Point of view: Thromboembolic risks associated with catheter ablation for atrial fibrillation

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1. What is the background of thromboembolic complications in the setting of catheter ablation of atrial fibrillation?

Embolic events are a known complication of catheter ablation, indeed of cardiac catheterisation in general but have been infrequent in the era dominated by ablation of paroxysmal supraventricular tachycardias. In the current context of expanding indications of catheter ablation, particularly for atrial fibrillation and to a lesser extent for left atrial flutter and ventricular tachycardia, thromboembolic complications have become commoner. The MERFS survey found a 0.06 % risk of embolic events among 1715 patients right sided ablation procedures (1). A recent world-wide survey of ablation for atrial fibrillation found a 0.94 % embolic event risk amongst 7154 patients undergoing left atrial ablation (2).

As opposed to tamponade or local bleeding, an embolic event, particularly within the circulation of the central nervous system can have profound and permanent sequelae. Moreover, the therapeutic options in the event of an embolic event are limited. This is why, I consider an embolic event among the most feared complication of catheter ablation of atrial fibrillation. Certainly, although an atrio-esophageal fistula is even more lethal it is thought to be significantly rarer.

Typically, an embolic event occurring during or soon after a catheter ablation procedure is considered a procedural complication. When the procedure is performed with heavy sedation or under general anaesthesia, cerebrovascular embolic events may be difficult to recognise and become apparent only later. Although a definitive time window has not been defined, complications occurring within the first 24 hours after the ablation are almost certainly procedure linked. In the event of cerebrovascular emboli, the use of full dose anticoagulation during and after the procedure increases the risk of aggravation because of secondary hemorrhage

2. What factors contribute to the risk of thromboembolism in the setting of catheter ablation for atrial fibrillation?

Factors contributing to the risk of thromboembolism in the above setting may conveniently be considered under three categories:

a. Those present before the procedure

b. Those operative during the procedure

c. Those operative after the procedure.

a. Before the procedure, the underlying arrhythmia and underlying (cardiovascular) disease are major factors that determine the likelihood of a pre-existing intracardiac or left atrial thrombus. Atrial fibrillation per se, co-existing risk factors such as age, hypertension, diabetes mellitus, congestive heart failure, and mitral valve disease are all important predictors of the risk of embolic events, although different pathophysiologic mechanisms may be responsible. Atrial fibrillation, congestive heart failure and mitral valve disease are all conditions producing or contributing to intracardiac stasis, whereas hypertension, diabetes mellitus and age probably contribute to acceleration or promotion of the atherosclerotic process, thereby promoting atheroembolic events.

b. During the ablation procedure the presence of foreign bodies in the circulation such as catheters, sheaths and guidewires activate the coagulation cascade and promote the development of thrombi. The nature of the foreign surface and its surface area are both probably related to the extent of activation of the coagulation cascade. Additionally, depending on their design, catheters and sheaths produce areas of stasis – pockets protected from the flushing effects of blood flow. Typically unperfused sheaths are frequently subject to this problem and prone to develop insitu thrombus. This thrombus may be then pushed out into the circulation by a catheter or by a bolus of flush or simply by restarting an interrupted perfusion flush. Filamentous thrombi attached to the tip of sheaths very likely develop as a result of this mechanism.

   Further, air emboli can develop because of the sucking effect of withdrawing catheters from sheaths. Air is aspirated through the ‘non-return’ valves of sheaths which are not designed to be air tight and certainly not to prevent aspiration. As with in situ developing thrombi, these bubbles are pushed out into the circulation by catheters or boluses of flush.

   Blood proteins heated by tissue or by RF current may also be denatured into macro-molecules with embolic potential. Proteins are altered by temperatures exceeding 50° C but in vivo, soft coagulum (a dense mesh of denatured proteins with enmeshed red cells, without any visible fibrin stranding and occurring despite high concentrations of heparin) develops at interface temperatures of 70-80° C (3).

RF catheter ablation can generate embolic material in other ways as well: endothelium damaged by tissue heating activates the coagulation cascade; steam pops within heated tissue produce cratering and the exposed tissue also activates the coagulation cascade. Rarely, catheter fragments, atheroembolic or calcific debris may be embolised during such procedures.

c. After the procedure, the tissue lesions produced by RF delivery provide a continuing stimulation of the coagulation cascade – probably till full endothelialisation is achieved. The duration of this at-risk period is unclear and although 3 months may be considered a reasonable period, it is possible that endothelialisation is completed much earlier. Mechanical recovery of atrial contractility undoubtedly plays an important role in preventing the development of stasis induced thrombi and at least two factors may be important in this context: the effect of RF lesion produced fibrosis versus the recovery of non-permanently damaged atrial myocardium. As indicated above, the processes of tissue healing may be expected to be completed by 3 months (or perhaps earlier). The reduction of atrial contractility after tachycardia termination – atrial stunning - is the second factor that modulates the overall effect on atrial contraction and may last for weeks to months after elimination of the tachycardia. On the other hand, if arrhythmias recur, the recovery from atrial stunning may be expected to be retarded, probably in proportion to the residual arrhythmia burden.

3. How can the risk of thromboembolic complications be minimised?

In view of the multiple possible mechanisms of thrombus generation outlined above, three main strategies may be outlined:

Pre-procedural detection of pre-existing thrombi or preventing their development

Oral anticoagulation (with an INR between 2 and 3) is the most effective treatment measure currently available for patients at risk for thromboembolic events, however even when the INR is carefully maintained within the prescribed range, this treatment does not provide a 100% protection from thrombo-embolic events. The cumulative thrombo-embolic risk in many patients is a combination of atrial fibrillation related stasis as well as athero-embolic (artery to artery emboli) risk with differing responses to oral anticoagulation. In any case, the risk of catheter manipulation

dislodging pre-existing thrombi is probably greater than that related to cardioversion (electric or pharmacologic) and in my opinion, justifies the routine pre-procedure use of transesophageal echocardiography despite effective continuous anticoagulation for 4-6 weeks. Although a TEE – alone approach has been advocated, I believe a dual layered screening (oral anticoagulation plus TEE) is more effective in reducing embolic complications. Ideally, the TEE should be performed just before the procedure and in particular, any substantial windows of ineffective anticoagulation between the cessation of oral anticoagulation and the procedure should be avoided with the use of Heparin. Of course, in order to permit safer transseptal puncture, IV heparin administration is usually terminated 4-6 hours prior to the procedure.

Preventing the development of thrombi or other emboligenic material during the procedure
Although there is little hard evidence, heparin is used almost universally during the procedure to the above end. Most laboratories use bolus doses of Heparin while others use a continuous infusion and the choice of one over the other may have more to do with convenience. In my lab, I use a bolus dose of 80 IU/Kg administered intravenously as soon as left atrial access with a long sheath is secured. Thereafter, ACTs are performed at 45 minute intervals and further boluses of 1000- 4000 IU of heparin administered in order to maintain the ACT between 200 and 250 seconds.

There is some evidence in the literature to support the use of higher target ACTs to reduce the thromboembolic risk (4), however it is prudent to remember that the protection provided by Heparin is associated with a bleeding risk, particularly of tamponade. Although some labs administer heparin before the transseptal puncture, we rely on heparinised flush to prevent thrombus development within the sheaths during this period. In my lab, 2000 IU of Heparin is added to 500 cc of normal saline to constitute a continuous perfusate for the side arm of the long sheath. The use of a perfusion pump allows the reliable delivery of 100-150 cc of heparinised flush per hour inspite of variations in residual lumen resistance typically during catheter exchange. Although retrospective, a single center experience clearly documented the clinical benefit of continuously perfusing left atrial sheaths at this flow rate (5).

The use of an open tip irrigated catheter reduces or eliminates the generation of soft coagulum or char on the catheter tip by cooling the interface and diluting the concentration of plasma proteins and is therefore believed to be an important safety measure (6). When using a non-irrigated catheter, enforcing a lower tip electrode temperature is logical although much less effective particularly with large tip catheters. Avoiding pops and the associated cratering is also important

and using the lowest effective power generally helps in achieving this aim. We do not add heparin to the irrigation perfusate because the amount of fluid and heparin delivered will then depend upon the duration of ablation making it difficult to maintain a target ACT.

Finally, simple measures such as flushing all sheaths and lumen bearing catheters (with heparinised saline) before introduction and aspiration (a passive bleed-out works particularly well for low pressure left atrial sheaths because negative pressure aspiration with a syringe frequently sucks in air through the back-bleed valve) are very effective in avoiding in situ thrombus development within sheaths which could then be embolised by subsequent catheter introduction. Air emboli are a significant but usually benign problem, producing transient ST elevation typically in a right coronary artery distribution (likely because the right coronary ostium is superiorly placed with the patient supine) with infrequent accompanying chest pain. While the typical syndrome resolves within a few minutes, it is possible that such a benign evolution may not always be the case particularly in the presence of significant coronary artery disease.

The role of intracardiac echo is unclear: it certainly offers the possibility of very good monitoring during the procedure, however, the ability to titrate RF power using micro-bubble emanation is limited when using the irrigated tip catheter (7). The additional cost, instrumentation and expertise required for its optimal use further weigh against its routine use.

Preventing thrombo-embolic complications after the procedure

At the end of the procedure, the achievement of hemostasis at puncture sites has to be balanced against the continuation of anticoagulation. Heparin administration is suspended for an hour or two to allow compression to be effective. Hemostasis is simplified if no arterial puncture has been performed (or a small – 5Fr- introducer used) and simple compression for a few minutes can be followed by the prompt resumption of IV heparin in therapeutic doses for the next 12-24 hours, typically till the next day morning. Because the risk of local bleeding as well as tamponade is high during this period, IV heparin is preferable over low molecular weight subcutaneous heparin because of its shorter half-life, the availability of quick ACT or PTT testing and of protamine reversal. Oral anticoagulation is usually restarted the same evening, without a loading dose and low molecular weight heparin is continued after stopping IV heparin till the achievement of an effective INR.

4. What are the long-term implications of catheter ablation of atrial fibrillation for thromboembolic complications?

There is little if any evidence to support recommendations about the continued use of anticoagulation after catheter ablation of atrial fibrillation. It must be pointed out that even outside the setting of catheter ablation of atrial fibrillation, there are few recommendations concerning the duration of anticoagulant treatment and in general the consensus has been to recommend anticoagulation without further qualification or for at least 4 weeks (8).

In the absence of evidence based recommendations, one has to rely on empiric reasoning. Atrial fibrillation being a major risk factor for thromboembolic events, its elimination is expected to reduce but perhaps not eliminate the propensity for this complication particularly when coexisting risk factors (e.g. hypertension, diabetes, age) remain unchanged. However, anticoagulation is not recommended for these risk factors alone. It is therefore reasonable to consider withdrawing anticoagulation for patients who were anticoagulated only in the run-up to ablation in order to diminish the risk of an embolic peri-procedural complication or those in whom, in the absence of atrial fibrillation or sustained atrial arrhythmias, anticoagulation would not have been ordinarily indicated e.g. patients with AF and hypertension. On the other hand, I do not consider it reasonable to withdraw anticoagulation in patients who have echocardiographic evidence of significantly impaired atrial mechanical function inspite of stable sinus rhythm, although it must be acknowledged that we do not yet have universally acceptable and reproducible measures of atrial mechanical function. Clearly, in the presence of other indications for anticoagulation e.g. severe LV dysfunction, prosthetic valves, anticoagulation should be continued and probably indefinitely so. The situation is much more complex when ablation is successfully performed for patients with a prior history of a thromboembolic event attributable to atrial fibrillation. Since such a history constitutes a high risk marker of recurrence and since there is no evidence to prove that eliminating atrial fibrillation eliminates or diminishes this risk, I consider it prudent to continue anticoagulation for a significantly longer period after successful elimination of atrial fibrillation – at least a year. This allows additional time for verification of complete elimination of atrial fibrillation, time for complete recovery from stunning and from the effects of ablation. At this point, if both mechanically effective and stable sinus rhythm is convincingly demonstrated, the possibility of discontinuing oral anticoagulation (replaced by Aspirin) can be discussed with the patient. It must not however be forgotten that the limited follow-up presently available indicates a 1-2% late arrhythmia recurrence risk and therefore periodic surveillance for arrhythmia recurrence is probably necessary.

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