Novel oral anticoagulants in the electrophysiology lab: are we really ready to forget warfarin?

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This editorial refers to ‘Novel oral anticoagulants in a real-world cohort of patients undergoing catheter ablation of atrial fibrillation’ by C. Eitel et al., on page 1587.

Atrial fibrillation (AF) is the most common arrhythmia, affecting over 6 million people in Europe. Subjects suffering from this arrhythmia have a five-fold higher risk of stroke than those in stable sinus rhythm, and anticoagulation with vitamin K antagonists has proven able to reduce this risk by about 60%.

Recently, new oral anticoagulants (NOACs) have been introduced in the clinical practice and have proven non-inferior to warfarin in preventing thromboembolic risk in patients affected by non-valvular AF.1,2 Moreover, NOACs significantly reduce the risk of cerebral haemorrhage, act rapidly, and are easier to administer, considering that monitoring of the international normalized ratio (INR) is not required and a lower interaction with food and other drugs is described. However, these drugs display the limitation to have no antidote and the difficulty to assess patient compliance.

In the last 10 years, catheter ablation has become an effective therapeutic option for treatment of symptomatic and drug-refractory AF. Nevertheless, this therapy may be associated with complications, mainly thromboembolic events, cardiac tamponade, and vascular complications.1,3 Over the years, various antithrombotic treatments for use either during or after the procedure have been proposed to maximize protection against thromboembolic events and to reduce the risk of bleeding. However, the lack of prospective, randomized, large-scale studies has led to the emergence of different approaches, which are largely based on the operator’s experience.

There is a general agreement on the need to anticoagulate the patient in the period prior to the procedure following the same recommendations that pertain to AF cardioversion. The most widely adopted strategy is discontinuation of warfarin and bridging with low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) for several days before ablation. During the procedure, optimal anticoagulation with UFH is regarded as essentially maintaining the activated clotting time (ACT) at 300–400 s. After ablation, oral anticoagulation is promptly restarted and maintained for at least 3 months in all patients due to high risk of thromboembolism in the early post-procedural period.3 The restoration of anticoagulation with warfarin, however, requires LMWH or UFH as bridging therapy in the post-operative period which increases the risk of vascular complications.

In the last few years, several studies have suggested that AF ablation can be safely performed in patients who are continuously therapeutically anticoagulated with warfarin. This strategy also requires UFH administration during the procedure to maintain ACT equal or above 350 s. Santangeli et al.4 conducted a meta-analysis of the data from over 27 000 patients, in which the strategy of discontinuing warfarin before ablation was retrospectively compared with that of performing the procedure under therapeutic INR. Their results confirmed that performing radiofrequency catheter ablation on warfarin is an effective strategy for reducing thromboembolic risk without increasing major bleedings. However, in the event of persistent bleeding or cardiac tamponade, fresh frozen plasma, prothrombin complex concentrate, or recombinant activated factor VII should be available for replacement of coagulation factors reduced by warfarin in addition to protamine for reversal of heparin.3,4

The availability of NOACs has opened up new anticoagulation protocols during AF ablation. Given the rapid onset of action, these drugs have the potential advantage of not requiring any bridging with heparin in the immediate post-operative period. At the same time, however, the lack of an antidote makes it difficult to manage any major bleeding. In the last 2 years, several retrospective analyses have been undertaken to glean information on the possible use of NOACs during AF ablation. Dabigatran has been most extensively studied in this setting. Winkle et al.5 described their experience of using dabigatran after AF ablation on 123 consecutive patients. In their series, < 30% of patients were taking dabigatran before the procedure. In this subgroup of patients, dabigatran was discontinued 36–60 h before the procedure depending on renal function. During ablation, UFH was administered in all patients to maintain a target ACT value of 225 s. Immediately after the procedure, all the patients received LMWH, and dabigatran was started after 22 h. No thromboembolic or haemorrhagic events were recorded with...
this approach. Later, Lakkireddy et al.\textsuperscript{6} reported the results of a multi-centre observational study in 145 patients in whom dabigatran was discontinued on the morning of ablation and resumed within 3 h after haemostasis. This population was matched with an equal number of patients who had undergone ablation in the same period on uninterrupted warfarin therapy. In the dabigatran group, there was a significantly higher incidence of major bleeding (6 vs. 1\% $P=0.019$); the thromboembolic risk was also higher, albeit not significantly (2.1 vs. 0\% $P=0.25$). Increased bleeding rates observed in this study may have been due to overlapping of pharmacodynamic effects of dabigatran and UFH adjusted to maintain an ACT target higher than described in the previous study (300–400 s). On the other hand, a higher thromboembolic risk observed in patients taking dabigatran can be explained by a possible greater resistance to UFH described with this treatment.\textsuperscript{7} Of note, all patients who suffered a thromboembolic event had undergone extensive ablation for non-paroxysmal AF and stable INR values before the procedure were excluded.

Recently, therapy with NOACs (dabigatran and apixaban) was associated with a lower risk of periprocedural thromboembolic complications in patients undergoing ablation during therapeutic warfarin.\textsuperscript{7,10} The only study in non-paroxysmal AF suggesting that the role of atrial substrate, type of ablation procedure performed after the discontinuation of dabigatran, the results obtained so far cannot be generalized to all the NOACs. Ablation of AF using uninterrupted warfarin seems to be the most appropriate strategy. Alternatively, discontinuation of NOACs 24 h before the procedure and their resumption a few hours after ablation to avoid the bridge with LMWH seems prudent.\textsuperscript{13} Further data from prospective randomized studies will be necessary to obtain a clearer picture on the periprocedural management of NOACs in patients undergoing AF ablation and, if appropriate, to propose these new drugs as alternatives to warfarin in electrophysiology laboratories.

**Conflict of interest:** none declared.

**References**


