EDITORIAL

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Left atrial appendage occlusion procedures

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Atrial fibrillation (AF) is the most common cardiac dysrhythmia encountered by cardiac surgeons in their practice. The incidence of AF rises with age from approximately 0.1% in adults younger than 55 to 9% in individuals older than 80. The routine performance of detailed examinations before cardiac surgery entails that, in most cases, AF patients are receiving treatment; however, there are still patients who remain undiagnosed and unaware of the disease due to the lack of symptoms [1–3].

Atrial fibrillation is associated with a manifold increase in the risk of ischemic stroke. It also significantly increases the incidence of serious conditions, such as congestive heart failure, premature death, or thromboembolic complications. Therefore, we should all strive to treat AF in our patients and prevent the occurrence of associated complications [4, 5].

The most common treatment for AF patients which can be employed by any physician is currently oral anticoagulation (OAC). The principles of OAC use in AF patients are discussed in detail in recommendations issued by scientific associations.

The guidelines of the European Society of Cardiology (ESC) recommend that all patients diagnosed with AF should be assessed with regard to the risk of thromboembolic complications using the CHA_2DS_2-VASc scale; patients with scores of 1 or more should undergo effective stroke prevention, mostly in the form of OAC, which necessitates the evaluation of its effectiveness and safety with regard to the risk of hemorrhagic complications. A relatively precise assessment of this risk can be accomplished by using the HAS-BLED scale.

Considering the numerous possible contraindications for OAC, medication intolerance, and potential complications during OAC, this type of prevention cannot be successfully employed in all AF patients, as the risk of complications often exceeds the potential benefits of OAC.

Physicians have always searched for new treatments for their patients, including those in whom the current therapies are unsuccessful or cannot be used for various reasons. One of the methods for safeguarding patients from complications caused by AF, including ischemic stroke, has led to the strategy of performing left atrial appendage (LAA) occlusion.

The LAA occlusion (LAAO) has been associated with cardiac surgery procedures from its very inception. Initially, the procedures consisted in suturing the LAA during mitral commissurotomy, later also during mitral valve plasty and replacement.

In accordance with the currently binding guidelines, LAAO should be considered in all patients at high risk of hemorrhagic complications with HAS-BLED scores of 3 or more.

The latest ESC guidelines also recommend performing LAAO in patients with high risk of stroke and contraindications for OAC; surgical LAAO can also be considered intraoperatively in all patients undergoing any cardiac procedures [6–8].

Initially, cardiac surgeons performed LAAO with regular lung staplers, loops, or sutures; however, some of the clinical studies analyzing such procedures have proved that the effectiveness of this type of management is very low, and LAA occurs very often. Some researchers state outright that these methods are completely ineffective and offer only a false sense of security.

The conducted meta-analyses show that the results of nearly all older surgical LAAO methods are unequivocal to say the least.

The most effective current surgical procedure for achieving LAAO is to cut off the LAA and suture the stump using a regular surgical suture.

The LAA amputation was a part of surgical left atrial ablation proposed by Dr James Cox. The results showed that, after 10 years, as many as 99% of patients did not suffer from ischemic stroke. Unfortunately, we do not know to what extent these good results can be attributed to LAAO in comparison to the restoration of sinus rhythm.

A number of questions related to all the currently used surgical LAAO procedures are expected to be answered by the recently started multicenter Left Atrial Appendage Occlusion Study III (LAAOS III). The enrollment is ongoing, and it is hoped that the outcomes will result in the formulation of recommendations important for our community.

The only fully effective surgical LAAO system is the AtriClip, based on a metal clip placed over the LAA [9]. It is very easy to use and guarantees very good results, which

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has made it the most popular medical product for surgical LAAO. In Poland, good results with this system have been achieved by Prof. Suwalski's center in Warsaw, Prof. Zembala's Silesian center, and Prof. Kapelak's center in Krakow.

Technological progress associated with the development of percutaneous methods has enabled the performance of some myocardial revascularization procedures without the need to open the chest. Percutaneous techniques have also recently begun to be used in endocardial LAAO procedures.

Devices dedicated for LAAO (such as WATCHMAN, AMPLATZER Cardiac Plug, and LARIAT), introduced through a catheter into the LAA or used externally, enable the safe exclusion of the LAA from the circulation and are widely used, including in Poland.

The first device for percutaneous LAAO was the PLAATO system. Despite its great commercial success, it has been discontinued and is no longer available.

Another device for LAAO is the Amplatzer Cardiac Plug (ACP). Its significant advantage is that, after being properly placed in the LAA, its disc completely seals off the interior of the LAA.

The Watchman device, like the ACP and PLAATO, is made of a nitinol mesh. It is currently the best studied system for LAAO, and a great number of clinical studies and registries prove its efficacy. The prospective randomized multicenter study PROTECT AF analyzed the device, providing reliable results and conclusions. The study proved that the efficacy of the Watchman device in preventing stroke is at least as high as warfarin therapy, whereas the associated risk of hemorrhagic complications is significantly lower.

This conclusion was groundbreaking for all those involved in LAAO procedures, as it proved that LAAO can be a valuable alternative to OAC in the prevention of ischemic stroke in AF patients with contraindications for OAC.

The present-day knowledge on the results of using the ACP and Watchman implants in humans is quite extensive and very well documented. Registry studies analyzing all systems based on LAAO implants are ongoing, and, hopefully, they will provide results that will enable a precise evaluation of the efficacy of these devices.

It remains puzzling why the manufacturers of both implant-based systems recommend postoperative OAC after LAAO also in patients with contraindications for OAC. The reason is likely to be related to effective healing and implant coverage, but can this justify exposing the patient to the risk of hemorrhagic episodes? It should also be noted that long-term complications from the use of endocardial implants (which include both the ACP and the Watchman devices) remain unknown.

Subsequent generations of percutaneous implant-based systems should significantly reduce the number of complications and improve the safety of implantation. One should keep in mind, however, that the long-term influence of endocardial implants on human health is yet to be studied.

Time will tell whether the future will bring a mass recall of endocardial implants, as is the case with endocardial electrodes, which were supposed to be absolutely safe.

Experiences gathered from surgical and percutaneous LAAO systems and thoracoscopic left atrial ablation as well as cooperation between researchers from the University of California and the company SentreHeart Inc. have enabled the development of the novel LARIAT system. The system has the advantages of implant-based systems, but without their drawbacks and limitations. It also draws on the advantages of surgical systems without inheriting their limitations in the form of postoperative recanalization or the need for opening the chest. Its use is completely percutaneous [10, 11].

The LARIAT system is not a nitinol implant like the abovementioned ACP and Watchman devices, but rather it uses a simple loop from a traditional insoluble surgical suture. The loop is placed on the LAA externally and is very effective in excluding the LAA from blood circulation.

The system was initially used in vitro in order to ensure its proper functioning; the many subsequent tests in animal models demonstrated its safety and efficacy. The results of these studies were published in prestigious journals including *Circulation: Cardiovascular Interventions* and *Heart Rhythm*. Our center actively participated in these studies and experiments [12, 13].

The first use of the LARIAT system in a human subject took place at the Clinic of Cardiac and Vascular Surgery and Transplantology of the John Paul II Specialist Hospital in Cracow. Appropriate institutions including the Central Register of Clinical Trials (CEBK, *Centralna Ewidencja Badań Klinicznych*) and the Bioethics Committee of the Jagiellonian University approved the procedure, which took place in November 2009. The surgical team including Bartuś, Sadowski, and Kapelak performed the first procedure and several subsequent clinical trials, which unequivocally confirmed the safety and effectiveness of the analyzed LARIAT system [10].

The most important reports documenting the results of trials in human subjects are those published in the *Journal of the American College of Cardiology* (JACC), *Heart Rhythm*, and *Circulation: Arrhythmia and Electrophysiology* [10, 11, 14]; the author of the present paper was the first author of these articles and performed all the LAAO procedures on which the articles were based. The clinical studies and multicenter registries that we participated in resulted in obtaining the CE marking for the product and, subsequently, the approval of the Food and Drug Administration for its use in human subjects both in the USA and the European Union.

The LARIAT device is manufactured in one size and is suitable for almost any anatomical conditions, in contrast to all other implant-based systems, which require the production of several model sizes and precise preoperative measurements. This universality of the LARIAT system greatly facilitates the performance of the implantation procedure.

However, its most important and unique characteristic in comparison with all the other percutaneous LAAO systems is the fact that no OAC is required.

As there is no implant, and the suture is not in contact with the patient's blood, the only thing remaining in the

blood flow is the patient's own tissue, which is already covered with live endothelium.

This is obviously of paramount importance for patients with contraindications for OAC, who no longer have to be exposed to the risk of hemorrhagic complications.

Furthermore, this allows the prevention of all complications normally associated with OAC.

The lack of an endocardial implant eliminates the risk of complications related to the presence of a foreign body within the heart (including implant migration, embolization, and coagulation), which is unfortunately associated with all implant-based systems.

The effectiveness of the LARIAT system ranges from 96% to 100%, which is comparable with other LAAO systems. The rate of complications associated with the pericardial access after the use of the LARIAT system are reported by various centers around the world at 3–5%; the rate of complications associated with the LARIAT device itself is reported at 0%.

Our center in Krakow was able to significantly reduce the number of all complications thanks to extensive experience in performing these procedures. At present, our complication rate is approximately 1%; this includes patients with various severe concomitant diseases.

At this point, it is worth commenting on the individual publications from American centers which report higher rates of complications. In the opinion of the author of this article and many other specialists, the higher number of complications reported by these centers can be attributed to the limited experience of the operators and erroneous qualification of patients for LAAO.

The use of other pericardial access techniques (telescopic needle) and anti-inflammatory agents during the postoperative course significantly limits both short- and long-term complications, as proven by a study encompassing several hundred patients undergoing this procedure in the USA [15, 16].

Our most recent experiences also demonstrate that the LARIAT system is the only percutaneous device for LAAO which offers not only mechanical, but also electric isolation of the LAA. The results of these procedures were published in *Heart Rhythm* and *Circulation: Arrhythmia and Electrophysiology* [13, 14].

The electrical isolation of the LAA provided by the LARIAT system has been demonstrated in these publications, which may be very important in the case of patients with AF triggers within the LAA.

The performance of LAAO using the LARIAT system can simultaneously remove the cause of AF in these patients. Our experience includes several AF patients who never again suffered from an AF episode after being treated with LAAO using the LARIAT loop. Therefore, it appears that systems employing epicardial access and based on the well-known and safe surgical suture, such as the LARIAT system, are fundamentally better. This stems from their capability of providing complete mechanical isolation from the circulating blood and electrical isolation of the LAA without the use of extracorporeal circulation or the need to leave an implant within the heart. Many authors believe that implant-based methods will always be less attractive for the patient, as the presence of an endocardial implant and its contact with the blood current will always be associated with the risk of potential complications [17–20].

The LARIAT system has been successfully deployed in nearly 5000 patients in over 180 centers around the world. Since 2009, I have performed over 400 procedures using the LARIAT loop, which is the largest number of such procedures in the world.

I would like to encourage the readers to monitor the literature associated with LAAO and to attempt to perform these procedures on their own.

The efforts of our society (the Polish Society of Cardiothoracic Surgeons), especially Prof. Zembala, Prof. Maruszewski, and Prof. Różański, have resulted in the possibility of obtaining a certificate attesting to the skills required for LAAO. This is certainly a milestone that will enable cardiac surgeons to independently perform and account for all LAAO procedures.

Disclosure

Author reports no conflict of interest.

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