in thrombogenicity resultant from an incomplete exclusion.^{9,10} Endovascular LAA occlusion devices have become the most commonly used technique. Since 2006, the American College of Cardiology/American Heart Association guidelines have considered LAA ligation/exclusion, a reasonable therapy in patients with Afib or atrial flutter undergoing valve surgery in order to reduce the risk of thromboembolic events. Most recently, the 2021 European Society of Cardiology/European Association of Cardiothoracic Surgery (ESC/EACTS) upgraded this intervention to a level IIa recommendation (Table 1).^{11,12} These statements have endorsed the use of epicardial-based approaches. Despite their invasiveness, these procedures offer the theoretical advantage to avoid blood interaction with foreign material and the need for long-term anticoagulation, while achieving excellent exclusion rates with the caveat of being performed as a stand-alone procedure via thoracoscopy or via hybrid techniques transcatheterly.⁸

Some of these epicardial based techniques include: a) endocardial suturing, which has shown suboptimal results leaving residual communication in between the LAA and the left atrium in up to half of the patients; b) Surgical excision followed by double layered suture, the most effective technique for isolation with the downside that demands the utilization of cardiopulmonary bypass, preferably under cardioplegic arrest; c) Hybrid endo-epicardial procedures (i.e. Lariat) with an increased rate of procedural-related complications; and finally, d) Stapling closure devices.⁸ The later, have the technical advantage of being suitable off pump and are able to be performed as a stand-alone procedure via thoracoscopy. An important technical

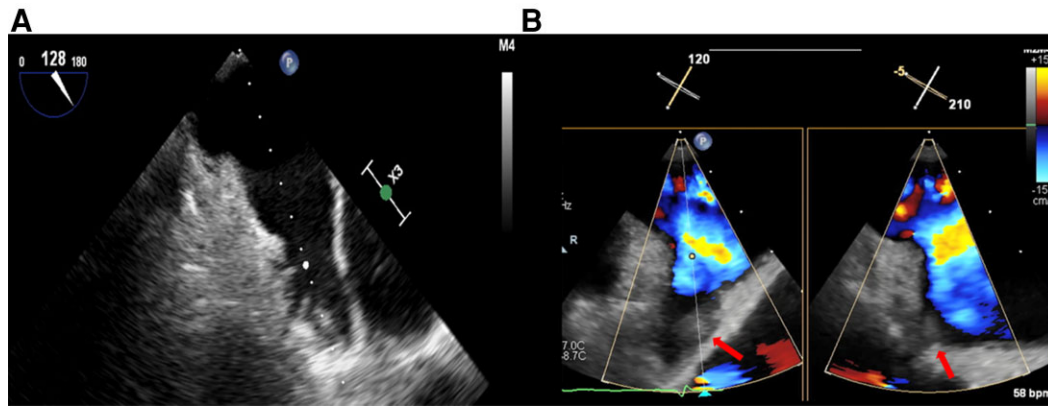


Figure 1 Preoperative and precardioversion transesophageal echocardiograms of Patient #1. (A) Preoperative transesophageal echocardiogram, mid esophageal left atrial appendage focused view at 128°, demonstrating absence of thrombus. (B) Precardioversion transesophageal echocardiogram after surgical left atrial appendage exclusion with *Atriclip* device, mid esophageal left atrial appendage biplane at 120° (left) and 210° (right) with colour Doppler interrogation at low velocities (15.4 cm/s) demonstrating lack of flow in the corresponding area of thrombus (arrow).

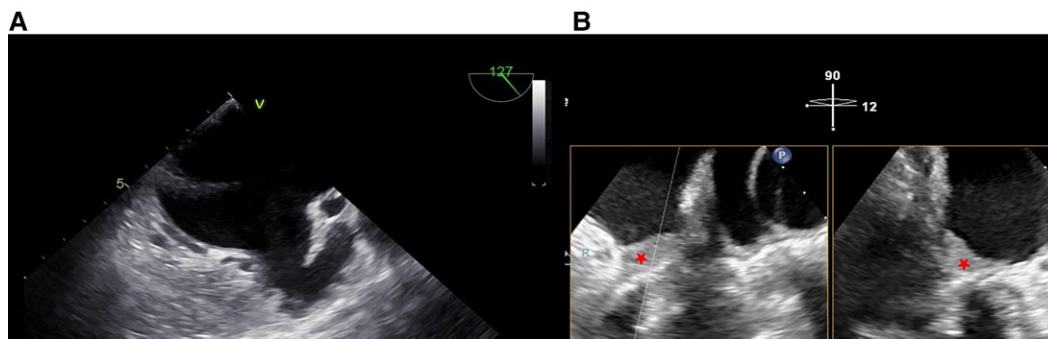


Figure 2 Preoperative and pre cardioversion transesophageal echocardiograms of Patient #2. (A) Preoperative transesophageal echocardiogram, mid esophageal left atrial appendage focused view at 127° demonstrating absence of thrombus and 'chicken wing' morphology. (B) Precardioversion transesophageal echocardiogram after surgical left atrial appendage exclusion with *Atriclip* device, mid esophageal biplane view of the left atrial appendage at 90° (left) and 12° (right), demonstrating the presence of a soft thrombus in the left atrial appendage stump (asterisk).

Table 1 Intersocietal guidelines recommendations regarding left atrial appendage occlusion and use of anticoagulation

Guidelines/year	Recommendation	Level of evidence
ESC/AECTS 2021 Diagnosis and management of atrial fibrillation	Long-term OAC therapy is recommended in patients after Afib surgery and appendage closure, based on the patient's thromboembolic risk assessed with the CHA ₂ DS ₂ -VASc score.	IC
ESC/AECTS 2021 Guidelines for management of valvular heart disease	LAA occlusion should be considered to reduce the thromboembolic risk in patients with AF and a CHA ₂ DS ₂ -VASc score ≥ 2 undergoing valve surgery.	IIa
ACC/AHA 2020 Guidelines for management of valvular heart disease	For symptomatic patients with paroxysmal or persistent Afib undergoing valvular surgery, surgical pulmonary vein isolation or a maze procedure can be beneficial to reduce symptoms and prevent recurrent arrhythmias.	IIa
ACC/AHA 2020 Guidelines for management of valvular heart disease	For patients with Afib or atrial flutter undergoing valve surgery, LAA ligation/excision is reasonable to reduce the risk of thromboembolic events.	IIa
ACC/AHA 2020 Guidelines for management of valvular heart disease	In patients undergoing LA surgical ablation of atrial arrhythmias and/or LAA ligation/excision, anticoagulation therapy is reasonable for at least 3 months after the procedure.	IIa

ACC, American College of Cardiology; AHA, American Heart Association; EACTS, European Association for Cardio-Thoracic Surgery; ESC, European Society of Cardiology.

challenge to keep present is the residual thrombogenic pouches that can be left in up to one third of the patients.¹³

Atriclip is a stapler exclusion device made of two parallel straight titanium tubes with elastic nitinol springs covered by knit braided polyester to enhance fibrosis⁸ (Figure 3). Results regarding the efficacy of stapling devices are mixed. Early data from Kanderian *et al.*,¹³ studying 137 patients with surgically excluded LAA, identified 12 individuals undergoing LAA stapling. Interesting, in this cohort, two patients (17%) remained with a patent LAA, seven (58%) had a remnant LAA (residual pouch >1 cm), and three (25%) had an excluded LAA with persistent flow. On the other hand, Salzberg *et al.*,¹⁴

demonstrated in 34 subjects treated with *Atriclip*, 100% LAA occlusion with intraoperative TEE without reported device-related complications and confirmed occlusion in all patients at 3 months with computed tomography (CT). Similar outstanding results were replicated in the EXCLUDE trial, in 71 patients treated with *Atriclip* concomitantly with other cardiac procedures. In this study, the rate of complete exclusion was 95.7% confirmed by intraoperative TEE and 98.4% at 3 months confirmed by TEE and CT.¹⁵ In terms of clinical efficacy, a recent systematic review by Toale *et al.*,¹⁶ including 68 studies of patients treated with *Atriclip*, described a low incidence of stroke or transient ischaemic attack post-clip around 0.2 to 1.5/100 patient-years.

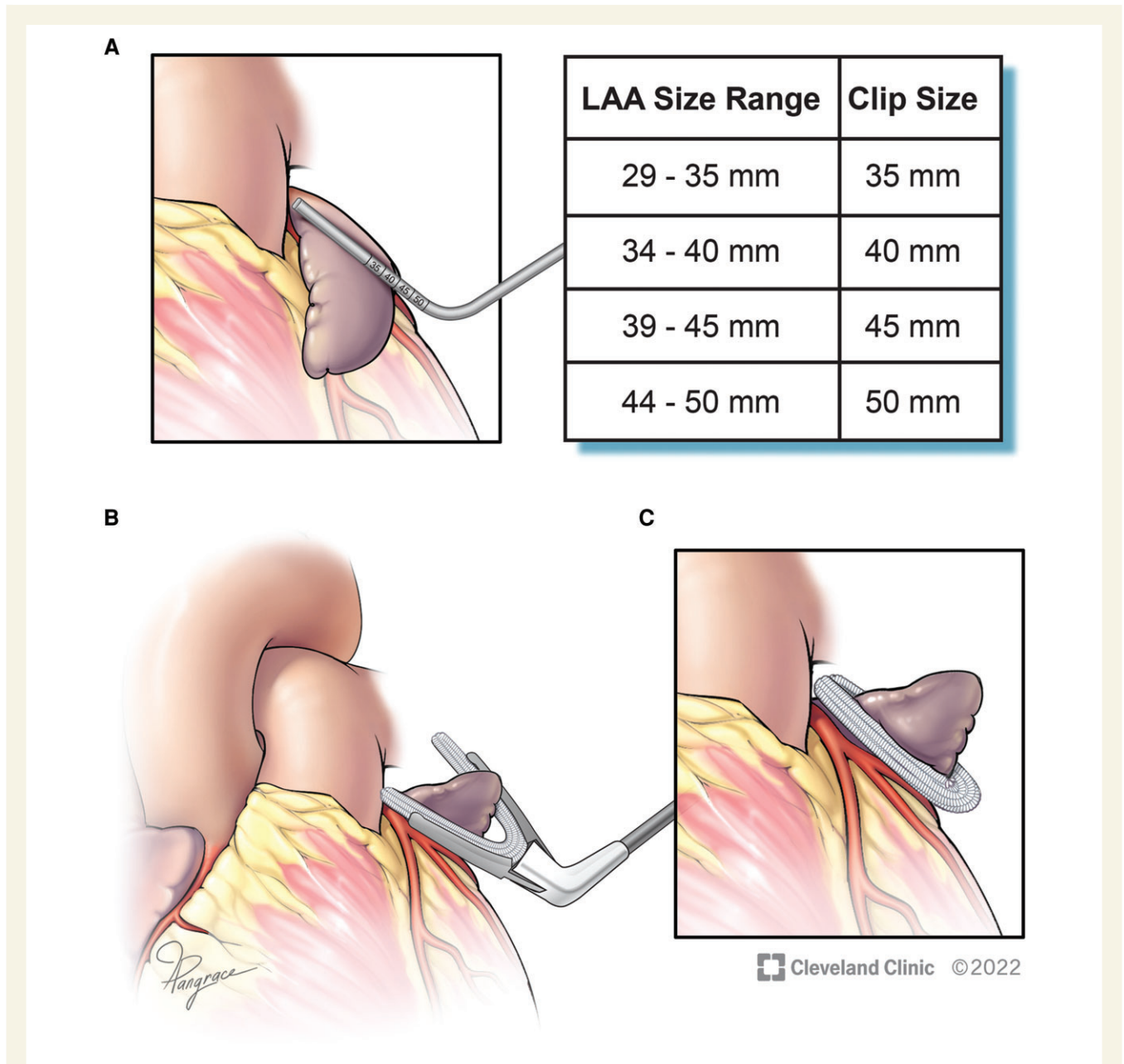


Figure 3 AtriClip implantation technique. (A) Utilization of the Gillinov–Cosgrove selection guide to determine correct selection of the clip size. (B) Approximation of the device and positioning at the base of the appendage. (C) Deployment of the clip and removal of the effector, leaving the clip in place.

The presence of thrombus in the LAA stump after *Atriclip* has been previously published. Patel et al. described a case of intraoperative LAA stump thrombus formation in a 84-year-old male undergoing aortic valve replacement and LAA exclusion with *Atriclip*, requiring re-arresting of the heart and removal of the thrombus via left atriotomy.¹⁷

Two plausible mechanisms should be considered when encountering patients with LAA thrombus after surgical stapling. The first, is the persistence of a thrombogenic nidus of remnant sizable pouch (>1 cm), and the second, the use of suboptimal anticoagulation or even in more rare instances, anticoagulation failure.^{13,18} The safety of stopping anticoagulation after *Atriclip* and the need for precardioversion TEE requires clinical equipoise. Current guidelines endorsed by the ESC and the EACTS granted a class IC recommendation for long-term OAC after LAA occlusion or surgical exclusion based on the patient's thrombotic risk utilizing CHA₂DS₂-Vasc risk score.² However, resuming of OAC after cardiothoracic surgery in the acute postoperative period should be done cautiously accounting for several variables such as: achievement of full hemostasis, removal of chest tubes and pacing wires, postoperative thrombocytopenia and anaemia, the presence of gastric dysmotility, the use of acid suppressive therapy and the level of kidney function, among others.¹⁹

In clinical practice, the most common justification for LAA occlusion/exclusion is the perceived high bleeding risk or contraindications for OAC.² However, no data are available comparing surgical LAA exclusion techniques replacing OAC. The recently published LAOS III trial, reaffirmed the incremental benefit of excluding the LAA surgically in addition to OAC.²⁰ The results from PROTECT AF and PREVAIL trials demonstrated that Watchman device was non-inferior for stroke prevention when compared with vitamin K antagonist; however, these results cannot be generalized to other surgical appendage exclusion techniques, and withholding OAC after LAA occlusion is likely to result in undertreatment.^{2,21,22}

These two cases are cautionary tales for relying on surgical exclusion of LAA to obviate the need for anticoagulation and precardioversion TEE in this group of patients. The authors favour the evaluation with TEE precardioversion in patients not receiving OAC, especially in those known to have > 1 cm residual LAA pouch, though this is based on anecdotal experience and further research in this topic is needed.

Lead author biography



Dr. Saberio Lo Presti completed his medical school at the University of Los Andes in Venezuela, his Internal Medicine Residency and Cardiology Fellowship at Mount Sinai Medical Center Florida, and currently is completing an Advanced Cardiac Imaging fellowship at Cleveland Clinic Ohio.

Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidelines.

Conflict of interest: Dr. Wazni reports personal fees from Boston Scientific, outside the submitted work. The rest of the authors have no relevant financial disclosures.

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