Original paper

Percutaneous closure of the left atrial appendage for secondary prevention of stroke in patients with atrial fibrillation and contraindications to chronic anticoagulant therapy

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Abstract

Introduction: Stroke accounts for approx. 90% of thromboembolic complications associated with atrial fibrillation. The use of oral anticoagulants is the most effective therapy but is associated with risk of haemorrhagic complications.

Aim: In this article, we describe a series of patients with atrial fibrillation, cardiogenic stroke history, and contraindications for long-term anticoagulant therapy, in whom an alternative method – percutaneous closure of the left atrial appendage – was performed.

Material and methods: Nine patients with atrial fibrillation and previous stroke were qualified for percutaneous closure of the left atrial appendage (5 men and 4 women, aged 45–78 years). Physical and neurological examinations were conducted in the qualification period, 1–3 days before the intervention, and 1–3 days and 1, 3, 6, 12, and 24 months following percutaneous closure of the left atrial appendage. Transoesophageal echocardiography was carried out in the qualification period, 1–3 days before the intervention, and at 1–3 days and 3 and 6 months following the procedure.

Results: No complications were observed in the perioperative period and during the follow-up period of 16–31 months. Echocardiographic examinations showed that occluders were present in the appropriate positions.

Conclusions: Percutaneous closure of the left atrial appendage can be an alternative form of secondary prevention of stroke in patients with atrial fibrillation and contraindications for long-term anticoagulant therapy or those who have problems managing drug treatment. Complex clinical assessment performed by a neuro-cardiac team allows safe and efficient invasive treatment.

Key words: atrial appendage, stroke, atrial fibrillation.

Introduction

Stroke accounts for approx. 90% of thromboembolic complications associated with atrial fibrillation (AF). Among individuals aged 60 years and below, the incidence of AF is estimated at 0.1–0.2%, while in individuals over the age of 80 it is 9.1–11% [1–3]. To assess the risk of a cerebrovascular event in patients with AF, the CHA_2DS_2–VASc score, which is a modified version of the $CHADS_2$ score, developed on the basis of the results of stroke prevention in atrial fibrillation (SPAF), is used [4]. Oral anticoagulant treatment (OAT) is recommended for stroke prevention in individuals with atrial fibrillation, and in patients who cannot tolerate it – antiplatelet therapy [5]. Percutaneous closure of the left atrial appendage (LAA), the place where the thrombus is formed in the heart, is another alternative. The results of the PROTECT-AF study prove that the effectiveness of this method in preventing AF complications is comparable to anticoagulant treatment [6, 7]. Taking into account the large number of patients with cardiogenic stroke, we started to use this method in a highly select group of subjects.

Aim

In the presented study we evaluate the effectiveness and safety of percutaneous closure of the LAA in our patients with AF and a history of cardiogenic stroke.

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Material and methods

Between January 2011 and April 2013, in 307 patients (of the 371 with suffered from cardiogenic stroke), warfarin or new oral anticoagulants (NOACs) were used in secondary prevention (Figure 1). In 53 individuals antiplatelet therapy was introduced due to the inability to use oral anticoagulation (difficulties in the monitoring of coagulation parameters and maintenance international normalised ratio (INR) in the therapeutic range, bleeding during anticoagulant therapy). Eleven patients, aged 45–79 years, 7 men and 4 women, were qualified for percutaneous closure of the LAA. The main inclusion criteria were as follows: the presence of atrial fibrillation, a past history of clinically apparent cardiogenic stroke (which had occurred > 2 months earlier), ineffectiveness of long-term oral OAT, its limitation, or contraindications for its use. The main exclusion criteria were as follows: the presence of thrombus in the LAA detected on transoesophageal echocardiography (TEE), left ventricular wall motion abnormalities, the anatomical structure of the LAA hindering occluder implantation, stroke of aetiology other than that associated with AF, and allergy to ionic contrast media. Physical and neurological examinations were conducted in the qualification period, 1–3 days before the intervention, and 1–3 days, 1, 3, 6, 12, and 24 months following percutaneous closure of the LAA. Transoesophageal echocardiography was carried out in the qualification period, 1–3 days before the intervention as well as at 1–3 days and 3 and 6 months following the procedure.

Finally, the procedure was carried out in 9 of the patients; the reason for abandoning the procedure in 1 case was technical and resulted from the anatomy of the appendage; in the other case, the reason was the presence of thrombus in the left atrium, detected twice on TEE.

The procedure was performed through a puncture in the femoral vein, under general anaesthesia, in the presence of a team of anaesthesiologists and an echocardiographist carrying out TEE in order to monitor the course of the procedure. The LAA was reached through a transseptal puncture. X-ray imaging with contrast enhancement was used for detailed assessment of the appendage's shape and dimensions. Amplatzer Cardiac Plugs, optimally sized for each LAA, were implanted with the use of an introducer system. Detachment of the occluder from the introducer system was preceded by echocardiographic assessment of its position.

Eight patients used dual therapy in the 6 months following the procedure: aspirin with clopidogrel. Afterwards, they continued treatment using only aspirin at a dose of 150 mg daily. One of our patients used acenocoumarol on a permanent basis due to an artificial heart valve.

Results

The characteristics of the patients qualified for percutaneous closure of the LAA are presented in Table I.

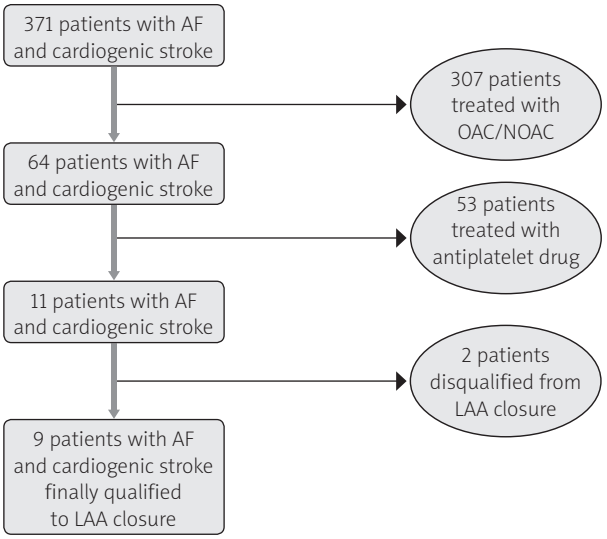

Figure 1. Flow chart for selection of patients for LAA closure

No complications associated with the procedure of LAA closure were observed in the perioperative period or during the 16–31-month follow-up period. No new cerebral ischaemia events were found in any of the patients in the 16–31-month follow-up period after the procedure. Transoesophageal echocardiography examinations performed at 1–3 days as well as at 3 and 6 months following the procedure showed normal and stable positioning of the occluders in each of the patients.

Discussion

Percutaneous closure of the LAA eliminates the region where thrombus most often forms in the heart. According to echocardiographic and post-mortem studies, over 90% of potentially embolic material forms in the LAA [8–11]. The use of an oral OAT is the best form of secondary prevention of stroke, but as many as 54% of patients with indications for such treatment do not receive it for various reasons [12, 13].

Factors limiting the use of OAT result not only from the caution of physicians, who are more afraid of iatrogenic bleeding than cerebral infarction, but also from common contraindications found in patients eligible for such treatment. The main restrictions in individuals over 80 years of age result from the propensity to fall (41%) and bleeding events (28%) [14–16]. Although the inclusion of NOACs in the secondary prevention of cardiogenic cerebral stroke has increased the safety of chronic anticoagulant therapy, approx. 20% of patients resign from it within 2 years of therapy due to complications and/or poor tolerance [17, 18]. Left atrial appendage closure is an alternative for patients with AF and a high risk of a cardiogenic cerebral events, in whom long-term OAT is associated with a high risk of complications or is impossible for various reasons.

Table I. Clinical characteristics of the patients finally qualified for LAA closure

Parameter	Patient									*N* (%)
	1	2	3	4	5	6	7	8	9	
Congestive heart failure The presence of signs and symptoms of either right or left ventricular failure or both, confirmed by non-invasive or invasive measurements demonstrating objective evidence of cardiac dysfunction, e.g. LVEF < 40%	+				+				+	3 (33.3)
Hypertension A resting blood pressure > 140 mm Hg systolic and/or > 90 mm Hg diastolic on at least 2 occasions or current antihypertensive pharmacologic treatment	+	+		+	+	+		+	+	7 (77.7)
Age ≥ 75	+		+	+	+					4 (44.4)
Age 65–74		+				+	+		+	4 (44.4)
Diabetes mellitus Fasting plasma glucose level ≥ 7.0 mmol/l (126 mg/dl) or treatment with oral hypoglycaemic agent and/or insulin					+	+	+		+	4 (44.4)
Stroke/TIA/thrombo-embolism	+	+	+	+	+	+	+	+	+	9 (100)
Vascular disease prior myocardial infarction, angina pectoris, percutaneous coronary intervention or coronary artery bypass surgery. The presence of any the following: intermittent claudication, previous surgery or percutaneous intervention on the abdominal aorta or the lower extremity vessels, abdominal or thoracic surgery, aterial and venous thrombosis		+			+				+	3 (33.3)
Sex, female		+				+	+	+		4 (44.4)
Bleeding						+	+		+	3 (33.3)
Labile INRs Therapeutic time in range < 60%	+		+	+	+					4 (44.4)
Drugs – antiplatelet agents or NSAIDs	+	+	+	+	+	+	+	+	+	9 (100)
Alcohol									+	1 (11.1)
Abnormal liver function				+					+	2 (22.2)
Abnormal renal function				+		+				2 (22.2)
CHA_2DS_2–VASc	6	6	4	5	8	6	5	4	7	5.66*
HASBLED	5	5	5	7	5	6	4	3	7	5.11*

**Mean value.*

So far, two randomised studies using percutaneously implanted WATCHMAN occlusion systems have been carried out [6, 19]. The results of the PROTECT AF study suggest that LAA closure is as effective in preventing stroke in patients with non-valvular AF as warfarin treatment [6]. Analysis of the endpoints of the study (stroke, cardiovascular death, death from an unknown cause, systemic embolism) showed an insignificantly lower number of events in the group of patients treated surgically in comparison with the group treated with warfarin. In view of the positive results regarding the method's effectiveness, safety analysis provided some disappointing data. Complications occurred in almost 11% of patients in the perioperative period, including pericardial effusion in 22 patients (4.8%), bleeding requiring transfusion of 2 units of packed red blood cells, or surgical interven-

tion in 16 patients (3.5%) as well as cerebral infarction in 5 patients (1.1%) [6]. The complications were related to operator experience over the course of the trial. Indeed, a subsequent non-randomised Continued Access PROTECT-AF registry (CAP) that involved more experienced operators demonstrated significantly fewer pericardial effusions (PEFs) and no instances of procedure-related stroke [20]. After 1588 patient-years of follow-up (mean 2.3 ±1.1 years), the primary efficacy event rates were 3.0% and 4.3% in the Watchman and warfarin groups, respectively (relative risk, 0.71; 95% CI: 0.44–1.30% per year). There were more primary safety events in the Watchman group (5.5% per year; 95% CI: 4.2–7.1%) than in the control group (3.6% per year; 95% CI: 2.2–5.3%; relative risk, 1.53; 95% CI: 0.95–2.70%) [7].

In the PROTECT AF study, almost 68% of patients were qualified with a $CHADS_2$ score of no more than 2 [6]. Therefore, taking into account the yearly risk of stroke and the risk in the perioperative period in the presented studies, qualifying patients for percutaneous closure of the LAA cannot be recommended in patients with low $CHADS_2$ and CHA_2DS_2–VASc scores.

During the Left Atrial Appendage Closure With Amplatzer Cardiac Plug in Atrial Fibrillation: Initial European Experience study, the LAA was successfully occluded in 132 patients (96% of the patients qualified for interventional treatment). Serious complications were observed in 10 (7%) patients, including pericardial effusion in 5 (3%) and cerebral infarction in 3 (2%) [15]. According to the results obtained from currently held studies and registers of patients after LAA occlusion, the incidence of all complications associated with the procedure relates to 2–7.7% of patients [21, 22].

All of our patients had a history of at least one cardiogenic, embolic stroke. Independent of cerebral ischaemia, iatrogenic intracranial haemorrhage during OAT occurred in 3 of our patients, nosebleeds in 2 (recurrent in 1 of them), bleeding from the genital tract in 1 patient, and urinary tract bleeding requiring a urologic intervention in 1. The state of the daily functioning of 6 patients qualified for treatment was good (they were self-reliant), while 3 required help, including 1 person who needed help with both verbal communication and mobility (Table I). We thought that LAA closure was ineffective in the prevention of stroke and iatrogenic bleeding events associated with OAT (including NOACs), making the continuation of therapy difficult despite indications. The results of the ASAP study indicate efficacy and safety of antiplatelet therapy in patients after LAA occlusion [23]. We did not observe any complications associated with the procedure or cerebrovascular events in any of the patients, either in the perioperative period or in the 16–31-month follow-up period. Follow-up TEE examinations at 3 and 6 months after LAA closure confirmed that the occluders were positioned correctly.

The yearly risk of stroke in our patients according to their CHA_2DS_2–VASc scores was 4–6.7%; at the same time, the patients were at a serious risk of bleeding (their average HAS BLED score was > 5).

Aspirin monotherapy is currently used in 8 of the patients (> 6 months after LAA occlusion). Due to cardiosurgical indications, we did not discontinue OAT in 1 individual. In our opinion, in the last case, removing a potential source of thrombus formation from the cardiovascular system was a beneficial effect of percutaneous closure of the LAA. In the remaining patients, percutaneous closure of the LAA made it possible to modify their therapies and reduce the risk of iatrogenic bleeding.

An ever-increasing number of patients undergoing LAA closure in the prevention of cerebral stroke allows us to gain experience, not only in terms of patient qualification but also management strategy. According to current guidelines, interventional percutaneous occlusion/closure of the LAA has a role in patients with thromboembolic risk, who cannot be managed in the long term using any form of OAT [24]. Results of the latest Gafoor *et al.* study have demonstrated the feasibility and efficacy of LAA closure devices also in the very elderly with AF [21].

Because patients in whom percutaneous closure of the LAA are considered to belong to groups with other numerous co-morbidities, their appropriate qualification and performance concerning the procedure requires close collaboration between a neurologist and a cardiologist who can deal with this problem.

Conclusions

Percutaneous closure of the LAA can be an alternative form of secondary prevention of stroke in patients with AF and contraindications for long-term anticoagulant therapy or those who have problems managing drug treatment. Complex clinical assessment performed by a neuro-cardiac team allow for safe and efficient invasive treatment.

Conflict of interest

The authors declare no conflict of interest.

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