Percutaneous Left Atrial Appendage Occlusion

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The left atrial appendage is known to be the origin of thrombi in >90% of patients with nonvalvular atrial fibrillation (AF), and in a recent registry the incidence was shown to be even higher (>99% of cases) [1]. Left atrial appendage occlusion (LAAO) is an important therapeutic option in for patients with AF, a high thromboembolic risk and a relative or absolute contraindication to long-term therapy with anticoagulant chronic oral treatment ACO [2].

The randomized clinical trials (RCTs) available, have shown that LAAO has an excellent safety profile, with an equal efficacy in preventing strokes compared to vitamin K antagonists (VKA) in patients without a contraindication to oral anticoagulants [3, 4]; promising data are emerging on the comparison with direct oral anticoagulants (DOACs) [5]. Currently, in the United States the FDA approval is given only for the use of the WATCHMAN device in patients eligible for short-term ACO treatment; this limits significantly the use of these devices in patients with a high hemorrhagic risk or a previous episode of bleeding. Whereas in Europe, the ESC guidelines recommend LAAO in AF patients with a history of intracranial hemorrhage or nonmodifiable risk factors (Class IIb, Level of Evidence B) [2]. Even though there is

no RCT yet supporting this recommendation, the evidence is based on an increasing number of real life registries that have been published in recent years, addressing the issue of LAAO in patients, who were excluded from RCTs for having a contraindication to anticoagulation.

Adedineswo et al. [6] conducted a retrospective observational study of 231 patients (33% female) who received a Watchman[®] device at Mayo Clinic sites. Patients had high thromboembolic and bleeding risk scores. The study showed no statistically significant difference in bleeding risk related to initial antithrombotic choice. However, patients with prior gastrointestinal bleed were more likely to have a clinically significant bleeding event in the first 6 weeks following smaller device sizes (21 mm). Furthermore, these devices were related to thromboembolic events.

This study is interesting and the results are certainly reassuring with respect to the short-term efficacy and safety of LAAC in such patients, adding valuable information to the previous real-world evidence in this field. However, it is necessary to highlight that, in consider-

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ation of the different guidelines in the United States, patients treated in the US are often less ill than those treated in Europe. In fact, the authors declare that 70% of patients are discharged with warfarin, 23% are discharged with NOACs, and only 7% are discharged with antiplatelet therapy. In Europe, however, most patients are discharged with antiplatelet therapy [6, 7]. On the other hand, the follow-up was short (only 45 days). Current US practice recommends that patients start warfarin therapy in the periprocedural period based on the design of the PROTECT AF and PREVAIL trials and the FDA approval documentation [3, 4]. DOACs such as dabigatran, rivaroxaban, apixaban, and endoxaban have been used in contemporary clinical practice following LAAO [8]; however, there are no RCTs or guidelines supporting this practice. Furthermore, current AHA/ACC/HRS guidelines acknowledge the uncertainties with appropriate patient selection and choice of a periprocedural antithrombotic regimen. DOACs are considered first line of therapy for stroke prophylaxis in patients with nonvalvular AF, and based on the lack of existing literature, evidence for DOAC use in patients with nonvalvular AF has been extrapolated to patients who receive a Watchman® device. Some observational studies have also demonstrated the safety of DOACs as well as antiplatelet therapy only, in the periprocedural period following Watchman® implantation [9].

Twenty-two patients (10%) experienced clinically significant bleeding within the first 6 weeks following Watchman® implantation. In crude models, the initial antithrombotic choice was not significantly associated with bleeding risk; however, patients who had a Watchman® device implanted due to gastrointestinal bleeding were more likely to experience a bleeding event compared to patients who had the device implanted due to intracranial pathology. Furthermore, patients who had a history of diabetes were more likely to experience a bleeding event whereas patients with a prior history of stroke/TIA appeared less likely to experience bleeding following Watchman® implantation. Overall, 17 (7%) patients experienced a thromboembolic event after the first 6 weeks from Watchman® implantation.

Another point of current controversy lies in the recommendation of antithrombotic therapy after the procedure. In the PROTECT AF study, ACO were administered for 45 days after implantation and were suspended if the TEE demonstrated an adequate closure of the left atrial appendage (LAA) [3].

Recently, the ASAP study [10] showed that ACO treatment for 45 days can be replaced by DAPT (acid acetyl-

salicylic 100 mg/day and clopidogrel 75 mg/day). Currently, most centers recommend DAPT for 1–3 months and antiplatelet monotherapy indefinitely. Device thrombosis is a rare complication, but it has been equally described with the Watchman™ and the ACP-AMULET devices. In most cases, it is resolved with anticoagulation for 2 weeks. A worrying fact is that the authors report a high mortality for all causes: 10% during a 45-day follow-up, much higher than that reported in the PREVAIL trials (2.6%) and in PROTECT AF (3.2/100,000 patients/year) [3, 4]. However, the authors did not find any variable associated to this fact.

The presence of periprosthetic leaks during follow-up still has an uncertain meaning. A sub-analysis of the PROTECT AF study did not detect a relationship between leaks and the appearance of clinical events [3]. On the contrary, in studies carried out on patients undergoing coronary heart surgery who underwent a prophylactic surgical closure of the OI, it was observed that an incomplete excision of the LA was associated with a higher rate of cardioembolic events [11]. At the moment we are still waiting for data on this topic in order to confirm or rule out this relationship, in the mean time we should try to prevent the occurrence of periprosthetic leaks. Regarding this aspect, slightly larger devices are recommended compared to the TEE and angiography measurements since this approach manages to reduce the residual leakage rate without increasing the risk rupture of the wall [7]. In order to better assess these aspects, larger prospective studies with longer follow-ups are needed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding sources were used.

Author Contributions

Drs. Antonia Sambola and Patrizio Mazzone have equally contributed in critical review of literature and redaction of editorial. Dr. Andrea Radinovic contributed in research of literature.

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