



Left atrial appendage closure with Watchman device in prevention of thromboembolic complications in patients with atrial fibrillation: First experience in Serbia

Zatvaranje aurikule leve pretkomore Watchman uređajem u prevenciji tromboembolijskih komplikacija kod bolesnika sa atrijalnom fibrilacijom: Prva iskustva u Srbiji

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Abstract

Introduction. Atrial fibrillation (AF) is the major cause of stroke, particularly in older patients over 75 years of age. European Society of Cardiology guidelines recommend chronic anticoagulation therapy in patients with atrial fibrillation if CHA₂DS₂-VASc score is ≥ 1 [CHA₂DS₂-VASc score for estimating the risk of stroke in patients with non-rheumatic AF consisting of the first letters of patients condition: C – congestive heart failure; H – hypertension; A₂ – age ≥ 75 years; D – diabetes mellitus; S₂ – prior stroke, transitory ischaemic attack (TIA) or thrombolism; V – vascular disease; A – age 65–74 years; Sc – sex category]. However, a significant number of patients have a high bleeding risk, or are contraindicated for chronic oral anticoagulation, and present a group of patients in whom alternative treatment options for thromboembolic prevention are

required. Transcatheter percutaneous left atrial appendage closure (LAAC) devices have been recommended in patients with contraindications for chronic anticoagulant therapy. **Case report.** We present our first three patients with nonvalvular AF and contraindications for chronic anticoagulant therapy who were successfully treated with implantation of LAAC Watchman device in Catheterization Laboratory of the Clinic for Cardiology, Clinical Center of Serbia in Belgrade. **Conclusion.** Our initial results with Watchman LAAC device are promising and encouraging, providing real alternative in patients with non-valvular AF and contraindication for chronic anticoagulant therapy and high bleeding risk.

Key words:

atrial fibrillation; cerebrovascular disorders; risk assessment; therapeutic occlusion; heart atria.

Apstrakt

Uvod. Atrijalna fibrilacija (AF) je glavni uzrok moždanog udara, posebno kod starijih bolesnika preko 75 godina. Preporuke Evropskog udruženja kardiologa preporučuju hroničnu antikoagulantnu terapiju kod bolesnika sa atrijalnom fibrilacijom i CHA₂DS₂-VASc skorom ≥ 1 [CHA₂DS₂-VASc skor za procenu rizika od nastanka moždanog udara kod bolesnika sa ne-reumatskom AF koji se sastoji od početnih slova boles-

ti: C – kongestivna srčana slabost; H – hipertenzija; A₂ – starost preko 75 godina; D – dijabetes melitus; raniji moždani udari ili tranzitorni ishemijski atak (TIA) ili tromboembolizam; V – vaskularne bolesti; A – starost 65–74 godine; Sc – polj]. Međutim, značajan broj bolesnika ima visok rizik od krvarenja ili kontraindikacije za hroničnu antikoagulantnu terapiju, i predstavljaju bolesnike kod kojih su neophodni alternativni načini lečenja u prevenciji tromboembolijskih komplikacija. Transkatetersko perkutano zatvaranje aurikule leve pret-

komore (LAAC) putem posebnih zatvarača preporučuju se kod bolesnika sa kontraindikacijama za hroničnu antikoagulantnu terapiju. **Prikaz slučaja.** Predstavljamo naša prva 3 bolesnika sa ne-valvularnom AF i kontraindikacijama za hroničnu antikoagulantnu terapiju kod kojih su uspešno ugrađeni Watchman LAAC zatvarači u Sali za kateterizaciju Klinike za kardiologiju Kliničkog centra Srbije u Beogradu. **Zaključak.** Naši inicijalni rezultati sa Watchman LAAC zatvaračima su obećavajući i ohrabrujući, a predstavljaju pravu alternativu za

bolesnike sa ne-valvularnom AF i kontraindikacijom za primenu dugotrajne antikoagulantne terapije, odnosno za one kod kojih postoji visok rizik od krvarenja.

Ključne reči:

fibrilacija pretkomora; cerebrovaskularni poremećaji; rizik, procena; okluzija, terapijska; srce, pretkomora.

Introduction

Left atrial appendage closure (LAAC) by transcatheter technique has been developed to prevent thromboembolic complications in patients with nonvalvular atrial fibrillation (AF) who cannot tolerate chronic oral anticoagulant therapy^{1,2}. In fact, it has been demonstrated that LAAC device can be used as an alternative to chronic anticoagulant therapy for stroke prevention in patients with nonvalvular AF, but the primary indications for LAAC include the patients with contraindications to chronic anticoagulant therapy³.

In patients with nonvalvular AF, left atrial appendage is in vast majority of cases the origin of thrombi and thromboembolic complications with stroke being most devastating and life-threatening⁴. Oral anticoagulant therapy with vitamin K antagonists, have been used for years to prevent thromboembolic complications but still a number of patients are undertreated with large periods of time out of therapeutic range⁵. Newer oral anticoagulant drugs have demonstrated superiority in relation to vitamin K antagonists in regard to efficacy and less intracranial bleeding, but still a number of patients cannot tolerate these agents due to high bleeding risk or adverse effects⁶.

Several transcatheter LAAC devices have been developed, but only Watchman (Boston Scientific, USA) has demonstrated long-term superiority over warfarin in two large randomized clinical trials, PROTECT AF and PREVAIL⁷⁻¹⁰. Thus, here we present our first three patients with nonvalvular AF and contraindications for chronic anticoagulant therapy who were treated with implantation of Watchman device in Catheterization Laboratory of the Clinic for Cardiology, Clinical Center of Serbia, Belgrade.

Case report

Study population

Implantation of Watchman LAAC device was performed between March 2014 and April 2015 in three patients with nonvalvular AF and contraindications for chronic anticoagulant therapy or high bleeding risk¹¹. The patients were considered for LAAC if noninvasive and invasive cardiologists concluded that they were not candidates for chronic anticoagulant therapy. All patients were informed about the risks and benefits of the procedure and provided informed consent for LAAC. All procedures were performed with the guidance of the experienced proctors for LAAC (MG and AVP).

Pre-procedure screening

Pre-procedure screening included detailed clinical examination, 2D echocardiographic and transesophageal echocardiographic (TEE) examination. Baseline TEE was required to exclude existing thrombus, to evaluate feasibility of the intervention and the morphology of the appendage ("WindSock type", "Chicken Wing type", or "Broccoli type") (Figure 1). Accurate TEE measurements in several planes (at 0°, 45°, 90°, 135°) (Figure 2) were important to determine dimensions of left atrial appendage (LAA) ostium and depth of the appendage¹². The sizing of the Watchman device is based on largest ostium diameter which should be in the range of available device diameter, with certain (up to 20–25%) recommended oversizing. The maximum LAA ostium size should be > 17 mm or < 31 mm to accommodate available Watchman device sizes.

Watchman device

Watchman LAAC device (Figure 3) consists of self-expanding nitinol frame covered with permeable (160 microns) polyethylene terephthalate (PET) membrane, with 10 anchors on the nitinol frame designed to fix and stabilize appendage tissue with device nitinol frame^{8,9}. They are manufactured in 5 sizes (21, 24, 27, 30 and 33 mm) that are delivered through 14F sheath inserted in the femoral vein. In most of the cases, double-curve sheath is used for implantation of the device. The Watchman device has CE and FDA marks.

Implantation procedure

All three patients were premedicated with aspirin 100 mg, clopidogrel 75 mg, and the left atrial appendage was one day before procedure checked for the presence of left atrial thrombus by TEE. In case of the presence of left atrial thrombus, the patient received anticoagulation for at least 15 days, and then again the left atrium was re-evaluated by TEE.

The procedure was performed in catheterization laboratory under general anesthesia and TEE monitoring, with pure percutaneous approach from right femoral vein. After insertion of 8F sheath into right femoral vein, transseptal puncture with Brocken-brough needle and insertion of transseptal sheath were performed. Transseptal puncture was performed with TEE guidance in the middle lower part of interatrial septum, using TEE bicaval view and aortic short axis view. At this time point, unfractionated heparin dose of

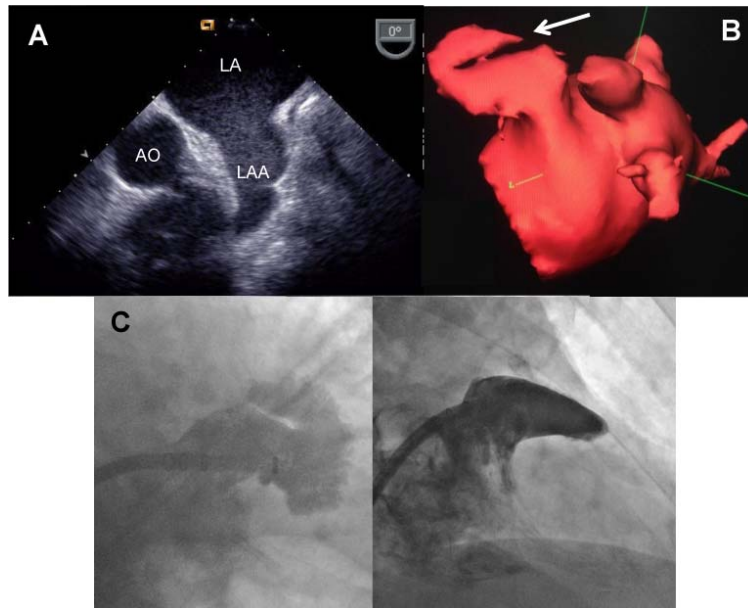


Fig. 1 – The "Chicken Wing" left atrial appendage morphology. Imaging modalities such as (A) transesophageal echocardiography, (B) computed tomography or (C) contrast angiography can be used to determine the shape of the left atrial appendage (arrow) to help planning device placement. AO - aorta; LA - left atrium; LAA - left atrial appendage.

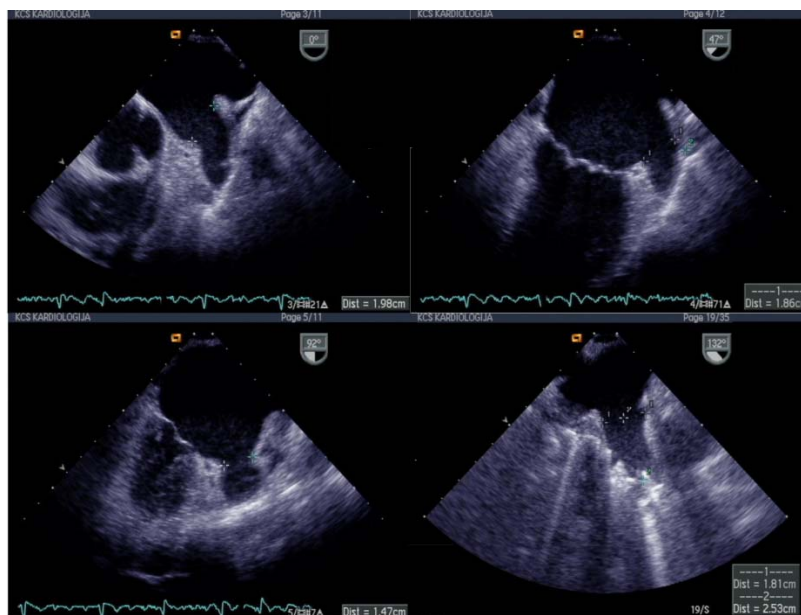


Fig. 2 – Transesophageal echocardiography measurements in several planes (at 0°, 47°, 92°, 132°) are important to determine maximal ostial diameter and depth of the left atrial appendage.



Fig. 3 – Watchman: Left atrial appendage closure device is a nitinol cage with a polytetrafluoroethylene membrane on the surface, and fixation anchors around the perimeter (Courtesy of Boston Scientific).

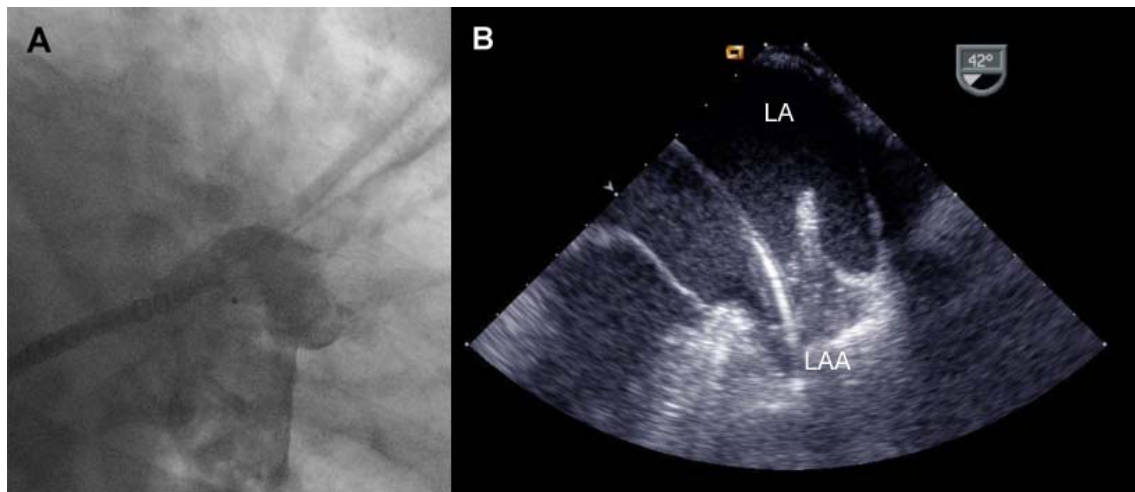
100 units/kg body weight was administered to reach activated clotting time of at least 250 seconds which was repeated every 30 min.

After transseptal puncture, super stiff J-tip guide wire 0,035" was positioned into the upper left pulmonary vein, and the device sheath was introduced into the left atrium. Then, pigtail catheter was introduced and positioned in the LAA for angiography performed in several views (right anterior oblique with caudal and cranial angulations) for LAA shape visualization and measurement. At the same time, once again TEE measurements of LAA orifice and depth were rechecked, and optimal device size was selected.

The 14F double curved sheath was advanced over pigtail catheter into LAA dominant lobe and positioned at the LAA orifice. Then, pigtail catheter was removed and the device preloaded into 12F delivery system was advanced and aligned with 14F sheath positioned at the orifice. Once the sheath was slightly retracted from the orifice, with the delivery system stable positioned at the orifice, the whole delivery system and 14F

sheath was withdrawn to expose Watchman device to adapt to LAA (Figure 4). The device was ready for the release when following criteria were met: position (device distal or at ostium with less than 40–50% of device depth protrusion of the shoulders), anchor stability (return to original position when retracting); size (device shoulder compressed up to 20% of original size by TEE); seal (residual flow less than 5 mm by TEE). When all these criteria were met, the device could be released by counterclockwise rotation. The position was finally checked by angiography (Figure 5) and TEE images (Figure 6) for residual seal and position.

One day after the procedure, TEE was repeated for the position of the device and the presence of pericardial effusion, and if absent the patients were discharged on oral anticoagulant therapy and aspirin for the next 45 days. If on repeated TEE after 45 days there was successful sealing around the device (complete or less than 5 mm residual flow) the patient was given clopidogrel for the next 6 months and aspirin indefinitely.



**Fig. 4 – Angiography (A) and transesophageal echocardiography (B) images showing the final position of the Watchman device before device release.
LA - left atrium; LAA - left atrial appendage.**

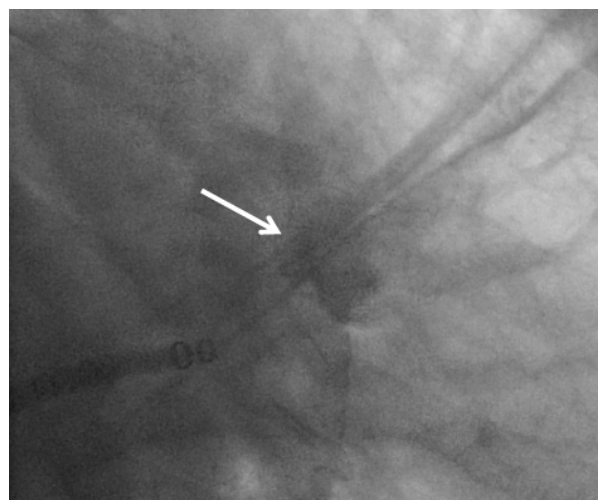


Fig. 5 – Angiography showing the final position of the Watchman device (arrow) after device release without residual peridevice shunt.

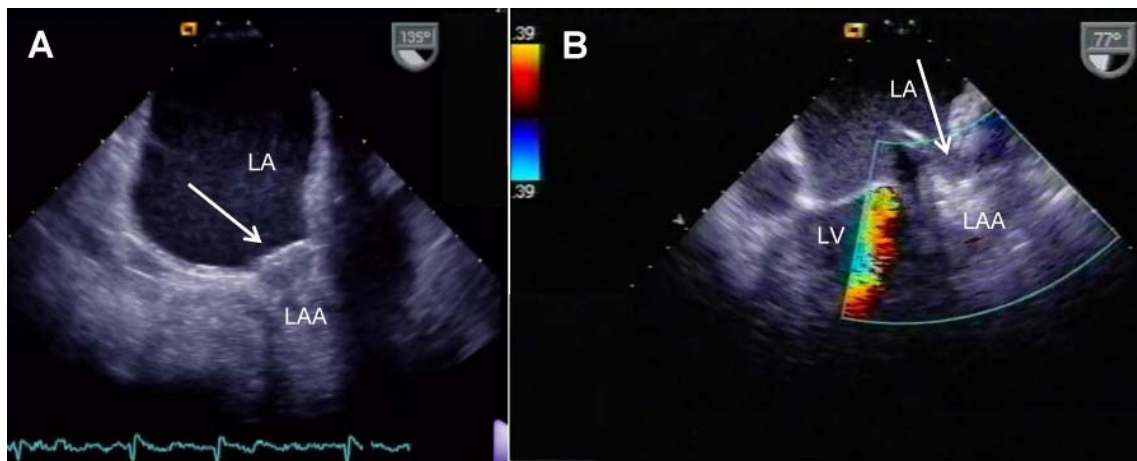


Fig. 6 – A) Transesophageal echocardiography showing the final position of the Watchman device (arrow); B) – Color Doppler echocardiography image showing the absence of residual shunt within the left atrial appendage.

LA – left atrium; LAA - left atrial appendage; LV – left ventricle.

Case 1

A 59 male patient was admitted to our hospital with a history of frequent episodes of paroxysmal AF for the implantation of LAA occluder. He had a moderately diminished renal function (stage 3A), well controlled arterial hypertension and prior history of two transient ischemic attacks (in January 2002 and in February 2014) even though he was on warfarin and later on dabigatran anticoagulant therapy. The patient also had at the end of 2013 and at the beginning of 2014 duodenal ulcer perforation which was conservatively treated. Thus, due to prior stroke despite anticoagulant therapy and high bleeding risk HAS-BLED score 4) [H – hypertension; A – abnormal renal and liver function; S – stroke; B – bleeding; L – labile INRs (International normalized ratio) D – drugs or alcohol], this patient was referred to implantation LAAC in order to prevent further thromboembolic complication of AF. He denied chest

discomfort during physical activity but he had palpitations and dyspnea on effort. On transthoracic echocardiography (TTE), left ventricular (LV) dimensions were normal, end-diastolic dimension (EDD) was 50 mm, and end-systolic dimension (ESD) 38 mm with preserved ejection fraction (EF), 67%. Left atrium (LA) was enlarged, 52 mm (volume 85 mL). Prior to the intervention on TEE, the presence of thrombus in LAA was excluded and maximum measured ostial dimension of LAA was 21 mm. Watchman LAA occluder size 24 mm was implanted in March 2014. Even though at the end of the procedure we found on TEE the residual jet leak measured about 5.3 mm (Figure 7A), angiographically we found only mild leak – dye filling of one-third of the LAA (Figure 7B). We decided to stop the procedure since the angiographic result was acceptable. As a result of the residual leakage due to probably smaller device size, the patient was left on anticoagulant therapy including dabigatran.

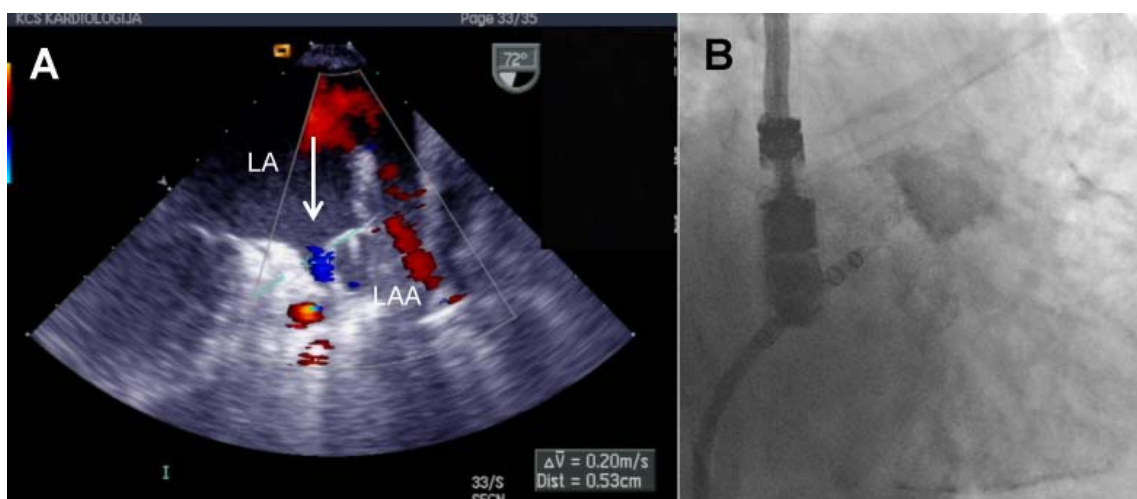


Fig. 7 – A) Color Doppler echocardiography image showing residual peridevice shunt within the left atrial appendage (arrow); B) Angiography showing mild leak – dye filling one-third of the left atrial appendage.

LA – left atrium; LAA – left atrial appendage.

Case 2

A 53 years old male patient with a prior history of permanent AF, kidney transplantations (1989 and 2003) due to terminal renal insufficiency and with chronic hepatitis B was referred to our hospital. He knew for the AF since 2013, and was unsuccessfully medically converted to the sinus rhythm both with amiodarone due to the rise of the liver enzymes and with propafenone therapy. Thus 2013, he was on the heart rate control therapy with beta blockers and on warfarin therapy. Also, because of chronic hepatitis B and moderately elevated liver enzymes, he was on antiviral therapy. Due to kidney transplant he was on immunosuppressive therapy. He denied chest pain at rest and during physical activity, palpitations or dyspnea on effort. He had also well controlled arterial hypertension. Because of the need of chronic anticoagulant therapy and high risk of bleeding due to his comorbidities (HAS-BLED score 3) he was referred to the percutaneous device closure of the LAA. Prior to the intervention, TTE and TEE were done. On TTE, LV dimensions were normal (EDD 47 mm, ESD 37 mm with preserved EF, 55%). LA was enlarged, 50 mm (volume 80 mL), with spontaneous echo contrast, but without thrombotic masses in LA. On TEE, prior to the LAAC, the presence of thrombus in LAA was excluded and the maximal dimension of LAA ostium was 23 mm. Initially, Watchman device 24 mm was selected and positioned, but due to high peridevice leak it was not released, but retracted and replaced for bigger device size 27 mm which was successfully implanted with good device deployment, very mild peridevice leak of up to 2 mm and angiographically only the trace of the dye in the LAA. After 45 days, TEE showed residual peridevice leak of up to 4mm, without thrombotic formations but because of spontaneous echo contrast in LA we decided to continue with anticoagulant therapy.

Case 3

A 53 years old male patient with a permanent AF was admitted to our hospital. He had a prior history of paroxysmal AF from 2006, with several unsuccessful cardioversions to the sinus rhythm, and since 2006 he was on warfarin. He had also well controlled hypertension and smoking habit. In July 2013, he suffered hemorrhagic stroke. He denied chest discomfort during physical activity but he had palpitations and dyspnea on effort. The decision to implant Watchman device was based on previous hemorrhagic stroke and consequently high bleeding risk (HAS-BLED score was 3) on anticoagulant therapy. Prior to the implantation of device TTE showed enlarged LV: EDD 58 mm and ESD 44 mm with slightly reduced EF 45%, without wall motion abnormalities. LA was enlarged 55 mm (volume 103 mL), with spontaneous echo contrast, but without thrombotic masses. On TEE precise measurements (maximal ostial LAA dimension of 26 mm), anatomy (lobularity and shape) and potential presence of thrombus in LAA were assessed. Next day, the implantation of Watchman device, size 30 mm, was successfully done with TEE periprocedure guidance. At the end of the procedure TEE showed good device deployment,

stability, no interference with surrounding structures and peridevice leak. Also after 45 days, TEE showed excellent device sealing of the LAA, without any peridevice leakage. Therefore, only antiplatelet therapy including clopidogrel for the next 6 months and aspirin indefinitely was continued.

Discussion

Our initial results with Watchman LAAC device in patients with non-valvular AF are promising and confirm previous experience and data⁸⁻¹¹. The technique appeared to be effective and safe in preventing thromboembolic complications in high risk patients.

AF is not only the major cause of stroke, particularly in older patients over 75 years, but also those strokes generating from AF are clinically more severe and disabling¹³. Thus, prevention of strokes in patients with AF is cornerstone of treatment and the European Society of Cardiology (ESC) guidelines recommend chronic anticoagulation if CHA₂DS₂-VASc [congestive heart failure, hypertension, age \geq 75 years, age 65–74 years, diabetes mellitus, stroke/transient ischemic attack/thromboembolism, vascular disease, sex (female)] are \geq 1³. However, a significant number of patients have a high bleeding risk, or are contraindicated for chronic oral anticoagulation, and represent a group of patients who required the alternative treatment options. In addition, although the rate of intracranial bleeding is less with novel anticoagulant (NOAC) drugs, the overall risk of bleeding is not significantly lower with rivaroxaban and dabigatran in comparison to warfarin^{14,15}. Other concerns and contraindications for oral anticoagulant therapy include renal and liver dysfunction, noncompliance and discontinuation (even more with NOAC), low adequate therapeutic range with warfarin, as well as interaction with food and drugs¹.

LAAC device technology has evolved significantly over last 15 years, with several devices being under clinical investigation⁷⁻¹¹. Out of few of them, Watchman device has demonstrated most relevant clinical results confirmed in 2 large randomized trials. First, the PROTECT AF study^{8,9} included 707 patients with CHA₂DS₂ \geq 1, randomized to device therapy and warfarin. Watchman was successfully implanted in 91% of the patients. The primary outcome was similar for Watchman and warfarin, with Watchman having more procedure adverse events and bleeding. However, after 45 months the primary efficacy endpoint was lower with the Watchman, as well as hemorrhagic stroke, cardiovascular death and overall mortality^{8,9}. In the second study, PREVAIL¹⁰ 407 patients were randomized to Watchman and warfarin, and successful implantation of the device increased to 95%. In addition, procedure time was significantly reduced, and there was also a decline in procedure-related adverse events. Even though recent meta analysis of the 2 randomized clinical trials and 2 nonrandomized registries demonstrated all-cause stroke rates similar between the device and warfarin group, pathophysiology of stroke was significantly different - more device patients experienced ischemic strokes, while more warfarin patients experienced hemorrhagic strokes¹⁶. Higher ischemic strokes rates might be explained

either by development of thrombus on the device or to the failure to completely obliterate LAA flow and as a result to have residual leak that might have embolic potential^{8, 9, 15}. Also, according to the same meta analysis, patients randomized to the LAAC had significant improvement in survival (freedom from cerebrovascular death) and significantly less bleeding complications compared to the patients on warfarin therapy when periprocedural bleeding was excluded¹⁶.

Implantation of the Watchman device carries substantial upfront procedural risk mostly observed at the beginning of the learning curve and became less frequent with more experience. Pericardial effusion either as cardiac tamponade or as an asymptomatic effusion is one of the most serious complications in LAA-occlusion procedures⁸. Transseptal puncture, manipulation of the guiding catheters, stiff wires and even aggressive movement of device itself might result in LAA injury causing pericardial effusion¹⁷. In the PROTECT AF trial 5% of patients with pericardial effusion required drainage or surgery^{8, 17}. In the Continued Access Protocol (CAP) registry, where experienced operators implanted Watchman devices, the rate of pericardial effusions decreased to 2.2%¹⁷. During the LAA occlusion procedure ischemic stroke due to air or thromboemboli occurred in 0.9% in the PROTECT AF trial while none in the CAP registry¹⁷. Percutaneous closure of the LAA may be also complicated by immediate or late device embolization which occurred in 3 (0.6%) patients in the PROTECT AF trial and none in the

CAP registry, thus proper selection of patients with favorable LAA morphology and appropriate device sizing are crucial to prevent this very serious complication¹⁷.

In regard to indication for implantation of LAAC devices, ESC has recently issued guidelines stating that LAAC device may be considered in patients with high bleeding risk and contraindications for long-term oral anticoagulant therapy, but also in patients with previous stenting and prolonged need for triple antithrombotic and anticoagulant therapy, previous stroke on warfarin, labile and poorly regulated INR and severe renal and hepatic diseases that preclude chronic anticoagulant therapy^{3, 18}. Practically, in those, and most often older patients with co-morbidities a number of clinical situations can be anticipated where long-term oral anticoagulant therapy should be avoided.

Conclusion

Our initial results with Watchman LAAC device are promising and encouraging, providing real alternative in patients with non-valvular atrial fibrillation and contraindication for chronic anticoagulant therapy and high bleeding risk. This initial results in our Center need to be extended with consistent application and performance as this and other highly sophisticated procedures for percutaneous treatment of "structural and valvular" heart diseases, but require considerable experience and a learning curve.

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