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REVIEW ARTICLE

How to prevent, recognize and manage complications of AF ablation?

Mauricio I. Scanavacca

Instituto do Coração (InCor), Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil

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Abstract Ablation of atrial fibrillation (AF) is one of most complex procedures in electrophysiology. Many technical improvements have been incorporated lately in order to improve clinical results and reducing risks. Currently, cardiac tamponade, stroke, PV stenosis, phrenic palsy and atrial esophageal fistula are still recognized as the major risks of AF ablation, although their managements have been much better established. The aim of this article is to review recent data in how to avoid, to identify and to treat such complications.

Introduction

Catheter ablation of AF is a complex interventional electrophysiological procedure that has changed along the time. Nowadays, many technological advances have been incorporated in clinical practice in order to improve success rate and to minimize complications. Despite that as the volume of AF ablation procedures grows the number of complications also is expected to increase.

The incidence of complications of catheter ablation of AF depends on the volume of procedures regularly performed by the center, techniques and strategies applied and clinical management of patients following AF ablation. In a US nationwide study involving more than 90 000 procedures, the overall incidence of complication in the hospital was 6.29%, with 0.46% of mortality.[1] Importantly, the tendency of complications rate increased along the period of 2000 to 2010 and confirmed that operators performing low number of procedures were an important predictor of complications.

The most frequent and severe complications of AF ablation are well established: cardiac tamponade, stroke, PV stenosis, phrenic palsy and LA-esophageal fistula with incidence dependently on the technique that have been used. The less severe complications are related to the vascular access, pericarditis, gastroparesis, pulmonary infection, stiff left atrium syndrome and silent microemboli.

The aim of this article is to review the main complications associated with current AF catheter ablation techniques as well as the strategies to recognize and to treat them.

Cardiac tamponade

Probably the general incidence of pericardial effusion during AF ablation is around 1.2% to 1.3%.[2,3] A recent meta-analysis of 34 943 ablation procedures reported a 0.9% incidence of tamponade,[4] however, it may reach up to 6%,[5] a rate much higher as compared to other electrophysiological

E-mail address: mauricio.scanavacca@gmail.com

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procedures. The main reasons for the higher incidence in AF ablation are the need for trans-septal punctures (usually two), the intense and long catheter manipulation in the LA, use of high power ablation with risk of steam pops and the need for intense systemic anticoagulation. Cardiac tamponade has been considered the most frequent cause of periprocedural death during AF ablation, thus its prevention and early diagnosis are life saving strategies.[6]

How to prevent

Trans-septal punctures performed too posteriorly may perforate the posterior right atrium and reach the pericardium space; very high punctures may also perforate the LA roof; as well as advancing the sheath system too deep into the LA may reach and perforate the LA appendage, left PVs or the lateral LA wall. Thus, using different fluoroscopic views as RAO to have a better anterior-posterior view of trans-septal puncture and LAO to evaluate how deep is the sheath system being introduced in LA may prevent trans-septal accidents. Advancing the trans-septal system over the wire positioned into the left superior PV is also a used strategy to prevent LA perforation. Recently, many operators prefer to use transesophageal or intracardiac echocardiogram for a safer access to the LA.

Direct catheter mechanical trauma, especially through the LA appendage and roof of the LA are an important cause of pericardial effusion. Performing LA mapping and ablation based on the force sensing catheter is expected to reduce the rate of tamponade, however, this has not been still confirmed in clinical trials. In the Smart AF trial the incidence of cardiac tamponade was 2.5% among 161 patients[7]; in the Toccastar Trial the tamponade incidence was much lower, however, no difference was observed in the two arms (Force sensing catheter=0.66%; standard irrigated RF catheter=0.7%, p=NS).[8]

The incidence of tamponade has been suggested to be lower during cryoablation. A recent prospective randomized controlled trial showed an incidence of tamponade of 0.3% in the Cryoballoon arm and 1.3% in the RF arm.[9] However, a meta-analysis of cryoballoon ablation with involving data of 1308 procedures reported an overall incidence of pericardial effusion of 1.5%.[10]

How to recognize

The majority of episodes of cardiac tamponade are successfully treated by immediate percutaneous drainage and anticoagulation reversal with protamine. However, early recognition and rapid drainage of cardiac tamponade are essentials to obtain a safe patient recovery.

An early sign of cardiac tamponade is a reduction in the excursion of the cardiac silhouette on fluoroscopy with a simultaneous fall in systemic blood pressure. An arterial line for BP monitoring detects and warns very early a hypotension and should be available for electrophysiologists and anesthesiologists during AF ablation. An available portable Echo machine is also important in the EP laboratory to confirm dubious cases and also useful before patient leave of the EP room. A practical strategy also to clarify dubious cases is to inject 10 microgms of isoproterenol IV and look at the left border of cardiac silhouette. A clear movement of the cardiac silhouette border excludes cardiac tamponade. ICE has also been helpful to early detection of a pericardial effusion. Another safe procedure is to maintain the patient in the hospital for at least one night following AF catheter ablation and to perform a transthoracic Echo before leaving to detect late pericardial effusions.

How to manage

Sub-xiphoid puncture is the best way to achieve the pericardial space and to perform fast hemopericardium drainage with a pigtail catheter. In general, pressure returns normal after 100-200 ml of blood are fast aspirated. Sometimes a small drainage is maintained following anticoagulation reversion and patients need to be monitored for ongoing bleeding with the drainage catheter for at least 12 hours post ablation. Rarely, high volume of drainage is maintained needing blood reposition. In this condition is important to have access to cell saver system to minimize blood transfusion and save time to organize a surgical repair. It has been reported that it may be needed in up to 16% of cases of cardiac tamponade following AF catheter ablation.[4,11]

Anticoagulated patients with warfarin or NOAC without interruption for the procedure need special attention. For those on warfarin, infusion of fresh frozen plasma is usually effective, and rarely, a prothrombin complex concentrate is needed.[12] For patients on dabigatran, the reversal agent Idarucizumab is now available to immediately reverse the anticoagulant effects of dabigatran.[13] Patients under rivaroxaban, apixaban and edoxaban can be their effects reversed with Andexanet alfa that is already available in Europe.[14]

Stroke

Cerebral embolism is critical complications of ablation of AF due its possible dramatic consequences. Ischemic stroke events typically occur within 24 hours of the AF ablation procedure with the higher risk period covering for the first two weeks following ablation.[15]

The mean incidence of thromboembolism associated with AF ablation has been reported to be between 1% and 2%.[2,3] However, introduction of rigid pre, intra and post procedural managements for stroke prevention have reduced the incidence in most centers to less than 1%.[7,9,15] In 26 (0.8%) embolic stroke events that occurred in a series of 3060 patients, severe impairment in long-term neurologic outcomes occurred in 3 (0.1%) patients; moderate impairment in 10 (0.33%), mild impairment in 9 (0.3%) and they were unknown in 4 (0.13%) patients.[16,17]

Clinical and technical aspects are implicated in the risks for a thromboembolic event during an AF ablation procedure. Patients with paroxysmal AF, small LA, with a low CHA2DS2-Vasc score and in sinus rhythm in last weeks prior ablation have lower risk in comparison to those in persistent AA, larger LA and higher CHA2DS2-Vasc score. Five main mechanisms may be also involved in the development of thromboembolic stroke during AF ablation: 1 – thrombus already formed before the procedure and dislodged during LA catheter manipulation or electric cardioversion; 2 – thrombus formation in trans-septal sheaths or on the ablation catheters positioned within the LA; 3 – thrombus formation at the tip of the ablation catheter during

RF delivery; 4 – thrombus formation at the ablation area due endothelium damage; and 5 – thrombus formation due to the prothrombotic state that occurs after ablation. The atria may be stunned for weeks post-procedure, leading to thrombotic conditions.

How to prevent

Stroke events have been reduced after applying strict preventive protocol that involve: pre-procedural anticoagulation strategies; transesophageal echo (TEE) before the procedure; full anticoagulation with rigid intra procedural control; careful attention to sheathes management and radiofrequency energy delivery to avoid char and clothes formation; and maintenance of effective anticoagulation in following weeks after AF ablation independently of CHA2DS2-Vasc score.[18,19]

Anticoagulation for at least 3 weeks prior ablation is frequently used in patients who have CHA2DS2-Vasc risk score of 2 or greater, especially if they are likely to be in AF at the procedure. However, it does not exclude the role of prior TEE before the procedure. TEE performed prior ablation in patients under anticoagulation have identified 1 to 2% of thrombus in LAA, manly in patients with persistent AF, larger LA and high CHA2DS2-Vasc score.[20]

Uninterrupted warfarin (without enoxaparin bridge) has been used by many centers since comparison studies showed lower bleeding complications, especially at the site of vascular access.[12] New oral anticoagulants have also been increasingly used since several meta-analyses have demonstrated similar efficacy and safety of dabigatran and the factor Xa inhibitors compared to warfarin for embolic prevention after prior and after catheter ablation.[21,22]

IV heparin is essential to prevent thrombus formation during the procedure. Around 10 000 IU is generally administered prior to or immediately after trans-septal punctures in order to avoid thrombus formation on the trans-septal sheath or on electrode catheter.[23] ACT is regularly checked every 30 min and additional IV heparin is infused to maintain ACT (activated clotting time) around 350 sec. A recent meta-analysis demonstrated that targeting ACT > 300 sec decreased the risk of thromboembolic complications without increasing the rate of bleeding.[24]

How to recognize

Symptomatic cerebral thrombo-embolic event is usually dramatic when ischemia or infarction results from arterial occlusion of an important cerebral artery. In such circumstances a clear motor deficit, dysphasia, dysarthria or disorientation are observed during the procedure, if patients are under sedation; or soon after they awake from anesthesia. Minor manifestations occur when smaller arterioles are involved, exception for ischemia of sensitive organs resulting in immediate visual or vestibular disturbs. In other circumstances patient may present even multiple small embolisms without significant neurologic manifestations. These asymptomatic cerebral embolisms have been related to future cognitive deficits.[25]

How to manage

The treatment of acute stroke detected after AF ablation procedures has traditionally been managed conservatively, however, recent observations suggest that an aggressive early management of acute stroke may attenuate their consequences, with either thrombolytic drugs or percutaneous interventional techniques.[26]

Pulmonary vein stenosis

The PV stenosis was the most important complication on the beginning of the experience with AF ablation when the strategy was focused on RF ablation of the foci deep inside of the PVs. At that time the incidence of PV stenosis reached up to 40% of the cases with huge consequences.[27,28]

Fortunately, this scenario has changed after moving the PV isolation strategies avoiding ablation inside the PVs. Ablation inside the PVs was associated with more than 5 fold risk for PV stenosis risk when compared with ablation outside the veins.[29]

Currently the incidence of symptomatic PV stenosis in high volume centers using PV antral isolation and performed by skilled operators is close to zero, although the incidence of asymptomatic PV stenosis still is not negligible.[30]

How to prevent

Antral ablation strategy changed completely the risk for PV stenosis in patients undergoing RF AF ablation. However, as the risk for esophageal lesions has become clear with antral ablation, some operators opt to go inside of a specific PV veins in close relation to the esophagus. This strategy eventually may increase the risk of PV stenosis even in the era of PV antral ablation. Patients undergoing to multiple procedures also have a higher risk of PV stenosis. Thus, PVi integrity evaluation by CT or MRI before repeating a procedure is essential.

Cryoballoon AF ablation strategy also has a low risk of PV stenosis using new generation big balloon as recently demonstrated in the randomized trial RF vs. Cryoballoon.[9]

How to recognize

PV stenosis symptoms may simulate different clinical situations as pulmonary embolism, pneumonia and cancer. They usually occur weeks to months after the ablation procedure and in general when there are two or more PVs involved. Common symptoms are cough, chest pain, dyspnea, hemoptysis, recurrent pulmonary infections and new pulmonary hypertension,[31] It is important to have in mind that severe stenosis can also remain asymptomatic, mainly when just one PV is involved.[32]

The severity of PV stenosis has been graduated according to the percentage reduction of the luminal diameter in mild (<50%), moderate (50%-70%), and severe (>70%). PV stenosis may progress in following 3 to 6 months after RF ablation. That is why early images examinations showing mild stenosis after of the procedure does not guaranty absence of important PV stenosis during a long term follow-up.

Many images methods may be used to confirm pulmonary vein stenosis diagnosis as CT imaging, MRI, perfusion scans, TEE or pulmonary venography. CT scan is usually preferred to define location and severity of PV lesions.[27,28]

How to manage
When one has a patient with a symptomatic PV stenosis he learns the importance of avoiding PV stenosis during PV ablation, once this treatment may be very complicated even by using interventional procedures. This is the reason why asymptomatic or mild symptomatic patients even with severe PV stenosis are usually managed conservatively.

Once the procedure is usually complex, pulmonary perfusion images are useful to identify the culprit(s) vein(s) to minimize excessive interventions and complications in patients with multiple PVs involved.[33]

Successful PV angioplasty or stenting usually results in a significant relief of symptoms; therefore, PV angioplasty is usually indicated in patients with limiting symptoms. However, PV restenosis may occur in up to 50% of patients after acute successful angioplasty. It seems that higher size stent ($\geq$10 mm) and drug-eluting stents present better results.[33,34]

There is no specific trial investigating the management of patients after PV stenting regarding anticoagulation and antiplatelet therapy. However, oral anticoagulation associated with Plavix and ASA for 6 weeks and subsequently ASA for lifetime has been suggested based on experience on coronary angioplasty studies. The most severe complications of PV stenosis interventions include cardiac tamponade, massive bleeding secondary to PV-rupture, stent thrombosis and embolization.[33,34]

Data from surgical procedures are very limited and they have been recommended just for very symptomatic patients with multiple PV stenosis and recurrent restenosis after interventional treatment.[35]

Phrenic nerve palsy

As PV stenosis in the past, right phrenic nerve palsy used to be an important complication of AF ablation when RF ablation was performed inside of right PVs. Currently, this complication has been reported in less than 0.5% when the isolation of right PV is not obtained during PV antra isolation and RF ablation is performed inside at carina the right PVs.[3,9,36]

Right phrenic nerve palsy risk has emerged more recently as an important complication again with the advent of cryoballoon PV isolation with an incidence of transient phrenic nerve palsy between 3.5 to 11%. Fortunately, with improved experience, permanent phrenic nerve palsy has been observed in few patients.[37,38] The reported incidence of persistent phrenic palsy was 0.3% in the Fire and ICE Trial.[9]

Attempts to isolate the superior vena cava have a higher risk (up to 10%) of right phrenic palsy.[39] Therefore, location of right phrenic nerve should be mapped before superior vena cava isolation in order to decide the risk and benefits ratio of performing such procedure. Rarely, left phrenic palsy may occur during RF ablation on the anterior wall of the LA appendage.

How to prevent
The most frequent strategy employed to prevent phrenic nerve palsy is to avoid delivering RF in recognized sites close to phrenic nerve. In that sites, the close proximity can be identified by delivering a high-output pacing that captures the phrenic nerve.

During cryoballoon ablation on right PVs the risk of phrenic palsy is considerable. Thus, cryoenergy is delivered under monitoring of diaphragmatic excursion with abdominal palpation during a high-output pacing in superior vena cava or right subclavia vein that captures phrenic nerve. Energy delivery is interrupted immediately when diaphragmatic excursion decreases. Using this maneuver most of phrenic palsy that occur is transitory.[40]

How to recognize
Absence or diaphragm excursion on fluoroscopy is the typical signal of phrenic nerve palsy during the procedure. Physical examination easily reveals paradox respiratory movement in abdomen and pulmonary auscultation shows absence of murmur in the right thorax. Most patients complains dyspnea soon after the procedure, however in few cases it may be asymtomatic.[39] The diagnosis is confirmed by new-elevated right diaphragm in post-procedure chest radiograph, fluoroscopy or ultrasound.

How to manage
Fortunately, most phrenic nerve injuries are transient and solves within minutes when diaphragmatic movements are monitored and ablation energy stopped. The risk for persistent palsy is higher when patient is under anesthesia and diaphragm movements are not monitored.

Most patients with persistent nerve palsy at hospital discharge recovers diaphragm movements in the follow weeks after ablation. A meta-analysis of 22 studies including 1308 patients who underwent cryoballoon ablation showed 4.7% of persistent phrenic nerve palsy at hospital discharge. However, only 0.37% had maintained their paralysis after 1-year.[39]

Unfortunately, there is no recognized treatment that can accelerate phrenic nerve recovers. However, respiratory physiotherapy improves clinical and functional status and should be recommended to all symptomatic patients.

Atrial esophageal fistula

The LA has a close anatomical relationship to the esophagus. Catheter ablation on the LA posterior wall may thermally damage the esophagus and eventually generate an esophageal ulcer that rarely may progresses to an atrial esophageal fistula (AEF) with catastrophic consequences.[41]

The occurrence of AEF as a consequence of AF catheter ablation was first described in 2004 after RF strategy changed from ostial to antral PV isolation.[42,43] The incidence of AEF post-ablation of AF is supposed to be around 0.1% of the procedures.[44] A recent study involving 8 centers in Brazil identified 10 cases of AEF (0.116%) in 8500 procedures in the period of 2004 to 2015.[45] Interesting, two cases representing an incidence of 1%, occurred in 2003 and 2004, when strategy to isolate PV was changed to antral PV isolation and AEF was still not recognized as a complication of AF catheter ablation. Other eight cases occurred from 2005 to 2015, representing an incidence of 0.1% after most groups introduced preventive measures such as reduced power during posterior wall ablation, monitoring temperature of the oesophageal, use of PPI and sucralfate after ablation. However, paid attention that four AEF cases occurred in the last

2 years of observation (2014 and 2015), when new technology to perform deeper lesions were introduced and representing an incidence of 0.23%, higher than in previous years.

How to prevent

Many groups do not use a specific method to prevent esophageal lesions beyond reducing RF power while ablation on LA posterior wall and performing the procedure with patient in conscious sedations since the esophageal pain induced by RF application warns the electrophysiologist for the risk. However, most centers monitor esophageal temperature to prevent thermal esophageal lesions.[46] An increase in esophageal temperature determines prompt interruption of the application and reducing the power and time in subsequent applications. However, different centers disagree about the limit of the temperature to interrupt the application, ranging from an increase in 1°C from the initial temperature to the limit 41°C.[47]

An important limitation of linear thermometer is that the absence of a critical elevation in esophageal temperature does not necessarily mean that the esophagus is distant, since due to its anatomical characteristics, it may monitor only one part of its lumen failing to measure the actual temperature of the contralateral margin. Another esophageal thermometer with multiple electrodes distributed along a probe with a sinusoidal format has been used to occupy all surface of the esophagus. The clinical use of this second system has shown higher sensitivity and readiness to detect increases in esophageal temperature, however, comparative studies are needed to clarify they benefit.[47] Another proposal still in evaluation is to move the esophagus with a mechanical system.[48,49]

The rate of esophageal erosion varies between 5 and 40% when upper gastrointestinal endoscopy is systematically performed in the days after the ablation, depending on the techniques used during the procedure.[41,44]

Cryo balloon ablation was supposed to be safer than RF regarding initial experience with first-generation balloons (23 mm) with no AEF reports. However, AEF has been reported with 28-mm second-generation balloons that present more powerful cooling at the PVs antra.[50] The occurrence of AEF has also been reported in patients in which PV isolation was performed by a circular and irrigated multielectrode system.[51]

How to recognize

Symptoms of AEF classically occur between 2 to 4 weeks after the ablation and they initially seem innocents. They include mild retrosternal discomfort, low fever, and mild leukocytosis without an apparent cause. If the process is not diagnosed and interrupted, it evolves rapidly to septicemia, hematemesis and cerebral septic embolism.

Complete recovery of the patient is rare when symptoms of AEF are completely manifested and most patients are unable to survive. Therefore, clinicians following up patients after AF ablation must be aware about the AEF symptoms and should make rapid decisions to make the diagnosis and start treatment.

Regular upper gastrointestinal endoscopy performed 24-72 hours after the ablation might identify patients with esophageal lesions and in risk however the cost-effectiveness of this approach has not been studied. Also there are no defined guidelines for the management of patients with esophageal lesions identified after AF ablation, just as there are no clinical studies proving the efficacy and safety of the procedures that have been used.

Chest computed tomography (CT) with oral contrast is the best method to investigate a possible fistula formation. Esophagoscopy should be avoided in this situation due to the risk of gas embolization if a fistula is present. Classical signs found on CT are the presence of gas images or infiltration of contrast in the mediastinum or pericardium.

How to manage

High doses of proton pump inhibitors (omeprazole or pantoprazole, 40 mg twice a day) for 30 days have been recommended to reduce the reflux of acid to the esophagus after ablation, independent of the findings of the esophageal temperature monitoring during the procedure.

Sucralfate 2.0 g may be added between meals in patients with esophageal lesions as erythema, erosion, and hematoma; additionally, a pureed light diet is also recommend. Bromopride 10 mg three to four times a day for 30 days may be helpful to improve the symptoms of gastroparesis.[52]

The patient must be admitted in hospital if presents fever, remaining fasting and monitored with leukogram and biochemical markers of inflammatory response. Patients without evidence of infection and normal CT are maintained in the hospital for monitoring while receiving clinical treatment for the ulcer.

Patients with an infectious response but without defined AEF at CT must be maintained in prolonged fasting along with parenteral nutrition, receiving atropine to reduce salivary secretion and broad- spectrum antibiotic therapy. A gastric surgery team must be called for a close follow up the patient because an emergency intervention may be required.[53]

CT or magnetic resonance imaging (MRI) scan is repeated 1 week later to monitor AEF progress. In the event of image evidence or clinical signs of fistula formation as cerebral embolism or hematemesis, the patient must be operated on immediately. A complete clinical recovery is possible when the procedure is performed early; otherwise, the rates of death or definitive impairments are high when it is postponed.[53]

Conclusions

In conclusion, catheter ablation is considered the most effective treatment of AF, and applied worldwide nowadays. Despite that, physicians should be aware about the risks and let their patients informed. It may promote an early identification of important complications, which is essential to permit a prompt treatment and to obtain a complete recovery of the patients.

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