

Periablative Anticoagulation Strategies in Patients with Atrial Fibrillation

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Abstract

Atrial fibrillation is associated with thromboembolic events that may cause important impairment on quality of life. Pulmonary vein isolation is the treatment of choice in cases that are refractory to medical therapy. Once sheaths and catheters are manipulated inside the left atrium, anticoagulation with heparin must be used during the procedure to protect patients from thromboembolic phenomena. Different strategies of anticoagulation are used at different centers. This review summarizes the pathophysiology of thrombus formation in the left atrium, defines which patients are under high risk and describes the main strategies used for anticoagulation.

Introduction

Atrial fibrillation (AF) is a common arrhythmia associated with significant morbidity and mortality.¹ Catheter ablation is indicated in patients with AF who are refractory or intolerant to antiarrhythmic medication.^{2,3}

Electrical isolation of the pulmonary veins is the cornerstone of any ablation approach. The goals of catheter ablation are to prevent AF by eliminating the initiating triggers and altering the arrhythmogenic substrate.^{2,4} This kind of treatment is generally safe and effective, but does pose some risk of thromboembolic complications due to the use of long intravascular sheaths, prolonged left atrial instrumentation and the lesions caused by RF delivery.

Stroke is the most feared complication associated with AF ablation, with reported rates of up to 6% in

patients undergoing to this procedure.⁴⁻⁷ Restoration of sinus rhythm per se also imposes some risk of embolism, but ablation adds substantial areas of damaged left atrial endothelium that may predispose to thrombus formation.³

The intensity and timing of anticoagulation are important issues when considering prevention of thromboembolic complications during AF ablation.

Soft Thrombus Formation

Soft thrombus is a mobile clot or fibrin formation that occurs during ablation probably by denaturation and aggregation of plasma proteins which may occur at blood temperatures between 50° and 80°C (Video 1). It usually occurs at the site with the highest temperature (the surface of the heated tissue) and has poor adherence to the ablation electrode and transeptal sheaths.⁸ Such a

formation may only be noticeable with intracardiac echocardiography (ICE), because it may not be associated with impedance rises⁹ and occurs even in patients submitted to increased intensity anticoagulation protocols.¹⁰⁻¹²

Some studies have shown that more aggressive heparinization strategies during the procedure results in a reduction of embolic complications.^{11,12} Wazni et al¹² compared different regimens of anticoagulation during AF ablation. The majority of patients in this study received a bolus of 10,000 U and the ACT was maintained around 350-400 seconds. In 180 patients ACT was maintained between 300-350 seconds in addition to an infusion of eptifibatid at a dose of 135 mcg/kg followed by 0,5 mcg/kg/min infusion adjusted to achieve greater than 85-90% suppression of platelet aggregation. At the end of the procedure, a single dose of Aspirin was administered and warfarin was restarted in all patients in the same day. In patients with persistent AF, bridging to warfarin was performed with enoxaparin 0,5mg/kg twice daily. There was a uniform reduction of periprocedural embolic events, but none of the anticoagulation protocol abolished catheter-associated char formation. There was a higher incidence of pericardial effusion without any reduction of stroke in the group receiving eptifibatid.

Char Formation

Char is the formation of hard coagulum due to tissue overheating during RF delivery and is generally observed at the end of the procedure, attached to the catheter tip¹² (Figure 1).

Kongsgaard et al observed that, in vitro, tissue overheating may occur despite low catheter temperatures.¹³ Without flow, the tip temperature initially exceeded the tissue temperature, but the tissue temperature exceeded the tip temperature after 18 seconds. With flow around the ablation site, the tissue temperature exceeded the tip temperature during the entire energy delivery, but in this case temperature curves were oscillating in the presence of flow around the ablation site.

Since char results from heated denatured fibrinogen, it is independent of thrombin; as such heparin cannot prevent its formation. The major strategy to avoid char formation is power titration,

which is possible using ICE. Direct visualization of the electrode surface and the detection of microbubbles are helpful in embolic prevention and allow early interruption of instrumentation for suction and removal once clot is detected. Bubble monitoring permits downward power titration before impedance rise and coagulum formation.^{12,14} (Video 2). That strategy is not usually applicable when open irrigation tip catheters are used, once the agitated saline droplets that leave the tiny catheter orifices at high velocity causes echogenic microbubble formation (Video 3), which may compromise the use of ICE for monitoring tissue overheating¹⁵. However, irrigated tip ablation limits the temperature at the catheter tip-tissue surface, reducing the risk of charring and thrombus formation.^{9,16}

Timing and Targets of Anticoagulation

Once vascular access has been obtained, before transseptal puncture, anticoagulation should ideally be initiated with unfractionated heparin, delivered based on body weight or time-based nomograms and monitored by regular ACT measurements. This strategy avoids LA instrumentation without therapeutic ACT levels, which may allow rapid thrombus formation¹⁷

Another strategy shown to prevent thrombus formation is continuous flushing of intravascular sheaths with heparinized solution.⁷ Cauchemez et al reported their experience with left atrial ablation using high-flow rate perfusion of long sheaths. In 153 procedures in 86 patients, they used two different protocols: the sheaths were continuously flushed with heparinized saline (1000U/L) at a flow rate of 3 ml/h ("low-flow"), or 180 ml/h ("high-flow"). They reported a strong relation between sheath perfusion rate and stroke, with a 17-fold higher risk using low flow perfusion than high perfusion sheaths.⁷

ICE also allows performance of transeptal punctures with ongoing anticoagulation, as it provides improved anatomic definition, direct visualization of sheaths and needle, and immediate identification of pericardial effusions.^{4,10,12,18} (Video 4)

Several studies have shown that more aggressive anticoagulation, maintaining ACT between 350 to 400 seconds, reduces periprocedural embolic

events, without increasing serious bleeding complications.^{10,12,19} Ren et al described different protocols of anticoagulation and analyzed the effects of increased intensity of anticoagulation during the procedure. They studied 511 patients divided in two groups: Group I – ACT 250-300 seconds and Group II – 300 – 410 seconds. Thrombus formation in the LA was monitored continuously with ICE imaging. Although there was a higher incidence of SEC in Group II (59,9% versus 16,7% in Group I), LA thrombus formation was observed in 11,2% patients of group I and only in 2,8% in group 2 ($p < 0,05$). When considering only patients with SEC, an incidence of 45% of thrombus formation in the LA was observed in the low ACT group, as compared with 4,6% in group II ($p < 0,0001$). There was no difference in procedural complications related to increased intensity of heparin anticoagulation.¹⁰

Prevention of Thromboembolic Events during and after AF Ablation

Oral et al described the prevalence and predictors of thromboembolism in patients with and without other risk factors for stroke who underwent to AF ablation. The procedure was realized in 755 consecutive patients with paroxysmal and chronic AF. The majority (56%) had at least 1 risk factor for stroke. The highest incidence of thromboembolic events was recorded within the first 2 weeks post procedure (0,9%) [20]. Warfarin was suspended after AF ablation in 79% of the patients with no risk factors, and in 68% in the patients with more than 1 risk factor. They reported also an incidence of up to 0,2% of stroke 6 to 10 months after ablation, 1 of whom still had AF, despite therapeutic INR²⁰

In that regard, in a recent study, Wazni et al evaluated strategies of periablation anticoagulation to minimize the risk of thromboembolic events in periprocedural period. They compared outcomes in 355 consecutive patients undergoing pulmonary vein antrum isolation of persistent atrial fibrillation. Patients were divided in three groups: group I (105 pts) received enoxaparin 1 mg/kg twice daily for bridging after ablation; group II (100 pts) received 0,5 mg/kg twice daily and group III (150 pts) were given their usual warfarin dose without interruption. All of the groups were comparable with respect to

age, gender and structural heart disease. Warfarin therapy was interrupted in groups I and II 3 days before (INR approximately 1,1 during the procedure). In group III, warfarin therapy wasn't interrupted and INR was [2,7+0,5. The maximum ACT during the procedure was comparable in both groups (>450 msec). More patients had spontaneous echo contrast in groups I and II. There were no thromboembolic events in group 3 patients. Symptomatic large pericardial effusion requiring pericardiocentesis occurred in two patients of group II. One patient in each groups I and III developed mild pericardial effusion that required no intervention. Hematomas were considered minor bleeding and occurred in 23 patients of group I and in 19 patients of group II. Nine patients of group III had hematomas.²¹ They concluded that maintenance of anticoagulation with warfarin to maintain therapeutic INRs is safe and that strategy may be an acceptable alternative to bridging strategies that use enoxaparin or heparin in the periprocedural period. This strategy is currently being used by several centers performing a high volume of AF ablation procedures.

Another important risk factor is the presence of spontaneous echo contrast (SEC), defined as slow swirling nonhomogenous amorphous echoes, visualized with intracardiac or transesophageal ultrasound (Video 5). It is a marker of a hypercoagulable state, since it results from red cell aggregation, which arises from an interaction between red cells and plasma proteins such as fibrinogen, at low shear rates. SEC is also associated with low left atrial appendage (LAA) velocities (< 20 cm/sec), commonly found in patients with AF.²² In these cases, more aggressive anticoagulation may help avoiding thrombus formation during the ablation procedure[10]. Wazni et al demonstrated that the maintenance of warfarin throughout AF ablation reduces dramatically the formation of SEC.^{14,21}

Conclusions

Pulmonary vein isolation is becoming the treatment of choice for symptomatic atrial fibrillation. The increasing number of procedures allowed electrophysiologists to become aware of the peculiarities and potential complications of this treatment. Thrombus formation is a feared complication related to this procedure, so many alternatives of anticoagulation are being tried to try to avoid it.

More aggressive anticoagulation with heparin during the procedure, maintaining ACTs in the range between 300-350 sec, reduces periprocedural embolic events without increasing hemorrhagic complications.

Continuation of warfarin throughout AF ablation without enoxaparin bridging is safe and efficacious and should be considered an alternative strategy to avoid embolic phenomena.

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