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Percutaneous Left Atrial Appendage Closure with the LAMBRE Device Protected by a Cerebral Protection System in a 76-Year-Old Man with Persistent Left Atrial Appendage Thrombus

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Male, 76-year-old
Final Diagnosis: Left atrial appendage thrombus despite optimal anticoagulation
Symptoms: Palpitations
Medication: —
Clinical Procedure: Cryoballoon-based ablation • percutaneous left atrial appendage closure • transesophageal echocardiogram
Specialty: Cardiology

Objective: Unusual clinical course

Background: Despite use of optimal oral anticoagulation regimens, left atrial appendage (LAA) thrombus may develop and persist in patients with atrial fibrillation (AF). The therapeutic options in this population are limited. Percutaneous LAA closure (LAAC) is performed to reduce thrombus formation and the risk of thromboembolism. However, this approach is prohibited in patients with LAA thrombus. We report the case of a 76-year-old man with AF and persistent LAA thrombus who underwent percutaneous LAAC with the LAMBRE device protected by the SENTINEL Cerebral Protection System (CPS).

Case Report: A 76-year-old man with history of persistent AF treated with pulmonary veins and LAA isolation developed LAA thrombus resistant to different anticoagulation therapies, including apixaban and Phenprocoumon, with a target international normalized ratio (INR) of 3-3,5. Repeated follow-up transesophageal echocardiography showed a persistent LAA thrombus despite optimal INR values. Thus, we performed a percutaneous LAAC using a double-umbrella-designed appendage occluder and a CPS to minimize the risk of intraprocedural cerebral embolization. The procedure was guided by transesophageal echocardiography and fluoroscopy. No signs of systemic thromboembolism were noted, and the CPS filters showed no evidence of thrombotic material.

Conclusions: This report shows that the use of a CPS during percutaneous LAAC may reduce the risk of procedural cerebral embolization and could be used as an alternative therapy for patients with contraindication or lack of effectiveness of oral anticoagulation.

Keywords: Atrial Appendage • Atrial Fibrillation • Intracranial Embolism and Thrombosis • Thrombosis


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Background

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in adults and is associated with substantial morbidity and mortality [1-3]. It is generally accepted that AF increases the risk of ischemic stroke 3-5-fold, with significant variability between patients due to differences in specific stroke risk factors [2,4].

It has been demonstrated that the presence of left atrial appendage (LAA) thrombosis is associated with a higher risk of ischemic stroke and transient ischemic attack (TIA) [5-8]. The prevalence of LAA thrombus in non-anticoagulated or suboptimal anticoagulated patients with AF is 5-27% [7]. In a recent metaanalysis, the prevalence of left atrial (LA) thrombus in patients with AF or atrial flutter under optimal anticoagulation was 2.7%, with no significant difference between patients treated with non-vitamin K oral anticoagulants (NOACs) and those treated with vitamin K antagonists (VKA) [7,9]. The management of these patients can be challenging, and consists of various therapeutic regimens, including a higher international normalized ratio (INR) target (3-3,5) in those under VKA or a switch to distinct anticoagulation therapy – VKA, NOACs, low-molecular-weight heparin (LMWH), or unfractionated heparin (UFH) [2,7,10]. Even so, the overall effectiveness of a second anticoagulation approach for thrombus dissolution is only 42.6% [11]. There are limited therapeutic options for patients with LAA thrombus unresponsive to various anticoagulation regimens [12].

Percutaneous LAA closure is accepted as a safe and effective treatment for patients with AF and contraindication to oral anticoagulation [2]. The basis of this therapeutic approach is the ability to close the LAA, a remnant of the embryonic LA, which is considered the main source of left atrial thrombi in patients with non-valvular AF, thus limiting thrombus formation and further embolization [13]. The LAmBRE device (Lifetech Scientific [Shenzhen] Co. Ltd., Shenzhen, China) demonstrated excellent implantation success rates and follow-up results, while providing a design that might provide an important advantage in patients with difficult LAA anatomy [14,15].

However, the use of appendage occluders in the presence of LAA thrombosis is prohibited due to the increased risk of intra-procedural cerebral embolization [12]. A possible approach to limit this risk is the utilization of a cerebral protection system (SENTINEL, Boston Scientific, Minneapolis, Minnesota), which has been approved for use during transcatheter aortic valve replacement (TAVR) procedures [16]. A recent publication reported the implantation of LAA occluders in patients with appendage thrombosis using cerebral protection systems to minimize the risk of cerebral embolization. This approach showed excellent results, but no LAmBRE device was used in the study [12].

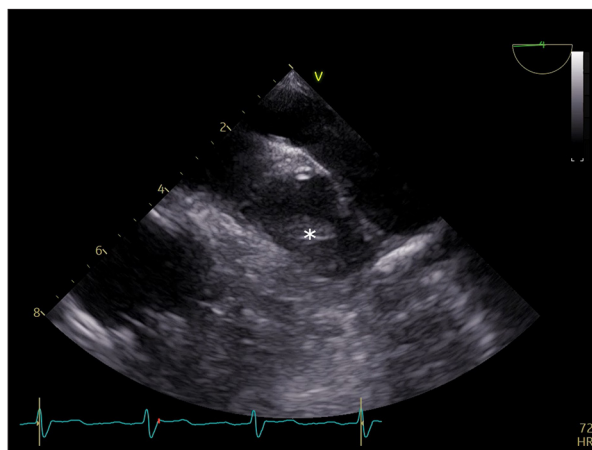


Figure 1. Transesophageal echocardiography (TEE) image recorded before the procedure. TEE image showing the thrombus (white star) and abundant sludge inside the left atrial appendage.

Therefore, this report presents the case of a 76-year-old man with AF and persistent thrombus of the LAA who underwent percutaneous LAA closure with the LAmBRE device supported by the SENTINEL Cerebral Protection System.

Case Report

A 76-year-old man with history of non-valvular, persistent AF (CHA₂DS₂-VASc score=5, HAS-BLED score=3), LAA thrombosis, and three-vessel coronary artery disease (CAD) treated with 1 drug-eluting stent (DES) on the left anterior descending (LAD) coronary artery presented to our department for a follow-up transesophageal echocardiography (TEE). The patient underwent cryoballoon-based pulmonary vein (PV) and LAA isolation 10 months before the current presentation and since then has been in sinus rhythm (SR) with no antiarrhythmic (AA) medication.

After ablation, the patient continued the previous anticoagulation therapy with apixaban 5 mg b.i.d. until the first follow-up TEE, at 1 month after the procedure, which revealed abundant LAA sludge and reduced LAA flow velocity, with no evidence of an organized thrombus. Apixaban was then changed to Phenprocoumon, with a target INR of 3-3.5. TEE 3 and 6 months after ablation revealed an LAA thrombus accompanied by abundant sludge despite optimal INR values (confirmed by multiple ambulatory determinations) (Figure 1). This was also confirmed at the 10-month visit.

Due to the unfavorable evolution under different oral anticoagulation regimens during the 10 months of follow-up, we decided to perform an LAA closure using the LAmBRE (Lifetech Scientific [Shenzhen] Co. Ltd., Shenzhen, China) device and

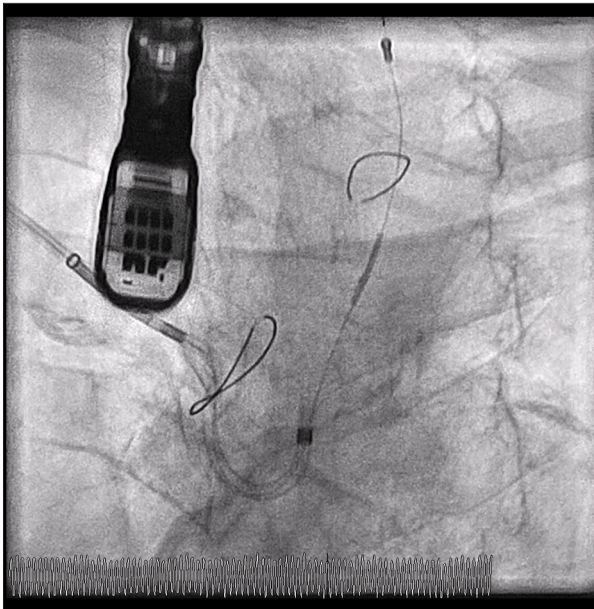


Figure 2. Fluoroscopic view of the SENTINEL system after delivery. Fluoroscopy image showing the cerebral protection system in place, with the distal filter opened inside the left common carotid artery and the proximal filter inside the brachiocephalic artery.

a cerebral protection system (SENTINEL, Boston Scientific, Minneapolis, Minnesota) to minimize the risk of intraprocedural cerebral embolization.

Written informed consent was obtained, and the patient was scheduled for the intervention. The procedure was performed under deep sedation utilizing midazolam, fentanyl, and a continuous infusion of propofol under TEE guidance. A right radial artery access was obtained, and a 6 French (F) sheath was placed at this level. Then, 2 ultrasound-guided right femoral vein punctures were performed (8 F and 10 F LAMBRE Sheath) and a multipolar catheter (Biosense Webster, Inc. Diamond Bar, CA, USA) was positioned into the coronary sinus (CS).

The angiography of the aortic arch, the brachiocephalic trunk, and the left common carotid artery was performed via a pigtail catheter placed in the ascending aorta through the radial artery sheath to describe the anatomy. Heparin was administered to maintain an activated clotting time (ACT) of ≥ 300 s [17]. The SENTINEL system was inserted using the radial artery access. Firstly, the proximal filter was deployed in the brachiocephalic trunk, then the distal filter was positioned in the left common carotid artery (**Figure 2**).

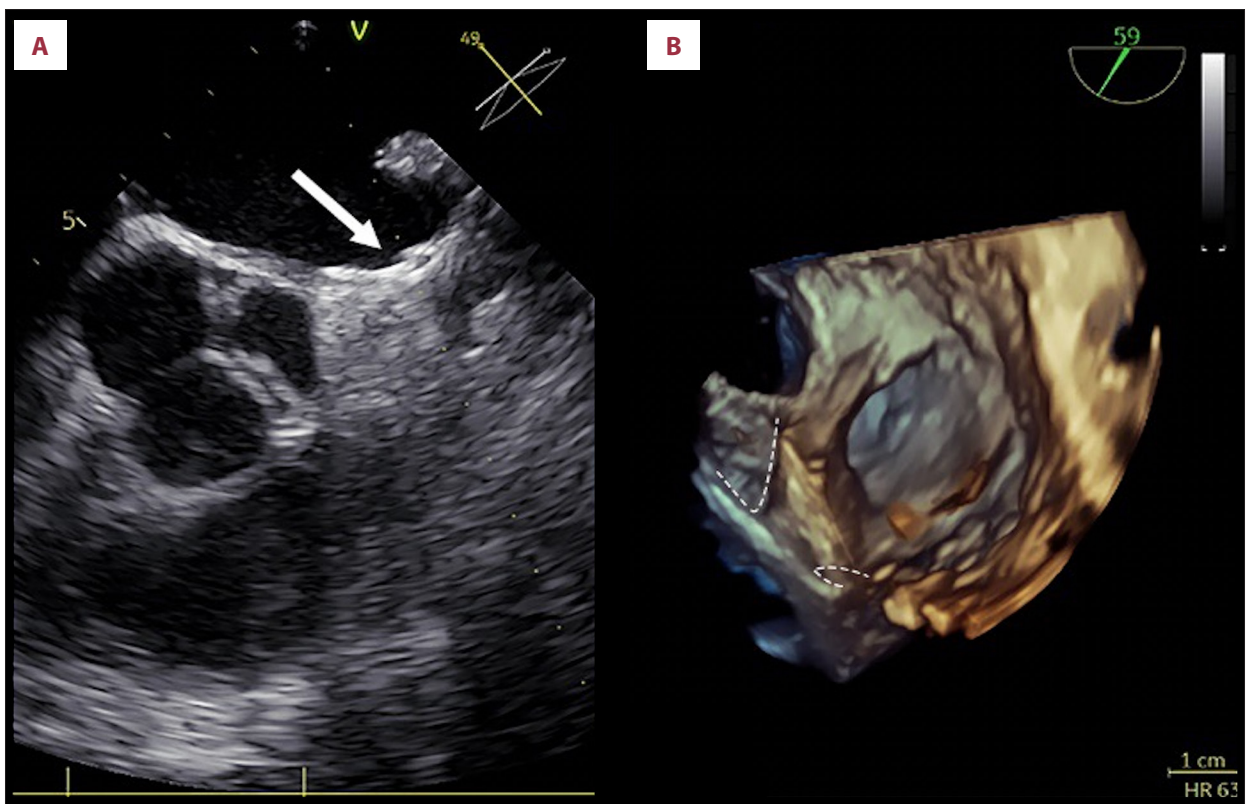


Figure 3. Echocardiographic images of the LAMBRE device after implantation. (A) Transesophageal echocardiography (TEE) image of the sealed left atrial appendage (LAA) after occluder (white arrow) implantation; (B) Three-dimensional (3D) echocardiographic image of the LAA occluder (bordered by dashed lines) after implantation.

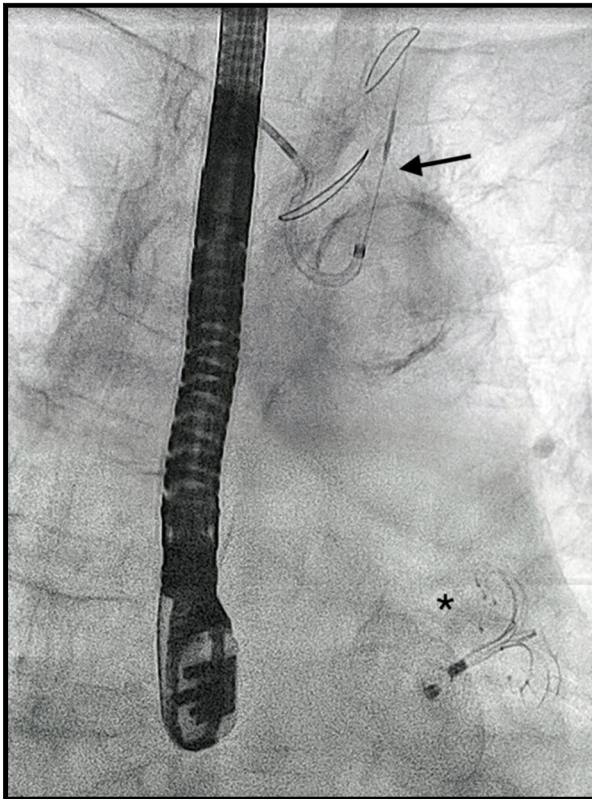


Figure 4. Fluoroscopic view of the LAMbre device and the SENTINEL system after delivery. Fluoroscopy image showing the left atrial appendage occluder after delivery (black star) and the cerebral protection device (black arrow) in place.

The LA access was obtained via a single transseptal approach via the right femoral vein under fluoroscopic guidance, using a modified Brockenbrough technique and an 8.5 F transseptal sheath (SL1 sheath, St. Jude Medical, Inc., St. Paul, MN, USA), which was continuously irrigated with heparinized saline [17]. After selective PV and LAA angiography, a spiral catheter (Lasso, Biosense Webster Corp., CA, USA) was placed in the LA and the electrical isolation of all PVs as well as of the LAA was confirmed. Subsequently, the SL1 sheath was changed over a guidewire with the LAMbre sheath. A pigtail catheter was advanced in the LA and a selective appendage angiography was performed to assess the landing zone diameter. Deep placement of the pigtail catheter inside the LAA was avoided to minimize the risk of thrombus dislodgement. The device landing zone diameter was measured by TEE and biplane angiography. The corresponding device was loaded on the delivery system and then advanced in the LA through the LAMbre sheath. To avoid intraprocedural systemic embolization, the LAMbre umbrella was partially opened at the LAA ostium, pushed inside, and afterwards completely delivered. The adequate positioning of the device was confirmed by bi- and three-dimensional TEE (Figure 3A, 3B). No evidence of peri-device leaks

was noted. The Tug-test showed no change in the position of the umbrella and the device was then successfully released (Figure 4). The transseptal sheath and the CS catheter were withdrawn. A figure-eight suture and a pressure bandage were used to prevent femoral bleeding.

Subsequently, the 2 filters of the SENTINEL system were closed, and the device was removed. A radial compression band (TR Band®, Terumo, Japan) was utilized to halt the radial artery bleeding. After the procedure, the filters of the cerebral protection device were analyzed, showing no evidence of thrombotic material or other tissue debris. No signs of systemic embolization, including ischemic stroke, were noted.

Treatment with apixaban 5 mg b.i.d. was initiated after the procedure, lasting for at least 3 months.

Discussion

The main finding of the present report is that in patients with AF-related LAA thrombus and contraindications or lack of response to oral anticoagulation, LAA closure supported by a cerebral protection system to minimize the risk of cerebral ischemic lesions represents an efficient alternative treatment. Moreover, the double-umbrella design of the LAMbre device could constitute an advantage for these patients, allowing minimal LAA manipulation during implantation [15].

The pathogenesis of AF is a complex and incompletely elucidated, with many data suggesting that electrical abnormalities, as well as atrial fibrosis, are important substrates for AF initiation and progression [18]. Recent publications reported the use of circulating micro RNAs (miRNAs) as potential blood-based biomarkers, since they were correlated with the 2 main pathophysiological processes involved in AF, as well as with the evolution after catheter ablation, suggesting the importance of epigenetic modulation in the initiation and progression of this pathology [18]. Among the electrical abnormalities involved in AF pathogenesis, the alteration in the regulation of intracellular calcium (Ca^{2+}) plays a central role. A recent study demonstrated that the responders to epicardial PV isolation (PVI) had significantly increased Sarcoplasmic Endoplasmic Reticulum Ca^{2+} ATPase (SERCA) levels in peripheral lymphocytes as compared to nonresponders. Moreover, the SERCA levels correlated with AF recurrence after epicardial ablation, suggesting that targeting SERCA might be an effective therapeutic approach in addition to catheter ablation [19]. It has also been suggested that inflammation might influence AF progression and recurrence after catheter ablation [20]. It has been demonstrated that intracellular oxidative stress in atrial myocytes leads to intracellular Ca^{2+} leak, thus contributing to the pathogenesis of AF [20]. However, the use of alpha lipoic acid as an oral

antioxidant treatment in patients undergoing catheter ablation for AF significantly reduced the common markers of inflammation after 1-year follow-up, but with no effect on the AF recurrence rate [21]. Another important aspect in AF pathology is the presence of autonomic dysfunction. This aspect was studied in diabetic patients, and it has been demonstrated that the autonomic dysfunction has a strong relationship with silent AF episodes in type 2 diabetes [22].

In the present case, the failure of various optimal anticoagulation regimens to produce thrombus dissolution left the patient with limited therapeutic options. It has been suggested that long-standing thrombi may become fixed and organized, thus decreasing the risk of subsequent embolization [2]. However, the presence of LAA sludge has been independently associated with an increased risk of thromboembolic events [23]. In consequence, the TEE aspect in our patient suggested a high risk of embolic events and a watchful-waiting approach seemed inappropriate. It is also important to note that the patient has been in SR since the ablation procedure. The electrical isolation of LAA leads to loss of mechanical function in this territory and might increase the risk of LAA thrombosis [24,25]. A recent publication reported the presence of LAA thrombi in 23.4% of patients with AF and history of appendage electrical isolation despite oral anticoagulation [26]. Thus, the thrombus formation in this case was most likely the consequence of LAA electrical isolation, and the presence of SR may further increase the risk of embolic events [26].

LAA closure is an alternative treatment for patients with AF and contraindication to long-term oral anticoagulation [2]. The non-inferiority of this treatment compared to both VKAs and NOACs in preventing AF-related ischemic stroke has been demonstrated by randomized controlled trials [27,28]. However, LAA closure in the presence of appendage thrombus may have catastrophic consequences in case of intraprocedural thrombus dislodgement and cerebral embolization [29].

The SENTINEL cerebral protection systems proved to be safe and effective for embolic protection during TAVR and has been approved by the US Food and Drug Administration for this purpose [30,31]. The use of cerebral protection devices during LAA closure procedures in the presence of LAA thrombus has been reported previously [12,32,33]. Boccuzzi et al reported the largest study, which included 27 patients treated with LAA closure supported by the SENTINEL cerebral protection system [12]. In that study, most of the patients were treated as mentioned due to contraindications of oral anticoagulation, with only 18.5% of them presenting anticoagulation failure. Eight (29.2%) patients presented macroscopic debris visible in the cerebral protection system filters at the end of the procedure. In that report, the technical and procedural success was achieved in all cases, with no procedural

adverse events reported and no evidence of embolic stroke. It is, however, important to note that none of the patients received a LAMBRE device [12]. Similar to this report, we were able to obtain procedural success with no procedure-related complications. Moreover, our patient had no evidence of macroscopic debris in the SENTINEL filters, a finding also observed in most of the patients in the previously mentioned study [12].

Only 1 paper has reported the use of the LAMBRE device in this setting so far [34]. In that paper, the authors presented the case of a 79-year-old woman in permanent AF who was referred for LAA closure due to oral anticoagulation contraindication, after having a hemorrhagic cerebrovascular accident. The preprocedural TEE showed the presence of a thrombus in the LAA. The procedure was performed using a SENTINEL device to minimize the procedural cerebral embolization risk, and successful LAA sealing was achieved, with no complications [34]. The main difference from our case is that our patient did not have a contraindication for oral anticoagulation, yet the treatment was ineffective in obtaining thrombus dissolution. Moreover, our patient received LAA electrical isolation and was in SR since then. Similar to the present report, the SENTINEL filters showed no evidence of any debris [34].

Our paper is the first to report a thrombosed LAA closure procedure secondary to LAA electrical isolation using the LAMBRE device and the SENTINEL system.

It is also important to note that this approach comes with certain limitations. The 2 arterial-delivered filters of the SENTINEL system do not protect the left vertebral and subclavian arteries or the descending aorta and coronary arteries [17]. Thus, intraprocedural systemic embolization can still have serious consequences and cautious manipulation of the LAA closure device is recommended. The double-umbrella design of the LAMBRE device might be a substantial advantage in preventing intraprocedural thrombus migration, allowing for partial device deployment at the LAA ostium, followed by complete delivery inside the appendage [15,29].

Conclusions

This report shows that the use of a cerebral protection system during percutaneous LAA closure can reduce the risk of procedural cerebral embolization and could be used as an alternative therapy for patients with contraindication or when oral anticoagulation is ineffective.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Wang L, Ze F, Li J, et al. Trends of global burden of atrial fibrillation/flutter from Global Burden of Disease Study 2017. *Heart*. 2021;107(11):881-87
2. 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(5):373-498 [published correction appears in *Eur Heart J*. 2021;42(5):507; published correction appears in *Eur Heart J*. 2021;42(5):546-47; published correction appears in *Eur Heart J*. 2021;42(40):4194]
3. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics – 2019 update: A report from the American Heart Association [published correction appears in *Circulation*. 2020;141(2): e33]. *Circulation*. 2019;139(10):e56-e528
4. Wolf PA, Dawber TR, Thomas HE Jr, Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: The Framingham study. *Neurology*. 1978;28(10):973-77
5. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. *Ann Thorac Surg*. 1996;61(2):755-59
6. Stoddard MF, Singh P, Dawn B, Longaker RA. Left atrial thrombus predicts transient ischemic attack in patients with atrial fibrillation. *Am Heart J*. 2003;145(4):676-82
7. Zhan Y, Joza J, Al Rawahi M, et al. Assessment and management of the left atrial appendage thrombus in patients with nonvalvular atrial fibrillation. *Can J Cardiol*. 2018;34(3):252-61
8. Andrade JG, Macle L, Nattel S, et al. Contemporary atrial fibrillation management: A comparison of the current AHA/ACC/HRS, CCS, and ESC guidelines. *Can J Cardiol*. 2017;33(8):965-76
9. Lurie A, Wang J, Hinnegan KJ, et al. Prevalence of left atrial thrombus in anticoagulated patients with atrial fibrillation. *J Am Coll Cardiol*. 2021;77(23):2875-86
10. Steffel J, Collins R, Antz M, et al. 2021 European Heart rhythm association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Europace*. 2021;23(10):1612-76 [published correction appears in *Europace*. 2021;23(10):1676]
11. Kofakowski K, Farkowski MM, Pytkowski M, et al. The comparative effectiveness and safety of different anticoagulation strategies for treatment of left atrial appendage thrombus in the setting of chronic anticoagulation for atrial fibrillation or flutter. *Cardiovasc Drugs Ther*. 2021; Online ahead of print [published correction appears in *Cardiovasc Drugs Ther*. 2021; Online ahead of print]
12. Boccuzzi GG, Montabone A, D'Ascenzo F, et al. Cerebral protection in left atrial appendage closure in the presence of appendage thrombosis. *Catheter Cardiovasc Interv*. 2021;97(3): 511-15
13. Asmarats L, Rodés-Cabau J. Percutaneous left atrial appendage closure: current devices and clinical outcomes. *Circ Cardiovasc Interv*. 2017;10(11):e005359
14. Ali M, Rigopoulos AG, Mammadov M, et al. Systematic review on left atrial appendage closure with the LAmbré device in patients with non-valvular atrial fibrillation. *BMC Cardiovasc Disord*. 2020;20(1):78
15. Schnupp S, Ajmi I, Brachmann J, Mahnkopf C. Lifetech LAmbré: A new promising and novel device in the interventional stroke prevention. *Future Cardiol*. 2019;15(6):405-10
16. Rogers T, Alraies MC, Torguson R, Waksman R. Overview of the 2017 US food and drug administration circulatory system devices panel meeting on the sentinel cerebral protection system. *Am Heart J*. 2017;192:113-19
17. Heeger CH, Metzner A, Schlüter M, et al. Cerebral protection during catheter ablation of ventricular tachycardia in patients with ischemic heart disease. *J Am Heart Assoc*. 2018;7(13):e009005
18. Sardu C, Santamaria M, Paolisso G, Marfella R. microRNA expression changes after atrial fibrillation catheter ablation. *Pharmacogenomics*. 2015;16(16):1863-77
19. Sardu C, Santulli G, Guerra G, et al. Modulation of SERCA in patients with persistent atrial fibrillation treated by epicardial thoracoscopic ablation: The CAMAF study. *J Clin Med*. 2020;9(2):544
20. Issac TT, Dokainish H, Lakkis NM. Role of inflammation in initiation and perpetuation of atrial fibrillation: A systematic review of the published data. *J Am Coll Cardiol*. 2007;50(21):2021-28
21. Sardu C, Santulli G, Santamaria M, et al. Effects of alpha lipoic acid on multiple cytokines and biomarkers and recurrence of atrial fibrillation within 1 year of catheter ablation. *Am J Cardiol*. 2017;119(9):1382-86
22. Rizzo MR, Sasso FC, Marfella R, et al. Autonomic dysfunction is associated with brief episodes of atrial fibrillation in type 2 diabetes. *J Diabetes Complications*. 2015;29(1):88-92
23. Lowe BS, Kusunose K, Motoki H, et al. Prognostic significance of left atrial appendage "sludge" in patients with atrial fibrillation: A new transesophageal echocardiographic thromboembolic risk factor. *J Am Soc Echocardiogr*. 2014;27(11):1176-83
24. Tilz RR, Liosis S, Vogler J, et al. Left atrial appendage thrombus formation less than 24 hours after empirical cryoballoon-based left atrial appendage isolation: A serious warning. *HeartRhythm Case Rep*. 2018;5(3):124-27
25. Heeger CH, Rillig A, Geisler D, et al. Left atrial appendage isolation in patients not responding to pulmonary vein isolation. *Circulation*. 2019;139(5):712-15
26. Fink T, Vogler J, Heeger CH, et al. Impact of left atrial appendage closure on LAA thrombus formation and thromboembolism after LAA isolation. *JACC Clin Electrophysiol*. 2020;6(13):1687-97
27. Reddy VY, Doshi SK, Kar S, et al. 5-year outcomes after left atrial appendage closure: From the PREVAIL and PROTECT AF trials. *J Am Coll Cardiol*. 2017;70(24):2964-75
28. Osmancik P, Herman D, Neuzil P, et al. 4-year outcomes after left atrial appendage closure versus nonwarfarin oral anticoagulation for atrial fibrillation. *J Am Coll Cardiol*. 2022;79(1):1-14
29. Chen S, Chun KRJ, Bordignon S, et al. Left atrial appendage occlusion using LAmbré Amulet and Watchman in atrial fibrillation. *J Cardiol*. 2019;73(4):299-306
30. Kapadia SR, Kodali S, Makkar R, et al. Protection against cerebral embolism during transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2017;69(4):367-77
31. Seeger J, Gonska B, Otto M, et al. Cerebral embolic protection during transcatheter aortic valve replacement significantly reduces death and stroke compared with unprotected procedures. *JACC Cardiovasc Interv*. 2017;10(22):2297-303
32. Marroquin L, Tirado-Conte G, Gracoñ R, et al. Management and outcomes of patients with left atrial appendage thrombus prior to percutaneous closure. *Heart*. 2022;108(14):1098-106
33. Beneduce A, Ancona F, Marzi A, et al. Percutaneous treatment of persistent left atrial appendage thrombus using watchman FLX no-touch implantation technique and cerebral protection system. *JACC Clin Electrophysiol*. 2019;5(10):1231-32
34. Mohandes M, Pernigotti A, Morr CI, Bardaji A. Percutaneous left atrial appendage closure in the presence of thrombus using LAmbré device and cerebral protection system. *Korean Circ J*. 2020;50(3):281-83