ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 10, Issue 12, Dec-2023 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980

ATRIAL FIBRILLATION:MODERN APPROACH TO TREATMENT

Kuchkarov B.O
Assistant of the department of "Internal medicine"
Andijon State Medical Institute
Uzbekistan,Andijon

The primary trigger for most episodes of atrial fibrillation (AF) is an electrical discharge(s) within one of the four pulmonary veins. The cornerstone of any procedure aimed at reducing AF burden is the electrical isolation of the pulmonary veins so that these discharges do not trigger the initiation of AF. In those with persistent and longstanding persistent AF, and in some patients with paroxysmal AF, additional areas, often in one or both of the atria or surrounding structures, are targeted for ablation, as they may also serve as a source of AF triggers or maintenance. Catheter ablation (CA) is the procedure that is used to prevent the initiation of AF by electrically isolating these triggers from the rest of the atrial chamber tissue.

Once a patient has been selected for AF ablation, the clinician performing the procedure or their designee should obtain informed consent from the patient. This involves shared decision-making after discussing the indications, benefits, risks, and alternatives of the planned procedure. Sedation options include general anesthesia that requires an endotracheal tube or monitored anesthesia care with sedation but not requiring intubation. Most procedures are performed under general anesthesia.

Medication management — Most physicians performing ablation will discontinue antiarrhythmic drugs prior to the ablation with the rationale that it may help to identify the triggers of the AF at the time of the procedure. We acknowledge that many other electrophysiologists will continue them. There are no well-performed studies to guide practice.

With regard to oral anticoagulation, randomized trials have demonstrated superior efficacy and safety of uninterrupted anticoagulation throughout the ablation procedure compared with temporary discontinuation of anticoagulation and bridging with low molecular weight heparin.

Ablation techniques and targets

Energy sources — There are three US Food and Drug Administration (FDA)-approved energy sources for AF ablation: radiofrequency energy, cryothermal energy in the form of cryoballoon, and laser balloon. This issue is discussed in detail elsewhere.
Pulmonary vein isolation — Complete electrical isolation of all PVs using circumferential, wide area pulmonary vein isolation (PVI) is the goal of most procedures. The following explains the rationale.
The initiation of AF requires a trigger either within or near the atrium (eg, PVs, crista terminalis, superior vena cava), and substrate within the atrium to maintain AF [9] .The anatomic significance of triggers and substrate differs somewhat, depending upon whether the AF is paroxysmal, persistent, or permanent. In patients with paroxysmal AF, PV triggers are the primary stimulus in most cases. As AF becomes more persistent, non-PV sources become more important [2]. The following important observations regarding triggers came from early studies of patients with paroxysmal AF and have guided the development of successful ablation techniques for AF [2-3].

- AF is commonly triggered by ectopic beats from muscle fibers (fascicles) extending from the left atrium into the PVs.

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- Ectopic foci are localized to the PVs in approximately 90 percent of patients with predominantly structurally normal hearts [3].
- Most patients have multiple foci that can act as triggers.
- Most (94 percent) of the foci are 2 to 4 cm inside the PVs, with the left superior vein being the most common site [2].
- The remaining foci are usually in the right or left atrium. The superior vena cava is a much less common site of triggering ectopic beats [2].

Because of these observations, early attempts at ablation targeted these focal ectopic beats within the PV [2]. This approach was limited by:

- Inconsistent ability to identify the triggering beats during electrophysiology study.
- Difficulties with precise localization of appropriate ablation sites.
- The risk of PV stenosis, which can occur following ablation within the PVs

These limitations lead to the adoption of ablative techniques focused on the complete electrical isolation of all PVs using circumferential wide area PVI. The majority of ablations performed use radiofrequency energy or cryothermy (cryoballoon ablation). Infrared laser received FDA approval in 2018.

Circumferential PVI involves the creation of confluent ablation lesions that encircle the ostia of all four PVs, usually in two pairs (ie, a left- and right-sided circles) [2-4]. The goal is to electrically isolate the PVs from the left atrium. For ablation using radiofrequency energy, power, duration, and the catheter contact force determine the size and the depth of the lesion created. It is generally felt that some lesions create edema but not scars, leading to temporary but not permanent ablation, and this ultimately leads to electrical reconnection of the left atrium to the PVs. Greater power, longer duration, and greater contact force improve the efficacy of the procedure but lead to an increase in complications such as cardiac perforation [5,6]. The efficacy and safety of high-power, short-duration ablation, which creates larger, shallower, and more homogeneous lesions, is under evaluation [7]. Circumferential PVI results in extensive ablation across a wider area of the left atrium. Because of the more extensive ablation, this technique may provide additional methods for preventing AF, including autonomic denervation, elimination of triggering foci outside the PVs, and alteration of the left atrial substrate necessary for perpetuating AF. However, more extensive ablation, particularly in the posterior left atrium, may increase the rate of complications, including the development of left atrial tachycardias or flutters months or years after the ablation. The relative efficacy and safety of these methods are discussed elsewhere.

Use of a contact force-sensing catheter — We use a contact force-sensing catheter in all patients with AF undergoing radiofrequency CA (RFA). The TOCCASTAR study found that patients who underwent CA with this catheter and who received a higher force (≥10 grams) had significantly lower rates of AF recurrence at one year.

Use of adenosine-guided pulmonary vein isolation — The administration of intravenous adenosine can be used to unmask dormant conduction at the time of CA. Reconnection rates are high in RFA, with three large studies finding rates of 21 (ADVICE), 27 (UNDER-ATP), and 34 percent [3-4]. The use of adenosine to guide additional CA has been shown to improve arrhythmia-free survival in some studies using RFA. Some technical aspects of the procedure are discussed separately.

In the ADVICE study, 534 patients with paroxysmal AF who had failed drug therapy underwent a standard PV isolation procedure using radiofrequency energy [3]. Patients were observed for spontaneous recovery of conduction over 20 minutes to allow for reconnected PVs to be reisolated before adenosine administration. Intravenous adenosine was then given to all patients. The 284

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patients in whom dormant conduction (evidence of persistent PV conduction) was unmasked by adenosine were randomly assigned to additional adenosine-guided ablation to abolish dormant conduction or to no additional ablation. Among the 250 patients without dormant conduction, 117 were enrolled in a registry. The primary endpoint of the time to first recurrence of symptomatic electrocardiographically documented atrial tachyarrhythmia was between 91 and 365 days. The following findings were noted:

- Dormant PV conduction was present in 284 (53 percent) of patients.
- Freedom from symptomatic atrial tachycardia occurred more often with adenosine-guided further ablation (69.4 versus 42.3 percent; hazard ratio [HR] 0.44, 95% CI 0.31-0.64).
- Among patients in the registry, approximately 56 percent remained free from symptomatic atrial tachyarrhythmia.
- The rate of serious adverse events was similar in both groups.

Limitations of this study include lack of generalizability (does not apply to patients undergoing cryoablation), lack of use of force-sensing catheters, which are used by many of our experts, and the use of "dormant connection" as an endpoint rather than AF recurrence.

In the UNDER-ATP trial, 2113 patients with paroxysmal, persistent, or long-lasting AF were randomly assigned to either adenosine-guided PV isolation (1112 patients) or conventional PV isolation (1001 patients) [3]. The primary endpoint was recurrent atrial tachyarrhythmias lasting for >30 seconds or those requiring repeat ablation, hospital admission, or usage of Vaughan Williams class I or III antiarrhythmic drugs at one year with the blanking period of 90 days post-ablation. Among patients assigned to adenosine-guided PV isolation, adenosine provoked dormant PV conduction in 307 patients (27.6 percent). Additional radiofrequency energy applications successfully eliminated dormant conduction in 302 patients (98.4 percent). At one year, 68.7 percent of patients in the adenosine-guided PV isolation group and 67.1 percent of patients in the conventional PV isolation group were free from the primary endpoint, with no significant difference (adjusted HR 0.89; 95% CI 0.74-1.09; p = 0.25).

The results were consistent across all the prespecified subgroups. Also, there was no significant difference in the one-year event-free rates from repeat ablation for any atrial tachyarrhythmia between the groups (adjusted HR 0.83; 95% CI 0.65-1.08; p = 0.16).

Based on these studies, the use an adenosine in patients undergoing CA with radiofrequency energy is at the discretion of the operator.

Confirmation of complete isolation — Unlike many other cardiac ablation procedures, AF does not need to be present or induced at the time of the ablation procedure nor is termination of AF or inability to reinduce the arrhythmia a required endpoint of the procedure. For PVI, acute procedural success is defined as electrical isolation of all PVs [4]. This is defined by entry block or the inability to electrically capture PV myocardial tissue distal to the area of ablation when pacing is performed proximal to the ablation line. To do this, a circular catheter is positioned just distal to the PV ostium for the purpose of recording electrograms within the PVs. Confirmation is attempted after a 30-minute waiting period after isolation.

Some operators also test for exit block, defined by the inability to capture atrial myocardium when pacing is performed within the PV distal to the ablation line. There is a high correlation between AF recurrences and the demonstration of persistent or recurrent conduction between the PVs and left atrium Recurrent PV conduction explains most cases of recurrence; it is thought to be due to recovery of function of tissue that has been acutely injured (ie, edema and inflammation) but not permanently

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scarred. Administration of adenosine has been shown to identify PVs with dormant conduction by transiently restoring excitability and conduction across circumferential ablation lines at risk of reconnection [10]. However, improvements in ablation tools and techniques have significantly reduced the routine use of adenosine. It is used at the discretion of the operator.

Summary and recommendations

- **Pulmonary vein origin of atrial fibrillation (AF)** – The primary trigger for most episodes of AF involves electrical discharges within one or more pulmonary veins (PVs). A principal goal of any procedure is to reduce the frequency of AF and electrically isolate the PVs so that these discharges do not activate atrial tissue.
- **Clinical goal of catheter ablation (CA)** – The major clinical goal of CA is a reduction in AF-related symptoms. CA is superior to medical therapy at improving a patient's quality of life. Therefore, it is generally reserved for individuals with symptoms attributable to the arrhythmia, which most often include palpitations, shortness of breath, or generalized fatigue. Even if they have no AF-related symptoms, older individuals with early AF (duration <1 year) and additional cardiovascular conditions also benefit from therapies aimed at maintaining sinus rhythm; these therapies include CA.

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