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Prevention of adverse ischemic events with Watchman device in non-valvular patients with atrial fibrillation and contraindications for long-term anticoagulation therapy

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Abstract

Aims. To evaluate efficacy and safety of endovascular occlusion of left atrial appendage (LAA) with Watchman device in patients, contraindicated for long-term anticoagulant therapy

Methods and Results. Watchman device implantation performed in 37 patients with non-valvular AF, CHA2DS2VASc score >2 (mean 4.73±1.15), HAS-BLED>3 (mean 3.84±0.76), with contraindications for long-term anticoagulation therapy, with > 6 months follow-up period. Technical success was achieved in 94.6% (35 patients). Periprocedural complications were device embolization in 1 patient and pericardial effusion, requiring treatment. During 14.8±6.7 months follow-up neither haemorrhagic/ischemic stokes or TIA were observed.

Conclusion. The LAA occlusion with Watchman device can be safely performed in selected patients with contraindications to oral anticoagulation (OAC).

Key words: Atrial fibrillation, Left atrial appendage closure, Watchman device.

Abbreviations

AF = atrial fibrillation;
LAA = left atrial appendage;
TEE = transesophageal echocardiography;
OAC = oral anticoagulation;
PCI = percutaneous coronary intervention

Introduction

Atrial Fibrillation (AF) is the most common rhythm disorder with clinical symptoms and the number of affected patients enlarges every year[1]. Ischemic events are the most dangerous complications of AF, neurological disorders and deficits are more severe than those outcoming from non-AF stroke[2], and ischemic stroke associated with AF are nearly twice as likely to be fatal as non-AF stroke[3].

Anticoagulation therapy is recommended to all AF patients with high individual risk of ischemic complications, also in the case of successful cardioversion. Major bleeding is a serious complication in patients undergoing anticoagulant therapy, more frequent for elderly people[4]. 10% of AF patients have contraindications for anticoagulation therapy because of the high risk of bleeding[5] and optimal therapeutic range of the anticoagulant therapy is achieved only in 50% of the patients[6]. Endovascular occlusion of LAA, as the main place of life threatening thrombus formation during non-valvular AF, is an alternative, save and effective method of thromboembolic events prophylactic in patients, contraindicated for anticoagulation therapy.

In the article we present our experience in LAA occlusion with Watchman device for the patients with non-valvular AF and contraindications for life-long anticoagulation therapy.

Methods

In Krasnoyarsk Regional Clinical hospital 59 patients with AF and with high individual risk of stroke (CHA2DS2VASc>2) and high risk of bleeding complications (HAS-BLED>3) were examined as a candidates for LAA occlusion with Watchman device. All patients had contraindications for long-term anticoagulant therapy. TEE echo was performed in all cases to exclude LA or LAA thrombus, to evaluate LAA and intraatrial septum anatomy. In 1 patient there was a need for computed tomography, for precise evaluation of LAA anatomy. In 5 cases implantation of Watchman device was not possible due to anatomical characteristics. 2 patients had LAA consisted from 2 big lobes, in 1 patient LAA ostium

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was 32 mm and in 1 patient maximal LAA diameter was 15 mm. For available Watchman modification LAA should have a diameter from 16 to 32 mm, with an appropriate depth.

Implantation was not possible in 1 female patient hypersthenic type (BMI 31), because of absence of visualisation in supine position, although in standard TEE LAA was visualized in 0^0, 90^0 and 135^0.

Eventually 54 patients were scheduled for the LAA closure procedure. We perform the analysis of 37 patients, with >6 months follow-up period.

In our clinic we perform the procedure under general anaesthesia, with TEE and fluoroscopic control. In the case of presence persistent foramen ovale or atrial septal defect it was used for septal crossing, without septal puncture. Implantation was considered successful, if Watchman device was implanted to LAA with total exclusion of LAA from blood circulation and absence of significant residual flow around device. All adverse events during procedure, hospitalisation and follow-up period were registered.

If the patient was on warfarin before the procedure, it was cancelled 4 days before the implantation with transmission on LMH. If the patient was on clopidogrel, it was not cancelled. In the case of absence of anticoagulant or antithrombotic treatment, loading dose of clopidogrel was administered on the day of procedure, after implantation and control TTE in the evening time, with transmission to 75 mg of clopidogrel next day. On the day of procedure heparin was administered intravenously in a weight dose 100 U/kg after transseptal puncture or crossing to LA, to achieve recommended activated clotted time (ACT) 200-300 seconds. Every 30 minutes ACT control was performed, if it was less then 200 seconds additional boluses of intravenous heparin were administrated. Further anticoagulation regime was administrated individually for each patient, according to recommended protocols, eligibility or contraindications for treatment, possibility of INR checking. TTE was performed 6-12 hours after the procedure and before patient's discharge.

After device implantation, patients were followed up at 3, 6, 12 months and once a year after 12th months by phone call. In the case of necessity hospital visit was administrated. Control TEE was performed at 6-8 weeks after the implantation, 6 months and in selected cases 12 months after the procedure to assess device position, residual peri-device flow and device-related thrombus. After total endothelisation, absence of thrombus and peri-device flow warfarin/clopidogrel was cancelled, while aspirin treatment stayed life-long.

Results

The mean age of patients was 65.0±7 years, 20 from 37 (54%) were females (Table 1). Attempt to implant Watchman device was performed in 37 patients. In 35 cases procedure was successful (Table 2). In one case Watchman device was not implanted due to anatomical characteristics (multi lobes anatomy, not possible to precise evaluation by TEE). One case of device embolization occurred. Mean CHA_2DS_2VASc score was 4.73±1.15, so the risk of stroke in analysed group was very high. 70.3% of patients had stroke previously; 18.9% had TIA; 5,4% had systemic thromboembolism (thromboembolism of brachial artery, with surgical intervention). More than half of these patients with adverse thromboembolic events took warfarin, with adequate INR level 2-3 with 60-80% therapeutic range.

Serious device and procedure related events occurred in 2 cases (5.4%). In one case device embolization was observed, after device releasing from delivery system, in spite of satisfactory compression on TEE, and tug-test both on TEE and angiogram. Watchman device migrated to LV, where it fixed in posterior mitral leaflet chords. Patient was send to surgery. Device was retrieved and MACE procedure was performed. 2 weeks after patient was discharged from hospital in sinus rhythm with low dose of antiarrhythmic drugs. In a second case, LA perforation with delivery system hap-

Table 1. Clinical characteristics, stroke and bleeding risks.

Characteristic	Value
Age, years + SD	65.0±7
Female, n (%)	20 (54)
BMI (kg/m2)	26 (23-29)
AF type: Paroxysmal AF, n (%) Persistent AF, n (%)	 12 (32.4) 25 (67.6)
Arterial hypertension, n (%)	37 (100)
Diabetes mellitus, n (%)	3 (8.1)
Thromboembolic event, n (%): Stroke TIA Peripheral thromboembolism	 26 (70.3) 7 (18.9) 2 (5.4)
Coronary arteries disease, n (%)	12 (32.4)
Vascular disease, n (%)	5 (13.5)
Heart Failure (NYHA III – IV), n (%)	5 (13.5)
Bleeding events, n (%)	2 (5.4)
Labile INR, n (%)	18 (48.5)
CHA2DS2VASc score, ±SD CHA2DS2VASc score, n (%) 2 3 4 5 6 7 8 9	4.73±1.15 1 (2.7) 4 (10.8) 16 (43.2) 5 (13.5) 7 (18.9) 3 (8.1) 0 1 (2.7)
HAS-BLED score, ±SD	3.84±0.76
Antithrombotic/anticoagulant drugs, n (%) none aspirin aspirin+clopidogrel warfarin NOAC	 4 (10.8) 9 (24.3) 3 (8.1) 17 (45.9) 4 (10.8)
EF, % ±SD	58±2.16

Table 2. Procedure characteristics, device-related adverse events and outcomes.

Characteristic	Value
Time of the procedure, ±SD, min	51±26
Technical success, n (%)	35 (94.6)
Implant failure, n (%)	1 (2.7)
Air embolization, n (%)	0
Device embolization, n (%)	1 (2.7)
Pericardial effusion, n (%)	1 (2.7)
Stroke/TIA, n (%)	0
All cause death	0
Femoral hematoma/bleeding	0
Femoral pseudoaneurism	0

pened, operator made a decision to finish implantation of 33 mm Watchman occluder. Pericardial centesis was performed, 400 cc of blood was evacuated. Two days after patient was transferred from ICU to cardiology department, discharged 7 days after without complains.

All patients, that underwent implantation procedure where available for follow up. TEE was performed 6-8 weeks after the procedure and in 6 months. In 1 case residual flow (3 mm) persisted after 7 weeks from implantation, 6 months later residual flow was not observed (Figure 1). No cases of device embolization or thrombosis in post-operative period were observed.

Annual ischemic stroke rate was expected to be 6.1%, based on CHA_2DS_2VASc score between patients in

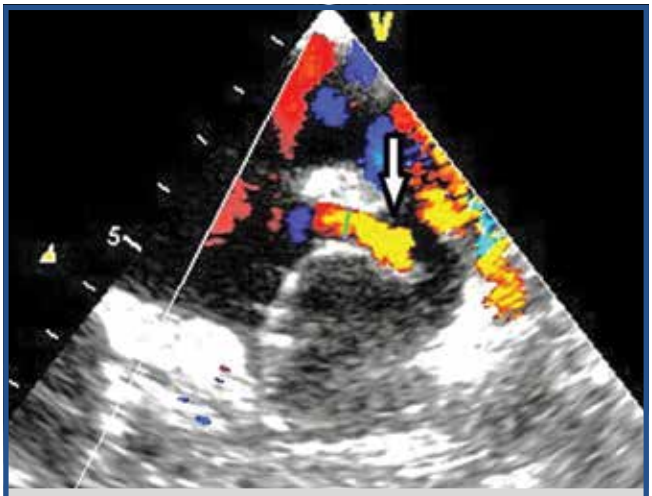

Figure 1. Persistent residual flow around Watchman device, 3 mm.

analyzed group. During 14.8±6.7 months follow-up period none of haemorrhagic/ischemic stokes or TIA were observed. During long-term follow up period 5 patients overcame open surgery, 2 patients now get combined treatment of oncological process (laringeal cancer, gastric cancer) The procedure of LAA closure, performed timely, dramatically decreased possible adverse thromboembolic events between these patients.

Discussion

In a group of the patients with non valvular AF, life-threating thrombus, causing stroke/TIA or systemic thromboembolism are formed in LAA in 90% of the cases[7]. Anticoagulant treatment is necessary for ischemic events prophylactic, but bleeding complications reduce frequency of admission of these treatment. Endovascular methods of LAA occlusion, as the main place of thrombus formation, got their fast development as a prophylactic method, with potentially lower risk of bleedings development.

Several devices for LAA occlusion are aloud to use in clinical practice. In Krasnoyarsk Regional Hospital we implant "Watchman LAA occlusion device" (Boston Scientific, USA), as the most examined, with efficacy, proved in several big randomised studies.

PROTECT-AF study, the only available randomized study, proved the efficacy of Watchman device, by demonstrating the noninferiority of the device-based prophylactic against standard anticoagulant therapy with warfarin. In additional safety end-points more adverse events were fixed in patients, undergoing device implantation – 5.5%[8]. In our clinical practice device-related safety events were observed in the same level – 5.4% (one device embolization with a need for surgical operation and one pericardial effusion due to LAA perforation). Significant decline in device/procedure related events with operator's experience was shown in CAP Registry (nonrandomized registry of patients undergoing Watchman implantation[9].

In an ESC Guidelines for the management of atrial fibrillation 2012, LAA percutaneous closure in patients with high stroke risk and contraindications for long-term oral anticoagulation has IIb class of recommendations and B level of evidence[10]. In ESC/EACTS Guidelines on myocardial revascularization 2014 percutaneous LAA closure and antiplatelet therapy is also recommended as a possible strategy in the patients with AF undergoing PCI in a case of high stroke risk and contraindications for long-term combined antiplatelet and anticoagulation therapy (Class IIb, Level of Evidence B)[11]. (Figure 2 a,b,c). In AHA/ASA Guidelines for the Primary Prevention of Stroke 2014 for the same group of patients it is recommended to perform LAA occlusion in a centre with low rates of periprocedual complications, and added that patient should tolerate the risk of at least 45 days of postprocedual anticoagulation (Class IIb; Level of Evidence B)[12].

Data of 4-year follow-up of the PROTECT-AF study have demonstrated statistically significant all-cause death reduction in the Watchman group compared to the control group due to reduction of the haemorrhagic strokes (0.4% vs 2.9% in a patients on warfarin, $p<0.001$)[13].

Based on this results, in October 2014 the Food and Drug Administration Circulatory System Devices Panel of the Medical Devices Advisory Committee voted in favor of the Device. By a vote of 6 to 5 (with 1 abstention) the Panel concluded that the benefits of the WATCHMAN Device outweigh the potential risks and that there is reasonable assurance that the Device is safe (12 Yes to 0 No). But on the question of reasonable assurance

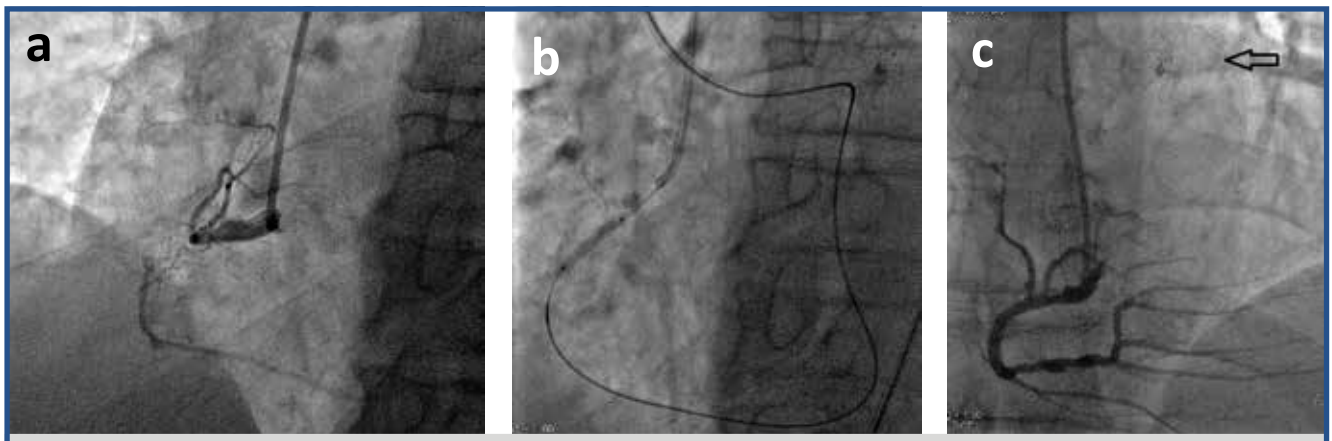

Figure 2. (a,b,c). Implanted Watchman device in patient with CTO of RCA, with retrograde recanalisation.
a – CTO of RCA in mid/3; b – balloon angioplasty after retrograde recanalisation; c – recanalised RCA+Watchman 24 mm device.

of effectiveness, the Panel vote was unfavorable (6 Yes to 7 No). It should be mentioned, that the vote was about using the device for the group of the patients, without contraindications for anticoagulant warfarin therapy. Probably, if a patients with contraindications for anticoagulant therapy and high risk of bleeding complications were discussed, the results of the vote could be different.

Finally, the WATCHMAN Device received U.S. Food and Drug Administration (FDA) approval on Friday, March 13, 2015. Now in the USA the WATCHMAN™ LAA Closure Technology is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who: are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores and are recommended for anticoagulation therapy; are deemed by their physicians to be suitable for warfarin; and have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.

The decision about method of ischemic events prophylactic for the patients with non-valvular AF should be taken individually for each patient, after precise analysis of potential risks of medicament strategies and innovative endovascular technologies, basing on available data and guidelines.

References

1. Fuster V, Rydén LE, Wann LS, et al. 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011;57:e101–e198.
2. Anderson DC, Kappelle LJ, Eliasziw M, et al. Occurrence of hemispheric and retinal ischemia in atrial fibrillation compared with carotid stenosis. Stroke 2002; 33:1963.
3. Lin HJ, et al. Stroke severity in atrial fibrillation: the Framingham study. Stroke 1996;27:1760-4.
4. Hylek EM, Evans-Molina C, Shea C, Henault LE, Regan S. Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. Circulation. 2007;115:2689-96.
5. Wysowski DK, Nourjah P, Swartz L. Bleeding complications with warfarin use: a prevalent adverse effect resulting in regulatory action. Arch Intern Med 2007;167:1414–9.
6. Glader EL, Sjolander M, Eriksson M, Lundberg M. Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke. Stroke. 2010;41:397-401.
7. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. Ann Thorac Surg. 1996;61:755-9.
8. Holmes DR, Reddy VY, Turi ZG, Doshi SK, Sievert H, Buchbinder M, Mullin CM, Sick P; PROTECT AF Investigators. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet. 2009;374:534-42.
9. Reddy VY, Holmes D, Kar S, et al. Safety of percutaneous left atrial appendage closure: results from the WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with AF (PROTECT AF) clinical trial and the Continued Access Registry. Circulation 2011;123:417–424.
10. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. European Heart Journal (2012) 33, 2719–2747.
11. 2014 ESC/EACTS Guidelines on myocardial revascularization. European Journal of Cardio-Thoracic Surgery 46 (2014) 517–592.
12. Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, Creager MA, Eckel RH, Elkind MSV, Fornage M, Goldstein LB, Greenberg SM, Horvath SE, Iadecola C, Jauch EC, Moore WS, Wilson JA; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, and Council on Hypertension. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association [published online ahead of print October 29, 2014.
13. Alli O, Doshi S, Kar S, Reddy V, Sievert H, Mullin C, Swarup V, Whisenant B, Holmes D Jr. Quality of life assessment in the randomized PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) trial of patients at risk for stroke with nonvalvular atrial fibrillation. J Am Coll Cardiol. 2013;61:1790-8.