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Catheter ablation of the cavo-tricuspid isthmus as a bridging therapy for symptomatic atrial fibrillation?

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Abstract

Atrial fibrillation and atrial flutter are the most common supraventricular arrhythmias. These arrhythmias often coexist, approximately one third of patients with atrial fibrillation presenting episodes of atrial flutter. Many physicians have difficulty making a correct diagnosis based on the electrocardiogram. However, it is fundamental for the choice of management strategy. Each arrhythmia has a different background, different sensitivity to pharmacological treatment and different approach to non-pharmacological treatment.

Key words: atrial fibrillation, atrial flutter, arrhythmia

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Introduction

Atrial fibrillation (AF) is the most common supraventricular arrhythmia and occurs in as much as 2–4% of the general population [1]. In the coming years, its incidence is expected to increase by as much as 2–3 times due to increasing life expectancy in the general population and more frequent search for previously undiagnosed cases of AF. The second most common supraventricular arrhythmia is atrial flutter (AFl). Many multi-centre trials emphasise the comorbidity of these two arrhythmias. According to the 2020 European Society of Cardiology (ESC) Guidelines for the management of these arrhythmias, pharmacological treatment and surgical treatment (ablation) are used. Decision concerning surgical treatment depends on the centre and the experience of the operating physician who performs the surgery. The long waiting time for ablation leads to establishment of the arrhythmia and worse long-term prognosis [2]. In addition, the form of AF (paroxysmal, persistent or longstanding persistent) affects both early and long-term effects of pulmonary vein isolation [2, 3].

Pathogenesis and indications for treatment of atrial fibrillation

Pathogenic mechanisms of AF are related to focal beats from pulmonary veins or multiple microreentries in the left atrium (Figure 1). The basis of treatment is pharmacotherapy – antiarrhythmic drugs (**class I** — for patients with no comorbidities, with no organic heart diseases [propafenone, flecainide] or **class III** — for patients with an organic heart disease [amiodarone]). Pharmacotherapy is effective in stopping and preventing the recurrence of AF, but in some patients it leads to conversion to another supraventricular arrhythmia — AFl. An invasive method for treatment of AF is catheter ablation, the purpose of which is to achieve pulmonary vein isolation (PVI). It is recommended for patients in whom either a class I or class III antiarrhythmic drug was ineffective or for patients who do not tolerate therapy using these drugs (**class of recommendation I, level of evidence A**) [1]. Radiofrequency ablation — also known as classic ablation — is difficult to perform, takes a lot of time, involves prolonged fluoroscopy and is characterised

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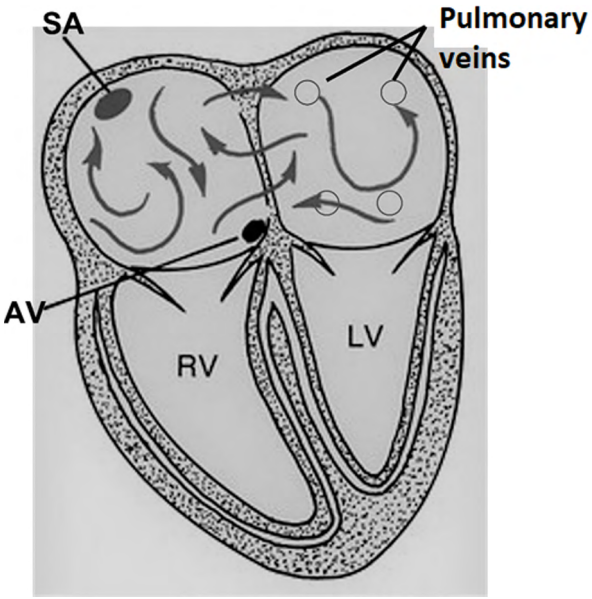

Figure 1. Atrial fibrillation — microreentry; AV — atrioventricular node; LV — left ventricular; RV — right ventricular; SA — sinoatrial node

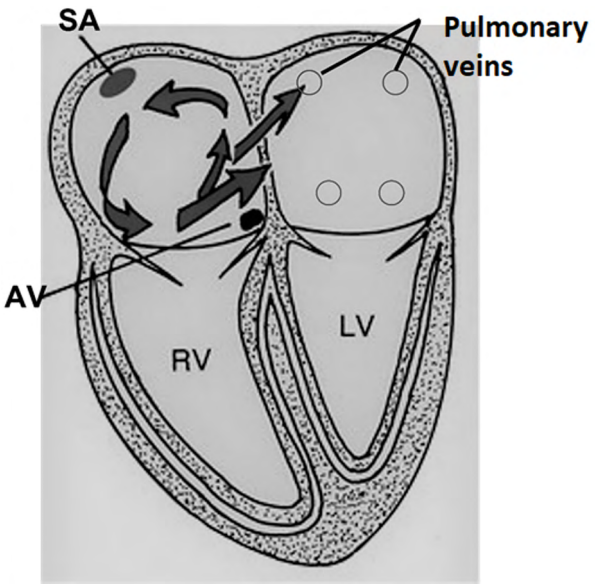

Figure 2. Atrial flutter — macroreentry; AV — atrioventricular node; LV — left ventricular; RV — right ventricular; SA — sinoatrial node

by a high rate of complications (pulmonary vein stenosis, post-ablation atrial tachycardia, atrioesophageal fistula). A newer method is balloon cryoablation of pulmonary vein ostia, which involves inducing left atrium tissue necrosis through a freezing/unfreezing process [2]. It is safer and associated with lower risk of complications. Both surgeries are characterised by comparable effectiveness in terms of maintaining sinus rhythm in long-term follow-up, i.e. 75% for paroxysmal and approx. 40% for persistent AF [2–4].

Pathogenesis and indications for treatment of atrial flutter

This arrhythmia is caused by macroreentry (Figure 2) in the right atrium, around the tricuspid ring. Antiarrhythmic treatment is ineffective for stopping and preventing the recurrence of this arrhythmia. The treatment of choice for AFl is radiofrequency ablation or cavotricuspid isthmus (CTI) cryoablation. It is indicated for poorly-tolerated recurring AFl flutter as well as AFl following pharmacological treatment of AF (**class of recommendation I, level of evidence B**) [1]. Ablation should also be considered for the first episode of AFl, and for well-tolerated and atypical AFl (**class of recommendation II, level of evidence A**) [1] The effectiveness of invasive treatment of AFl is nearly 100%.

Methods for preventing the recurrence of supraventricular arrhythmias

In the trial with the acronym of **STAR-AF II** (**Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial-Part II**), Verma et al. [5] tried to answer the question of whether electrical isolation of pulmonary vein ostia is sufficient to maintain the sinus rhythm in long-term follow-up. The trial included 589 patients with persistent AF, who were assigned to the following groups: I — PVI ablation (67 patients), II — PVI ablation plus ablation of areas of fragmented atrial potentials (263 patients) and III — PVI ablation plus linear ablation of the left atrial roof and the mitral isthmus (259 patients). The follow-up duration was 18 months. The primary outcome was no documented recurrence of AF lasting longer than 30 seconds after ablation. In their results, the authors stress that the duration of the procedure was much shorter for group I compared to groups II and III ($p < 0.001$). During follow-up, no recurrence of AF was observed for 59% of patients from group I, 49% of patients from group II and 46% of patients from group III ($p = 0.15$). In their conclusions, the authors emphasise that for patients with persistent AF, no reduction in the frequency of recurrence of AF was observed when ablative lines were applied in the left atrium in addition to pulmonary vein isolation. The relatively low effectiveness of ablation may stem from mechanisms which lead to unfavourable remodelling and fibrosis of the left atrium, such as: atrial myocardium stretching, AF episodes, other supraventricular arrhythmias or activation of the renin-angiotensin-aldosterone system.

Another frequently encountered situation is the primary occurrence of typical AFl and periodic AF episodes. What procedure should be performed in such a case? This question was tackled by authors of a pilot study (**Cavotricuspid isthmus ablation among patients with persistent**

atrial fibrillation as a bridging therapy to maintain sinus rhythm — a pilot study) [6], in which a hypothesis was assumed that sinus rhythm may be achieved through cavo-tricuspid isthmus ablation combined with pharmacological treatment using an aldosterone receptor antagonist. Follow-up, with a mean duration of 13.9 months, included 64 patients, assigned to 3 groups: I – AFl (n = 34); II – AFl with a history of AF episodes (n = 13); III – persistent AF despite antiarrhythmic treatment (n = 17). All patients underwent CTI ablation. For group II, antiarrhythmic treatment was commenced for all patients after the surgery, while for group III, the previously used treatment was continued. In addition, an aldosterone receptor antagonist was used for some patients from group I and all patients from other groups. During long-term follow-up, AFl recurrence was noted in 3 patients from group I (8.8%) and 1 patient from group II (7.7%) over 5 months; 1 AF episode was also observed. In group III, there were 7 AF episodes; for these patients, either another pulmonary vein isolation procedure was performed or AF was considered permanent. The rate of effectiveness of procedures in individual groups was 91% vs. 85% vs. 59% respectively ($p < 0.05$), and was statistically significant. In their conclusions, the authors emphasise that CTI ablation combined with antiarrhythmic treatment and aldosterone receptor antagonists may be an effective bridge therapy for patients with persistent AF before the final pulmonary vein isolation. It can be used to maintain sinus rhythm. Further multi-centre trials are needed to confirm this hypothesis.

In the work by Bianco et al. [7], the authors studied the frequency of occurrence of AF following CTI-dependent AFl ablation. The study included 84 patients with no prior history of AF who underwent CTI-dependent AFl ablation. During follow-up, with a mean duration of 26 ± 18 months, AFl recurrence was observed in 10 patients (11.5%), while 45 patients (53.6%) experienced their first AF episode. Throughout the entire study, no predictor variables for occurrence of a new AF episode were identified. This means that elimination of CTI-dependent AFl does not prevent the occurrence of AF episodes. This effect has been observed in numerous multi-centre clinical trials which studied the development of atrial arrhythmias, including AF, following CTI ablation due to AFl.

In relation to that, the latest data suggests that preventive ablation of pulmonary vein ostia may be an effective strategy for preventing new AF episodes in patients who undergo CTI-dependent AFl ablation. This is evidenced by results of the **PREVENT AF I** study [8]. Follow-up included 50 patients with CTI-dependent AFl with no prior history of AF and randomised into two groups, at a 1:1 ratio: I — CTI — only CTI ablation and II — CTI + PVI — CTI ablation combined with PVI cryoablation. It was emphasised in results that new AF occurred with statistically significantly lower frequency in the CTI + PVI group vs. the CTI group (12% vs. 52% respectively; $p = 0.003$). In addition, Romanov et al. [8] presented in their work the results of a prolonged 3-year follow-up for the **PREVENT AF I** study, noting the significantly lower rate of occurrence of any atrial arrhythmia in the CTI + PVI group compared to the CTI group (48% vs. 20%; $p = 0.01$).

Conclusions

On the basis of the latest ESC/Polish Cardiac Society Guidelines for management of AF, CTI ablation may be considered during AF ablation for patients with history of typical AFl, or if typical AFl was induced during ablation of pulmonary vein ostia (**class of recommendation IIb, level of evidence B**) [1]. However, what procedure should be used when the situation is reversed? Can/should simultaneous ablation of pulmonary vein ostia be considered in case of CTI ablation due to typical AFl and AF occurrence? On one hand, this would constitute a single, if prolonged, procedure, which could treat the patient, or at least minimise the frequency of occurrence of episodes of supraventricular arrhythmias: AFl and AF. However, given the lack of data from clinical trials, such strategy is not, at the moment, justified. For this reason, currently neither application of additional ablative lines in the left atrium nor PVI ablation are performed during CTI ablation. To conclude this article, it should also be emphasised that there is evidence that CTI-dependent AFl ablation is a safe and effective procedure, although it only solves the clinical problem of patients with isolated AFl. In long-term follow-up, the occurrence of AF following CTI ablation is frequently observed. On the basis of the presented results of trials and studies, the authors remain of the opinion that there is still no sufficient evidence to recommend the combination of CTI and PVI ablation in treatment of isolated AFl to prevent the occurrence of AF. More prospective multi-centre trials, with more patients and longer follow-up, are needed to assess the benefits of application of this treatment method.

Conflict of interest

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