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**“Analiza zastosowania zabiegów zamykania uszka lewego przedsionka jako metody
prewencji udarów mózgu u pacjentów z niezastawkowym migotaniem przedsionków.”**

**Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu
w dyscyplinie nauki medyczne.**

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SUMMARY

“Analysis of left atrial appendage closure procedures as a method of stroke prevention in patients with nonvalvular atrial fibrillation.”

Atrial fibrillation (AF) is the most common atrial tachyarrhythmia, and its prevalence increases with age. It is characterized by uncoordinated electrical activity of the atria, which causes loss of their contractile function. Atrial fibrillation is a major risk factor for thromboembolic events, regardless of whether it is paroxysmal, persistent or permanent. If left untreated, it is associated with a 5-fold increased risk of ischemic stroke.

Oral anticoagulation therapy is the default method for preventing thromboembolic events in patients with diagnosed AF. The 2024 European Society of Cardiology guidelines on atrial fibrillation replaced the previously used CHA₂DS₂-VASc score with the new CHA₂DS₂-VA score and recommends its use in all patients to stratify the risk of a thromboembolic event. It allows doctors to decide whether to initiate treatment with oral anticoagulants (OAC). In patients with 2 points or more, chronic anticoagulation therapy should be initiated (class of recommendation: I, level of evidence A), while in patients with 1 point, such therapy should be considered (class of recommendation: IIa, level of evidence C). The preferred treatment is the use of new oral anticoagulants (NOAC) instead of vitamin K antagonists (VKA) (class of recommendation: I, level of evidence A).

Among patients requiring OAC, there is a large group of patients in whom such treatment is contraindicated or ineffective. Contraindications to such treatment include a very high risk of bleeding or a history of serious bleeding, while therapy ineffectiveness is defined as appearance of thromboembolic event during appropriate anticoagulation treatment. Based on data from studies showing that over 90% of embolic material in patients with nonvalvular AF comes from the left atrial appendage (LAA), a procedure involving closure of the LAA was proposed. An effective procedure prevents the clot formation in the LAA and its

subsequent migration into the bloodstream. This approach appears to prevent embolic events while reducing the risk of bleeding associated with chronic OAC use. Currently, left atrial appendage closure (LAAC) is a non-pharmacological method for preventing thromboembolic events in patients with nonvalvular AF. The 2024 European Society of Cardiology Guidelines on Atrial Fibrillation indicate that LAAC may be considered in patients with contraindications to long-term OAC (class of recommendation: IIb, level of evidence C).

Left atrial appendage closure is an invasive procedure and is associated with complications such as ischemic stroke, major bleeding, tamponade, and vessel injury. In addition, successful occluder implantation is associated with the possibility of device-related thrombus (DRT) development, therefore post-procedural antithrombotic treatment is recommended. This approach is intended to reduce the risk of DRT. Initially, VKA was used after the procedure, however, due to the high risk of bleeding in the population undergoing the procedure, a search for alternative treatment methods began. The use of NOAC or antiplatelet drugs has been the subject of many clinical trials, which have shown that such treatment can be effective with a preserved safety profile. There are currently no clear recommendations for post-procedure pharmacotherapy. Randomized trials are underway and will help us standardize pharmacotherapy after a successful LAAC procedure, but until then, experts recommend individualizing the treatment.

The first study retrospectively analyzed 91 patients who underwent LAAC using the WATCHMAN device at a single academic center. The aim of the study was to evaluate the procedure, the periprocedural period, and the efficacy and safety of postprocedural antiplatelet therapy. The device was successfully implanted in 90 patients. Major bleeding with BARC (Bleeding Academic Research Consortium) scale > 3 occurred in 3 patients, tamponade in 3 patients, and 1 person died of cardiovascular causes. Additionally, 1 non-cardiovascular death occurred. After the procedure, until the follow-up transesophageal

echocardiography (TEE) examination, 85 patients received dual antiplatelet therapy consisting of acetylsalicylic acid and clopidogrel. The remaining 3 patients were discharged with a recommendation for single antiplatelet therapy with one of the above drugs. After a median of 67 days after the procedure, all patients underwent clinical evaluation, and follow-up TEE examination was performed in 78 subjects. The primary endpoint assessing the safety of the therapy, defined as major bleeding, occurred in 2 patients, none of whom required hospitalization or blood transfusion. However, the primary endpoints assessing the efficacy of the therapy occurred in 4 patients (1 ischemic stroke, 1 cardiovascular death, and 2 non-cardiovascular deaths). The control TEE examination did not reveal any significant peri-device leak (PDL), and a DRT was found on the device in 5 patients. The results of the study show that antiplatelet therapy after LAAC seems to be an effective and safe treatment option.

The aim of the second study was to assess the frequency of thrombus formation on the WATCHMAN device and to determine the predictors of its occurrence. The study group consisted of all patients who had a control TEE examination after successful implantation of the occluder. Device-related thrombus was found in 5 patients. Compared to the group of patients without DRT, patients with DRT were younger, had a lower left ventricular ejection fraction, a lower LAA emptying velocity, and had the device implanted deeper in the LAA. All patients with confirmed DRT received anticoagulation with low-molecular-weight heparin, achieving thrombus resolution without bleeding complications.

The last study presents a summary of the current knowledge on LAAC using the WATCHMAN device. The essence of the procedure, indications, and different versions of the occluder are discussed in detail. Possible forms of anticoagulation after successful LAAC are also presented. Complications of the procedure, such as DRT and PDL, were analyzed and methods of their treatment were discussed.

In summary, in the series of publications constituting the following dissertation, the developing LAAC method was analyzed, which is an alternative to OAC in patients with nonvalvular atrial fibrillation and contraindications to anticoagulation therapy. Based on the publications, it seems that antiplatelet therapy after LAAC is effective and safe in high-risk patients. Moreover, taking into account the risk factors for DRT, we are able to better individualize post-procedural treatment, minimizing the risk of DRT. The review paper discusses the most important aspects of the interventional method of stroke prevention and the data presented in this paper are a useful tool in everyday clinical practice.