Case Report

Percutaneous left atrial appendage closure—An alternative strategy for anticoagulation in atrial fibrillation and hereditary hemorrhagic telangiectasia?

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Abstract: Many patients with hereditary hemorrhagic telangiectasia (HHT) are unable to sustain oral anticoagulation (OAC) because of severe epistaxis, gastrointestinal (GI) bleeding and the risk of life-threatening bleeding from cerebral arteriovenous malformations (CAVMs) or pulmonary arteriovenous malformations (PAVMs). In patients with atrial fibrillation (AF), most thromboembolic complications arise from the left atrial appendage (LAA) and percutaneous transcatheter LAA closure proved to be non-inferior to OAC at mid-term follow-up. We report our experience with LAA closure in HHT with a follow-up of 12 months. Percutaneous LAA closure was performed in five patients with both HHT and high thromboembolic risk AF (CHA_2DS_2-VASc score ≥2) without peri-procedural complications. At 3 months no thromboembolic event occurred. After 12 months one patient had a transient ischemic attack while another patient had recurrence of stroke, this latter patient had a significant stenosis of the carotid artery and an incomplete closure of the LAA without any signs of thrombus on echocardiogram. Both patients had a non-treatable pulmonary right-to-left shunt (RLS). Percutaneous closure of the LAA may provide an alternative strategy to long-term OAC therapy in HHT patients with AF induced high stroke risk and intolerance for OAC.

Keywords: Hereditary hemorrhagic telangiectasia (HHT); atrial fibrillation (AF); Watchman; left atrial appendage (LAA) closure; stroke; bleeding

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide and is a major risk factor for cerebral embolic stroke (1-3). Oral anticoagulation (OAC) is highly effective in stroke prevention (1). However, a substantial number of patients are unable to sustain chronic OAC. Among these are patients with hereditary hemorrhagic telangiectasia (HHT).

HHT is an autosomal dominant inherited disease characterized by vascular malformations ranging from small telangiectases in skin and mucosal membranes to large arteriovenous malformations in brain, liver and lungs (4). These patients frequently encounter severe epistaxis and gastrointestinal (GI) bleedings leading to anemia and a substantial decrease in quality of life (QOL). Furthermore, since cerebral arteriovenous malformations (CAVMs) and pulmonary arteriovenous malformations (PAVMs) increase the risk of life threatening bleeding, a relative or absolute contraindication for OAC exists (5).

Most thromboembolic complications in patients with AF arise from the left atrial appendage (LAA) (1,6).

This is the first case series describing the feasibility of percutaneous LAA closure in HHT patients with AF and a high thromboembolic risk (7).

Case reports

Between 2010 and 2012, five consecutive patients (patient number 1-5, 3 males, mean age 71.4±5.0 years) with HHT and high thromboembolic risk AF (median CHA_2DS_2-VASc score of 4, range, 2-5) (1) received a LAA closure device. The baseline characteristics are described in *Table 1*.

Before LAA closure, patients 1 to 4 used OAC (CHA_2DS_2-VASc score 2, 5, 2, 4 respectively). All patients had progressive bleeding problems during this therapy and patient 1 and 2 needed several blood transfusions. Patient 5 (CHA_2DS_2-VASc score 5) only used aspirin because of a history of severe epistaxis and both an ischemic and hemorrhagic stroke.

Table 1 Baseline characteristics

Characteristics	n (N=5) [%]
Age (years)	71.4±5.0
Sex	
Male	3 [60]
Female	2 [40]
CHA_2DS_2-VASc-score	4 [2-5]
HHT type	
Type 1	1 [20]
Type 2	4 [80]
PAVMs	3 [60]
HAVMs	0 [0]
Bleeding tendency	
Epistaxis	5 [100]
GI bleeding	2 [40]
Hb (mmol/L)	6.7±0.3

Values are in number [percentages (%)], mean ± standard deviation (SD) or median with range. HHT, hereditary hemorrhagic telangiectasia; PAVMs, pulmonary arteriovenous malformations; HAVMs, hepatic arteriovenous malformations; GI, gastrointestinal; Hb, hemoglobin.

LAA closure

Before closure of the LAA, a three dimensional transesophageal echocardiogram (3DTEE) was performed to evaluate the anatomy of the LAA and to exclude pre-existent thrombus formation (*Figures 1*,*2*).

All procedures were performed as written before (3). In all cases the implantation of the LAA closure device (Watchman Left Atrial Appendage Occlusion Device®, Atritech Inc., Plymouth, Minnesota, USA) was acutely successful and there were no peri-procedural complications.

Directly after implantation, patient 1, 3 and 4 continued OAC, patient 5 continued aspirin and patient 2 combined aspirin and clopidogrel.

Follow-up

At three-month follow-up, TEE showed residual flow from LA to the LAA in patient 5 as a sign of incomplete LAA closure. No thromboembolic complications occurred. All patients discontinued OAC because of progressive bleeding; four patients switched to aspirin and patient 5 stopped the aspirin.

At 12-month follow-up (*Table 2*), one symptomatic episode was documented as a transient ischemic attack (TIA) in patient 1. The MRI showed no signs of ischemia. The TEE 2 months before and after the event showed a

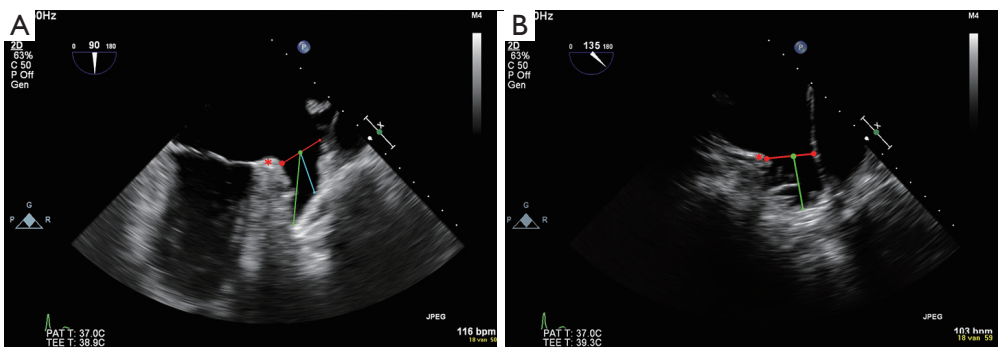

Figure 1 (A) 2D TEE before LAA closure; two-chamber view at 90°; (B) 2D TEE before LAA closure; long-axis view at 135°. Red line: landing zone; green line: LAA total depth; blue line: LAA depth perpendicular to landing zone; red astrix: circumflex coronary artery. TEE, transesophageal echocardiogram; LAA, left atrial appendage.

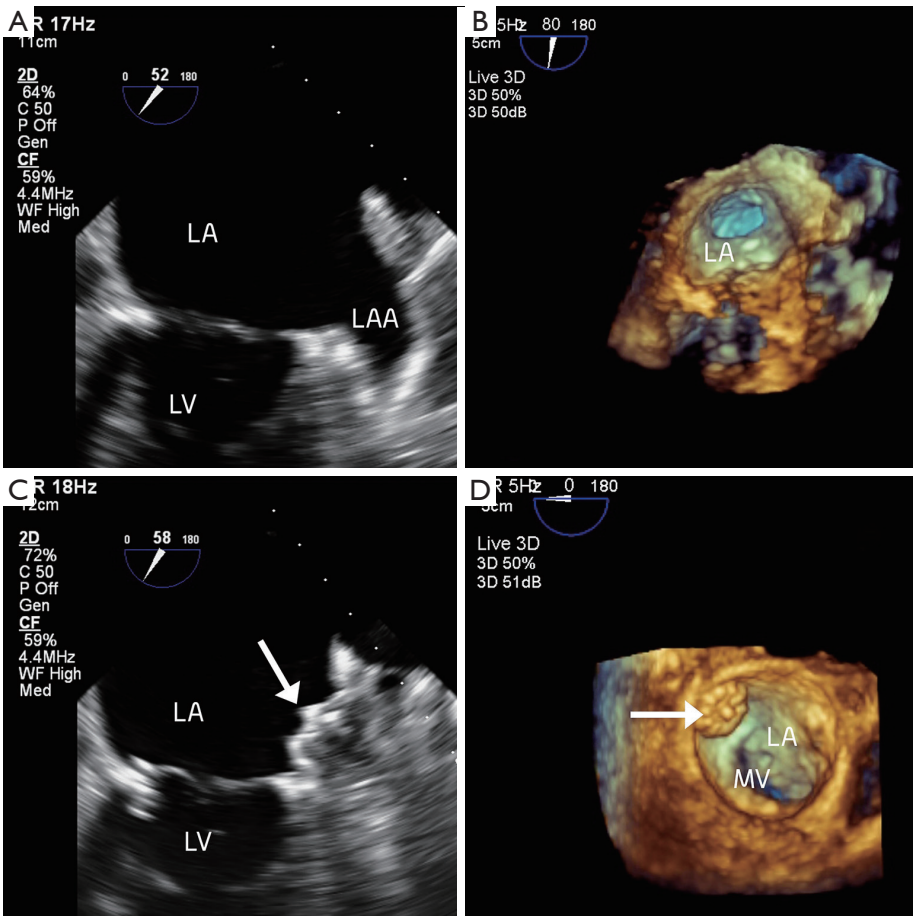

Figure 2 (A) 2D TEE of LAA, LA and LV before LAA closure; (B) 3D TEE of LAA and LA before LAA closure; (C) 2D TEE of LA, LV with the Watchman® closure device in the LAA; (D) 3D TEE of MV and LA with the Watchman® closure device in the LAA. 3D TEE, three dimensional transesophageal echocardiogram; LAA, left atrial appendage; LA, left atrium; LV, left ventricle; MV, mitral valve.

Table 2 Results at 12 month follow-up

Variables	Results, n [%]
Complete closure	4 [80]
TIA	1 [20]
CVA	1 [20]
Systemic embolus	0 [0]
Therapy	4 [80]
Acenocoumarol	1 [20]*
Aspirin	1 [20]
No therapy	3 [60]

Values are in number [percentages (%)]. *, acenocoumarol was restarted in one patient after a TIA. TIA, transient ischemic attack; CVA, cerebrovascular accident.

small residual flow but the criteria for complete closure were still fulfilled and no thrombus was seen. This patient had a history of smoking, had non-treatable PAVMs and was treated with thalidomide for refractory epistaxis. At the time of the event, the patient used no OAC or antiplatelet therapy. Although the exact cause of the TIA remained unknown, this patient restarted OAC which resulted in severe GI bleeding. Due to recurrent symptomatic AF rhythm surgery with LAA resection was performed.

A minor stroke was reported in patient 5. This patient had a significant stenosis of the carotid artery and embolized PAVMs with a persistent right-to-left shunt (RLS) on contrast echocardiogram. At follow-up, an incomplete LAA closure but no thrombus formation was seen. In the

remaining three patients, OAC was withheld without any complications.

Discussion

The treatment of patients with HHT and high thromboembolic risk AF is an increasing problem. Current guidance on the use of antiplatelet and anticoagulant agents in HHT is based on anecdotal evidence and expert opinion (5,8). This leads to insufficient treatment in many patients with a high stroke risk. In the United Kingdom, over 50% of the HHT patients were advised not to use OAC or antiplatelet therapy (8).

To decrease the risk of thromboembolic complications originating from the LAA, a percutaneous LAA closure may be performed safely. At mid-term follow-up, LAA closure proved to be non-inferior with regard to the prevention of stroke, systemic embolism and cardiovascular death in a large study with 707 patients (6).

In this current study, there was a CHA_2DS_2-VASc score of 4 estimating a yearly stroke risk of 4.0% (9). The thromboembolic complications that occurred during follow-up could be caused by either paradoxical embolization trough PAVMs, carotid artery disease, incomplete closure of the LAA or the use of thalidomide. A PAVM causes a permanent RLS that bypasses the pulmonary capillary filter, which carries the risk of cerebral paradoxical embolization (4,10). An incomplete closure of the LAA may provoke thrombus formation and might allow thrombotic embolization of LAA thrombus through the remaining defect, although current evidence seems contradictory (6,11,12). A small peri-device flow (jet width ≤5 mm) is seen after LAA closure in >30% and the PROTECT-AF trial revealed that this is not associated with an increased thromboembolic risk (12). In this case-series, thalidomide could also have contributed to thrombus formation. Thalidomide is frequently used for the treatment of refractory incapacitating epistaxis in HHT and the thrombotic complications are well known in cancer patients treated with thalidomide (13).

Currently, no guidelines regarding the treatment of patients with an incomplete LAA closure and an absolute contraindication for OAC exist. One report describes the safety of percutaneous LAA closure with another LAA closure device [the Amplatzer cardiac plug (ACP)] in 60 patients (no HHT patients) with a contraindication to OAC (14). After LAA closure, antiplatelet therapy was started without any thromboembolic complications (device related thrombus occurred in 3.5%) (14). Although there is less evidence, the ACP device may be an option for patients in which the LAA anatomy is not suitable for implantation with a Watchmann device (15).

There is no literature on the use of LAA closure without OAC or antiplatelet therapy. However, this therapy seems most important in the first months after implantation when endothelialization of the device is not complete.

Recently, it has been suggested that HHT patients tolerate antiplatelet therapy better than OAC (8). Besides this bridging therapy with OAC might not be necessary after LAA closure, based on the recent ASAP trial (16). Therefore, LAA closure seems especially valuable in HHT patients with intolerance for OAC who otherwise would be treated with antiplatelet therapy alone.

The treatment strategy in patients with both HHT and AF induced high stroke risk remains challenging and no sufficient answer for this specific population has been found. Treatment with OAC may lead to progressive and severe bleeding with a decrease in QOL. However, guidance for the treatment of patients with an incomplete LAA closure in this specific subgroup is lacking. Secondly, other thromboembolic risk factors may exist, especially in HHT.

Based on our current experience, a tailor made approach is necessary in which the choice for OAC or LAA closure should be based on the thromboembolic risk, the presence of visceral arteriovenous malformations and the bleeding tendency of the patient. We recommend to select patients with HHT for percutaneous LAA closure when OAC is not tolerated and after an observational period with and without antiplatelet therapy prior to LAA closure.

In conclusion, percutaneous closure of the LAA may provide an alternative strategy to OAC therapy in HHT patients with AF induced high stroke risk and intolerance for OAC. Future larger studies are needed to reveal the risks and benefits of this therapy in patients with HHT.

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