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Original Article

Early and Middle-Term Results and Anticoagulation Strategy after Left Atrial Appendage Exclusion Using an Epicardial Clip Device

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Objective: The present study aimed to evaluate short- and middle-term results and postoperative anticoagulation of left atrial appendage (LAA) exclusion with an epicardial clip device.
Materials and Methods: From September 2017 to August 2019, 102 patients at our institution underwent epicardial LAA exclusion using the AtriClip device. Anticoagulation therapy was resumed in the very early postoperative period and continued for at least three months after surgery. The patients' data were obtained by reviewing their medical records retrospectively.
Results: The mean and median durations of follow-up was 510 ± 184 days and 482 days (range, 216–938 days), respectively. Successful LAA exclusion was confirmed in all but one patient. No device-related complications occurred during surgery. Postoperative computed tomography (CT) findings revealed no migration or displacement of the clips in any patient; however, small clots were observed at the LAA stump in seven patients. Stroke-free rate during the follow-up period was 98.9%.
Conclusion: LAA exclusion using the AtriClip device was a feasible treatment method in terms of its early and middle-term safety and efficacy. In addition, our postoperative anticoagulation strategy could be optimal for maximizing the procedure's merits, although further studies, involving a larger number of patients and longer duration of follow-up, are needed.

Keywords: anticoagulation strategy, left atrial appendage exclusion, epicardial closure device

Introduction

Atrial fibrillation (AF) is a well-known risk factor for disabling stroke; patients with AF are five to six times more likely to have a stroke than patients with normal sinus rhythm.[1,2] A previous report estimated that 20% to 30% of strokes can be attributed to embolic events that develop as a result of AF.[1] In addition, there is evidence that up to 90% of embolic strokes occurring in AF patients originate from the left atrial appendage (LAA).[3] Over the past few decades, oral anticoagulation (OAC) has been the gold standard for stroke prevention in patients with nonvalvular AF. However, the currently used anticoagulation strategy is associated with a risk of major bleeding and intracranial hemorrhage (2.3% and 0.9% per year, respectively).[4] Furthermore, older age can lead to poor OAC compliance, which could expose older patients to a greater risk of stroke. Moreover, several major studies have reported that, even in those who receive optimal anticoagulation,

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patients with AF with previous stroke have an 8% to 10% risk of recurrence.[2)]

For these reasons, a new therapeutic strategy, targeting the LAA (including resection or exclusion) for stroke prophylaxis in AF patients as a potential alternative that avoids the use of OAC,[5,6)] has been explored recently.

The AtriClip device (AtriCure, Inc., Mason, OH, USA) is designed to be placed epicardially at the base of the LAA to exclude blood flow into the LAA's trabeculated area. Although the device's efficacy and safety have been accepted widely in Europe and the United States,[1)] the optimal postoperative anticoagulation treatment strategy remains controversial. The present study's goals are to investigate the short- and middle-term results of LAA exclusion using the AtriClip device in our hospital and to examine our postoperative anticoagulation strategy.

Materials and Methods

A total of 102 patients at our institution underwent LAA exclusion with the AtriClip device from September 2017 to August 2018. All patients were included in the present study. Our institution's ethics committee approved using the LAA exclusion device, and all patients provided written informed consent preoperatively. The design of this study was approved by the committee as well. The early mortality rate was 3.9% (four patients), and these patients were excluded from the analysis of clinical outcomes. Patients in whom an LAA thrombus was detected preoperatively were not suitable for this procedure. LAA exclusion was performed concomitantly with cardiovascular surgery, via median sternotomy, or as a stand-alone surgery via left mini-thoracotomy or median approach. Candidates for the stand-alone LAA exclusion were patients with an acute or subacute thromboembolic brain infarction derived from AF, who were at high risk of recurrent stroke. The indication was discussed meticulously between the cardiovascular team and neurosurgical experts. Although thoracoscopic left atrial appendectomy is widely recognized as an option for stroke prevention in nonvalvular AF,[7)] these patients were not candidates for this procedure because of their vulnerability to single-lung ventilation. Percutaneous catheter ablation was performed postoperatively for eight patients (22.9%) who were assessed to be suitable for rhythm control therapy by cardiologists. The maze procedure was basically performed for patients of mitral surgery if a patient has a clear documented history of AF, considering the amplitude of fibrillatory waves on V1 and V2 electrocardiogram (>0.2 mV), the duration of AF (<10 years), and left atrial diameter (<65 mm).

The AtriClip device is a clip made of two parallel, rigid titanium tubes with elastic nitinol springs, covered with a knit-braided polyester sheath. There are four different clip sizes available (35, 40, 45, and 50 mm), and clip selection is based on the size of the LAA base, which must be measured intraoperatively. All patients underwent intraoperative transesophageal echocardiography (TEE) to confirm successful LAA closure. Successful closure was defined as the absence of a residual stump (<1 cm) and no persistent flow into the LAA.[1,2)] An early postoperative computed tomography (CT) scan was evaluated by experienced radiologists to assess the clip's stability and thrombus at the LAA stump. All patients except those with severe renal dysfunction underwent a repeat CT scan after approximately three months. OAC was resumed on the day of surgery or one day postoperatively after hemostasis was checked and continued until at least three months after surgery. OAC cessation was considered cautiously and comprehensively based on the patients' medical history, other risks of thromboembolic events, use of a prosthesis, and CT scan findings.

We retrospectively reviewed the patients' medical records to obtain patient characteristics and perioperative data. Kaplan–Meier analysis was performed for statistical analysis using StatMate V software.

Results

Table 1 summarizes the patients' characteristics, including age, sex, preoperative stroke events, bleeding complications due to anticoagulation, CHA_2DS_2-Vasc score, HAS-BLED score, type of AF, surgical approach, concomitant procedure, and use of cardiopulmonary bypass. The patients' mean age was 72.2 ± 9.8 years. Forty-one patients (40.2%) had a history of stroke, and three patients (2.9%) had previously suffered from bleeding complications. The mean CHA_2DS_2-Vasc and HAS-BLED scores were 3.7 ± 1.8 and 2.3 ± 0.98, respectively. Sixty-five patients had a clear documented history of AF (paroxysmal, 13.7%; chronic, 50.0%). Sixty-two patients (60.8%) underwent concomitant surgery (coronary artery bypass grafting, 7.8%; aortic valve replacement, 11.8%; mitral valve plasty, 11.8%; aortic dissection, 27.5%; and other, 2.0%) via median sternotomy. In contrast, 40 (39.2%) operations were performed using left mini-thoracotomy or median approach as a stand-alone procedure for stroke prophylaxis in patients with AF.

Table 1 Patient background characteristics

Variables	n = 102
Age, years	72.2 ± 9.8
Male, n (%)	61 (59.8)
Female, n (%)	41 (40.2)
Preoperative stroke, n (%)	41 (40.2)
Preoperative bleeding complication, n (%)	3 (2.9)
CHA_2DS_2-Vasc score	3.7 ± 1.8
HAS-BLED score	2.3 ± 0.98
Type of AF	
Paroxysmal, n (%)	14 (13.7)
Chronic, n (%)	51 (50.0)
Approach	
Median sternotomy, n (%)	67 (65.7)
Left mini-thoracotomy, n (%)	35 (34.3)
Concomitant procedure	
Standalone, n (%)	40 (39.2)
CABG, n (%)	8 (7.8)
AVR, n (%)	12 (11.8)
MVP, n (%)	12 (11.8)
Aortic dissection, n (%)	28 (27.5)
Others, n (%)	2 (2.0)
Use of CPB, n (%)	67 (65.7)

AF: atrial fibrillation; CPB: cardiopulmonary bypass; CABG: coronary artery bypass grafting; AVR: aortic valve replacement; MVP: mitral valve plasty

Cardiopulmonary bypass was performed in 67 patients (65.7%). The mean and median durations of follow-up for the entire cohort was 510 ± 184 days and 482 days (range, 216–938 days), respectively.

Table 2 shows the clinical outcomes, including the rates of successful intraoperative LAA exclusion, injury of the LAA or the adjacent structures, postoperative migration and displacement of clips, LAA thrombus, OAC cessation in the postoperative period (i.e., later than three months), and postoperative stroke events. Intraoperative TEE confirmed successful LAA exclusion in all but one patient (**Fig. 1**). That patient had a severely thickened left atrial wall due to prolonged chronic heart failure, which made placing the clip device very difficult. No device-related injuries of the LAA or its adjacent structures (pulmonary artery and vein, left circumflex artery, and great cardiac vein) occurred during the operation. No patients had migration or displacement of clips, as confirmed by postoperative CT scan. However, seven patients had small clots at the stump of the LAA postoperatively, which were confirmed to have disappeared in all patients on the CT scan obtained approximately three months later (**Fig. 2**). The overall OAC cessation rate was 61.8% at the end of the study. A stroke event was detected in only one patient during the follow-up period.

Table 2 Clinical outcomes

Variables	n = 102
Successful LAA exclusion, n (%)	101 (99.0)
Injury of LAA or adjacent structures, n (%)	0 (0)
Migration or displacement of clip, n (%)	0 (0)
Postoperative LAA thrombus, n (%)	7 (6.9)
Rate of OAC cessation in postoperative period (>3 months), n (%)	63 (61.8)
Postoperative stroke events, n (%)	1 (0.98)

LAA: left atrial appendage; OAC: oral anticoagulation

The patient had dysarthria on postoperative day 2 despite an optimal anticoagulation therapy since one day after the surgery, which was relieved completely in about one week. However, neurosurgical experts found that the stroke was of cerebrovascular origin. CHA_2DS_2-Vasc score and HAS-BLED score of the patient were 3 and 3, respectively. Postoperative CT scan revealed no LAA clots at the stump of the clip. The stroke-free rate during the follow-up period was 98.9% according to Kaplan–Meier analysis (**Fig. 3**).

Discussion

Surgical procedures targeting the LAA

Currently available surgical methods for isolating blood flow to the LAA can be divided into two different categories, based on whether they involve LAA resection or exclusion. LAA resection is not a simple procedure. Obtaining an adequate suture line can be difficult; additional sutures or ligations are sometimes needed. Inadequate LAA resection can severely undermine the effectiveness of LAA resection as prophylaxis against stroke. Moreover, inadequate resection is sometimes associated with injury to the LAA, which can lead to devastating bleeding. Some reports have stated that residual blood flow through the closure line into the appendage could be detected in up to one-third of patients who underwent LAA closure with an intracardial suture.[1] In addition, it has been reported that patients with remnant flow into the LAA after closure have a greater likelihood of thrombosis in the left atrium.[2] Thus, these surgical procedures are not feasible options for stroke prevention in patients with AF.

The AtriClip device

The AtriClip epicardial exclusion device allows the LAA to be excluded without resection. Some reports have shown excellent short-term safety and efficacy

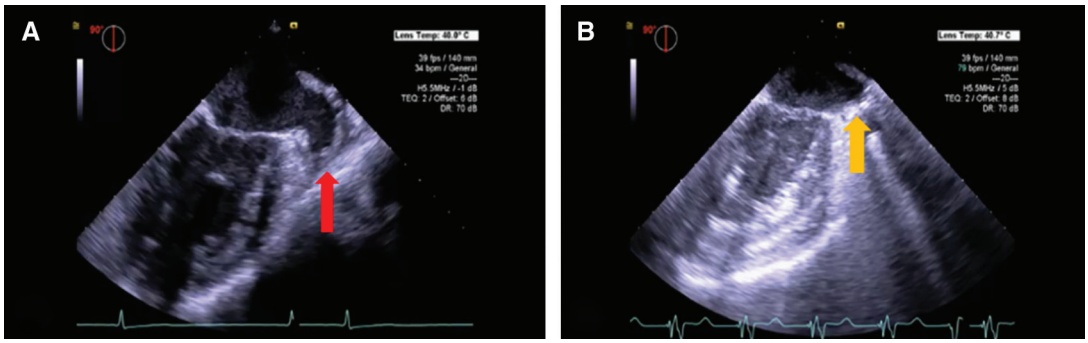

Fig. 1 Intraoperative TEE. (**A**) Intraoperative TEE demonstrating a large and patent LAA before AtriClip device placement (red arrow). (**B**) Intraoperative TEE demonstrating successful LAA exclusion after clip placement (yellow line). TEE: transesophageal echocardiography; LAA: left atrial appendage

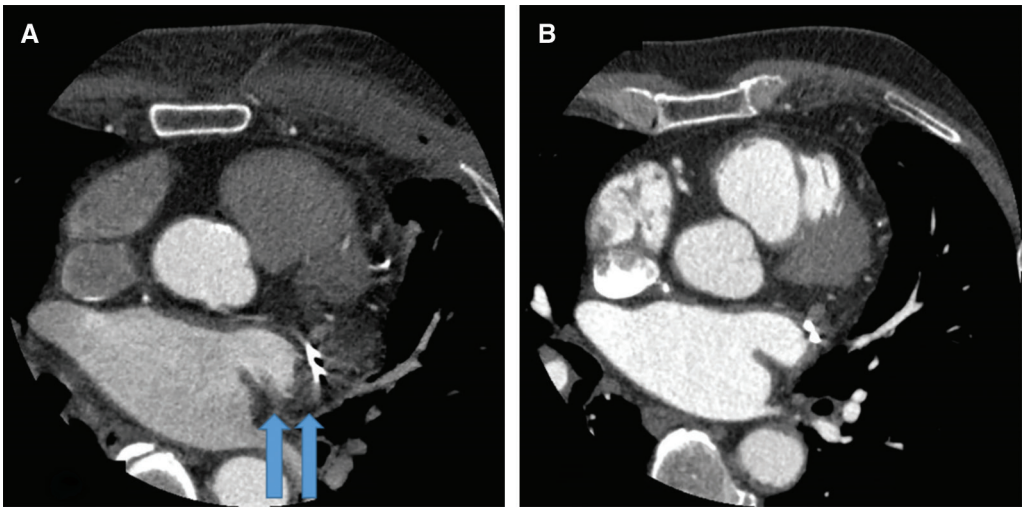

Fig. 2 Small clots after the operation. (**A**) Early postoperative CT scan demonstrating small clots (allows) at the stump of LAA. (**B**) Late postoperative CT scan revealing the disappearance of the clots. CT: computed tomography; LAA: left atrial appendage

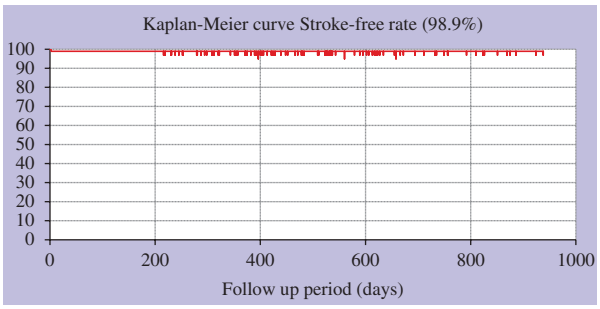

Fig. 3 Kaplan–Meier curve of postoperative stroke-free rate.

outcomes using the AtriClip device.[1,2] In addition, according to the European Society of Cardiology guidelines and the UK National Institute for Health and Care Excellence guidelines, LAA occlusion may be applied if anticoagulation is contraindicated because of elevated CHA_2DS_2-Vasc and/or HAS-BLED scores or if the patient cannot tolerate it.[8] Moreover, prospective device trials have demonstrated the LAA's durable occlusion for more than three years with excellent clinical outcomes.[9,10] For these reasons, the AtriClip device is considered a safe, efficient alternative to OAC for treating patients with AF. Our study demonstrated excellent short- and middle-term results of the AtriClip device, which were almost identical to previous reports.[1,2]

LAA clots at the stump of the AtriClip

In our research, seven patients (6.9%) had small LAA clots at the stump of the clip device; the likely cause was indirect laceration of the atrial intima, which seems to be an inevitable but serious complication. The results of this study indicate that three months of optimal OAC therapy

can resolve these stump clots with no associated thromboembolic events. In addition, some reports have indicated that a new endothelial coverage can be expected at the stump of the clip approximately 90 days after implantation.[11] Thus, OAC therapy should be continued for at least three months postoperatively.

Anticoagulation strategy

The choice of anticoagulation strategy is one of the most important issues for maximizing the AtriClip device's benefits. However, there is no clear consensus regarding OAC therapy after AtriClip implantation. At present, we use the following OAC strategy: OAC is resumed on the day of, or one day after, surgery and continued for three months postoperatively. The medication taken preoperatively by each patient is routinely selected as the postoperative OAC.

Moreover, whether OAC can be discontinued after surgery remains debatable. In our strategy, OAC cessation can be considered cautiously after three months if the patient provides sufficient informed consent and has no reason to require OAC, including LAA clots, prosthesis, risk factors for thrombosis, or other thrombosis (e.g., deep vein thrombosis). Despite the substantial benefit of OAC cessation for patients, OAC should not be stopped if there are any concerns of thromboembolic events.

The ultimate goal of LAA management is to prevent stroke caused by LAA in patients with nonvalvular AF. Considering the CHA_2DS_2-Vasc scores of our entire cohort, the estimated risk of stroke recurrence is 4.0% per year. However, in our study, the stroke-free rate during the follow-up period was 98.9%, which was confirmed by Kaplan-Meier analysis. This result may imply that our OAC strategy facilitates the AtriClip device's efficiency and could be suitable as a medical management option after the procedure.

Limitations

The present study has some limitations. First, this is a short- and middle-term study with a mean follow-up period of approximately 510 days. Second, the number of patients included is relatively small. Finally, the study is retrospective in nature.

Conclusion

LAA exclusion using the AtriClip device is feasible in terms of short- and middle-term safety and efficacy. In addition, our anticoagulation strategy increased the benefits of LAA exclusion using the AtriClip device. Our study results suggest that this strategy might be suitable for stroke prevention after AtriClip placement. Nevertheless, further studies, including a larger number of patients and a longer follow-up period, are warranted.

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Disclosure Statement

The authors declare no conflicts of interest in association with the present study.

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