Venice Chart International Consensus Document on Atrial Fibrillation Ablation: 2011 Update

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For the Venice Chart composition (Committees, members, affiliation) see Appendix.

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Introduction

This Venice Chart International Consensus Document on atrial fibrillation (AF) ablation represents an update of the initial document published in the *Journal of Cardiovascular Electrophysiology* in 2007.[1] Since then, many technological developments and progress have been made and AF ablation has become a well-established, widespread treatment for patients with AF.

Anatomy of Structures Relevant to Atrial Fibrillation Ablation

Over the last decade, ablation of AF has focused on the left atrium (LA) and this has stimulated further investigation on gross and microscopic anatomy of the LA and of the neighboring structures. Knowledge of their architecture and mutual relationships is necessary to access, map, and ablate the LA in a safe and successful way.

The anatomy and position of the fossa ovalis are major determinants for the electrophysiologists' ability to safely access the LA through transseptal catheterization. The dimensions of the fossa ovalis (average vertical diameter of 19 mm, average horizontal diameter of 10 mm, thickness of 1–3 mm)[2] allow a safe double transseptal puncture. Table 1 reports the congenital or acquired disorders of the chest and cardiovascular structures possibly affecting the location of the fossa ovalis and, therefore, resulting in a more difficult transseptal access. Similarly, multiple previous transseptal catheterizations causing fibrosis of the fossa ovalis are the major variables associated with difficult puncture and penetration of the transseptal needle.[3] Transseptal catheterization in the presence of a device occluding the fossa ovalis is possible, because its position is more cranial as compared to the fossa ovalis position.[4] However, a careful approach and additional imaging are mandatory.

Three-dimensional (3D) imaging of the LA and pulmonary veins (PVs) shows a wide range of variants of their anatomy.[5] Specifically, the typical PV branching pattern with 4 distinct PV ostia (Fig. 1C) is present in approximately 20–60%, while a very frequent anatomical variant is the presence of a short or long common left trunk, observed in up to 75–80% of cases. The presence of supernumerary PVs, mainly right middle PV or right upper PV, is reported in 14–25% of cases. The criss-cross of myocardial fibers and the increased thickness of the muscular sleeves at the interpulmunary isthmus between the orifices of the ipsilateral PVs with the possibility of epicardially located intervenous muscular connections (Fig. 1B) may represent the anatomical basis for the complexity to achieve a permanent PV isolation by ablation techniques.[6] Another critical structure for ablation procedure is the ridge or carine between LA appendage and left PVs (Fig. 1A). The ridge may be flat, round, or pointed

TABLE 1

Congenital or Acquired Disorders of the Chest and Cardiovascular Structures Potentially Affecting the Location of the Fossa Ovalis

–Kyphoscoliosis
–Straight back syndrome
–Pectus excavatum
–Obesity
–Persistence of left superior vena cava
–Pericardial agenesia
–Dextrocardia
–Aortic or mitral valve disease
–Marked dilatation of the ascending aorta
–Marked left ventricular hypertrophy
–Previous cardiac surgery

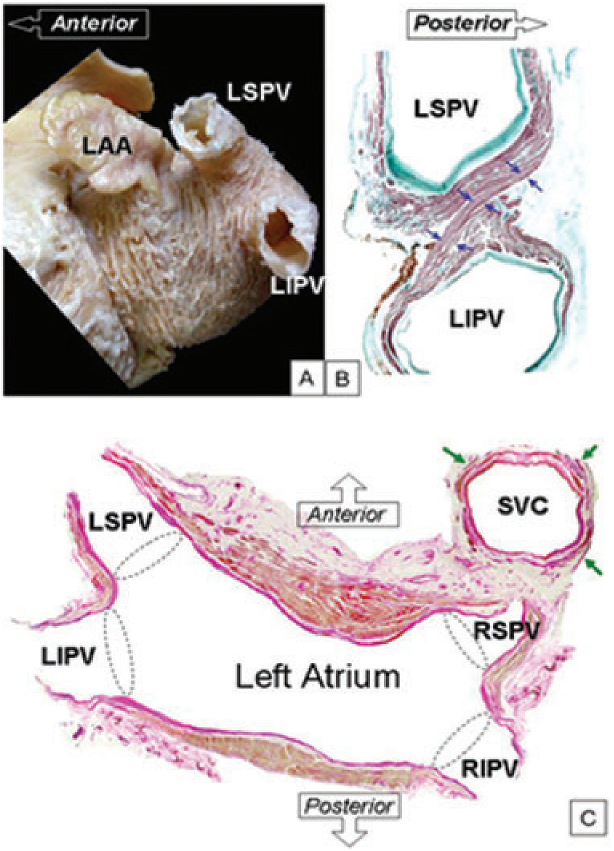

Figure 1. *(A) The left atrium viewed from the left side and dissected to show the myocardial strands extending over the left superior and inferior pulmonary veins (LSPV, LIPV). The left atrial appendage (LAA) is finger-like in shape. (B) This histologic section taken through the left pulmonary veins shows myocardial strands crossing between the veins (blue arrows). Masson's trichrome stain. (C) This histologic section shows the 4 pulmonary veins with myocardial extensions (stained brown) over the outer surface of the veins. The ovals indicate the veno-atrial junctions. Note the non-uniform thickness of the left atrial walls. The superior caval vein (SVC) is seen in cross section with its myocardial sleeve (green arrows). Elastic van Geison stain. RIPV, RSPV = right inferior, right superior pulmonary veins.*

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TABLE 2

Key Points Regarding the Anatomy of Structures Relevant to AF Ablation

–Some congenital and acquired disorders of the chest and cardiovascular structures, multiple transseptal catheterizations, and the presence of a device occluding the fossa ovalis are all potential causes of more difficult transseptal access.
–Owing to the wide range of anatomical variants, 3D reconstruction of LA and PVs by means of imaging techniques is considered essential to perform AF ablation in a safe and successful way.
–Understanding the anatomical relationship between the LA and both the esophagus and the phrenic nerves is crucial to avoid collateral damage of these structures during AF ablation.

in profile and is <5 mm wide in 75% of hearts suggesting that achieving catheter stability for adequate contact can be challenging most cases.

Understanding the anatomic relationship between the LA/PV orifices and the left atrial ganglionated plexi (GP) explains how ablation in the LA not only results in PV electrical disconnection but it may cause also modification of the autonomic tone influence with an impact on the electrical activity.[7] Transmural lesions[8] in the medial region of the LA, septum and/or proximal coronary sinus (CS) may disrupt interatrial conduction pathways alternative to conduction over the Bachmann's bundle and, consequently, alter the postablation atrial propagation pattern.

The very strict anatomical relationship between the LA and both the esophagus and the phrenic nerves[9,10] is the major cause of concern of collateral damage to these 2 structures during AF ablation, resulting rarely in severe patient injury. Assessment of the individual anatomy, reduced power and continuous monitoring of the effect of ablation on these structures are all possible means to avoid their permanent or severe damage.

The key points regarding the anatomy of structures relevant to AF ablation are reported in Table 2.

Pathophysiology of Atrial Fibrillation

The pathogenesis of AF is often multifaceted and the arrhythmia may develop in different disease conditions as well as in the normal heart. It is well recognized that increased atrial mass, decreased conduction velocity, and decreased atrial refractoriness with increased dispersion are all pro-fibrillatory factors. Irrespective of the underlying mechanism, the onset and maintenance of AF requires an event (trigger) that initiates the arrhythmia and the presence of a predisposing substrate that perpetuates it. Additional factors (e.g., inflammation or autonomic tone) may also cooperate as "modulators" in facilitating initiation or continuation of AF.

Diseases Associated with AF and the Role of Fibrosis

Although approximately 10% of AF patients have no evident cardiac disorder (so-called "lone" AF), the arrhythmia usually occurs in patients with structural heart disease. Hypertension, coronary heart disease, valvular heart disease, dilated cardiomyopathy, and heart failure are the most frequent pathological conditions associated with AF. Atrial enlargement is often present, although it is difficult to establish if it represents the cause or the consequence of AF. Atrial fibrosis and loss of myocardial tissue may be either a substrate for AF (due to coexisting heart disease) or a result of fibrillating atria and part of the so-called structural remodeling.[11]

Genetic Factors and Ion Channel Diseases

A number of studies provide irrefutable evidence for a genetic component in the case of lone AF.[12] Genetic linkage analyses have revealed AF chromosome loci for genetic defects in various potassium channels and the gap junctional protein Connexin40.[13] Relatively rare forms of familial AF have also been associated with inherited channelopathies such as Brugada, long QT and short QT syndromes, as well as with cardiomyopathies.[13,14]

Electrophysiological Mechanisms

Increased automaticity and single and multiple circuit reentry can cause AF. These mechanisms are not mutually exclusive; it is likely that areas of focal firing and areas of reentry are present simultaneously in varying degrees in the majority of patients.

AF Triggers and Sources

The PVs are an important source of ectopic beats; they are capable of initiating frequent paroxysms of AF, which can be eliminated by treatment with radiofrequency ablation.[15] Other anatomical structures that may also provide ectopic beats triggering AF are the superior vena cava, the vein of Marshall, the musculature of CS, the posterior wall of the LA, and LA appendage.[16]

The Third Dimension

The 3D anatomical structure of the atrial muscle is likely to be a crucial factor in determining the ultimate fibrillatory behavior. Indeed, high frequency stimulation of the PVs originates wavebreaks in areas of abrupt fiber orientation and wall thickness changes in the posterior wall of the LA.[17]

Role of the Autonomic Tone

The autonomic tone is thought to play an important role in the pathogenesis of AF. Vagal stimulation shortens refractory period, and sympathetic stimulation increases calcium loading and automaticity. Combined, these actions result in early afterdepolarizations and triggered firing that may initiate AF.[18-21] Interruption of nerves from the GP to the PVs may explain the frequent elimination of focal firing produced by PV isolation procedures during ablation therapy. These findings support the role of GP activity in the onset and perpetuation of AF, and may explain the success of early ablation studies targeting only the GP.[22]

Structural and Electrical Remodeling

Once established, AF begets AF through a self-perpetuation process called structural and electrical remodeling.[23,24] At the structural level, AF causes atrial fibrosis, dilatation, increased compliance, and reduced contractility. Ultrastructural changes of myocytes lead to the so-called dedifferentiation, because myocytes return to the fetal phenotype.[11] At the electrical level, progressive shortening and dispersion of refractory periods are the main changes occurring during AF.

The key points regarding the pathophysiology AF ablation are reported in Table 3.

TABLE 3

Key Points Regarding the Pathophysiology of AF

–The pathogenesis of AF is often multifaceted. Increased atrial mass, decreased conduction velocity, and decreased atrial refractoriness with increased dispersion are all profibrillatory factors.
–The onset and maintenance of AF requires an event or trigger (usually ectopic beats originating in the PVs or other anatomical structures) that initiates the arrhythmia and the presence of a predisposing substrate (atrial enlargement, atrial fibrosis, loss of myocardial tissue, etc.) that perpetuates it.
–Additional factors (e.g., inflammation or autonomic tone) may also cooperate as modulators in facilitating initiation and continuation of AF.
–Once established, AF begets AF through a self-perpetuation process called structural (atrial fibrosis, dilatation, etc.) and electrical (shortening and dispersion of refractory periods) remodeling.

Techniques and Technologies for AF Catheter Ablation

At present, multiple approaches for catheter ablation of AF have been developed. The current techniques focus on the elimination of mechanisms involved in the initiation and maintenance of AF, which are essentially represented by triggers (PVs and non-PV foci) and substrate (autonomic and electrophysiologic). The different techniques proposed for catheter ablation of AF include PV isolation, electrogram-based ablation or complex fractionated atrial electrograms (CFAEs) ablation, linear lesions, autonomic GP ablation, AF nests ablation, and sequential ablation strategy.

PV Isolation

"PV isolation" is considered the cornerstone of current AF catheter ablation techniques and is aimed at the electrical disconnection of the PV from the adjacent LA. The PV isolation comprises segmental/ostial PV ablation, circumferential PV ablation, and circumferential/antral PV isolation (Fig. 2).

Segmental/ostial PV isolation

A truly segmental PV isolation requires ablation inside the vein or very close to the output into the atrium[15,25] (Fig. 2A). It is now appreciated that ablation in the PVs themselves needs to be avoided as much as possible, primarily due to concern for development of PV stenosis. Therefore, the segmental/ostial PV isolation technique in the strictest sense has generally fallen out of favor. For segmental/ostial PV isolation, a circular mapping catheter (CMC) of variable diameter (15–25 mm) is inserted into the LA through a long introducer via the transseptal route, and is positioned sequentially at the ostia of the 4 PVs[25] (Fig. 2A). Alternatively, a multielectrode array system can be used. The ablation catheter is positioned at the ostium of the vein on the atrial side; a series of segmental lesions are then created until isolation of the vein can be demonstrated by disappearance of the venous potentials on the CMC (i.e., entrance block). Electrical disconnection of the PVs can be also demonstrated by pacing from inside the PVs (i.e., exit block). Ablation can be performed in sinus rhythm or during AF. The literature data display complete agreement as to the need to achieve isolation of all 4 PVs.

Circumferential PV ablation

Circumferential PV ablation using 3D electroanatomical mapping was initially described by Pappone *et al.*[26,27] Initially, the lesion set was limited to wide (>0.5 cm outside PV ostia) circumferential lesions around and outside the PV ostia but over time it was modified with wider (1–2 cm outside PV ostia) circumferential lesions (Fig. 2C). Radiofrequency (RF) energy is applied continuously on the planned circumferential lines, as the catheter is gradually dragged along the line, often in a to-and-fro fashion over a point. Successful lesion creation at each point is considered to have taken place when the local bipolar voltage has decreased by 90% or to <0.05 mV. This technique, as initially designed, did not involve verification of PV isolation (Fig. 2C). Many other centers have adopted this technique, some of which have added circular mapping to verify PV electrical isolation.

Circumferential/antral PV isolation

The key to this technique for PV isolation is delivery of the ablation lesions to the vestibule or "antrum" of the PV, which is the funnel-shaped portion of the LA (or perhaps more accurately the PV) that is proximal to the PV-LA junction or so called "ostium." The antrum includes the entire posterior wall and extends anteriorly to the right PVs on the septum (Fig. 2B). Various tools, according to operator preference, can monitor the identification of this region during the ablation procedure. *Selective pulmonary venography* is used by many centers to establish the relevant anatomy. *Intracardiac echocardiography* (ICE) offers a better definition of the LA and proximal PV anatomy and allows localizing catheter position.[28] *Computerized 3D mapping and navigation* techniques (Carto, NavX, etc.) are useful means to clarify the anatomy of the region and provide a method of nonfluoroscopic catheter guidance. These techniques might be made more anatomically accurate by registration with other imaging techniques such as *magnetic resonance* (MR) or *computed tomography* (CT). Technologies to perform "near real time" imaging in the EP laboratory, such as with *rotational angiography*, are available and might help to address some of the shortcomings of preprocedural imaging, but to date are still not sufficiently effective to result in widespread adoption.

The use of a CMC for PV isolation procedures has become incredibly widespread. For the CMC guided ablation technique, 1 or 2 (double Lasso technique; Fig. 2D)[29] CMCs are placed within the ipsilateral superior and inferior PVs or within the superior and inferior branches of a common PV during RF delivery. RF ablation is applied until absence or dissociation of all PV potentials are documented by CMCs within the ipsilateral superior and inferior PVs.

RF ablation catheter technologies might include standard tip (e.g., 4 mm), large tip (e.g., 8 mm), and closed or open irrigation. With the use of nonirrigated or closed-irrigation ablation catheter technologies, many centers employed ICE during lesion delivery to assess for the formation of microbubbles[30] and to monitor in this way tissue overheating.[31] With the use of open-irrigation ablation catheters this is no longer relevant.

New tools and techniques to perform PV isolation

There has been development of new technologies to assist the operator with PV isolation for AF catheter ablation.

Various *balloon-based technologies* have been under investigation, generally designed specifically to deliver arcs or circumferential lesions at the PVs.[32] Such technologies

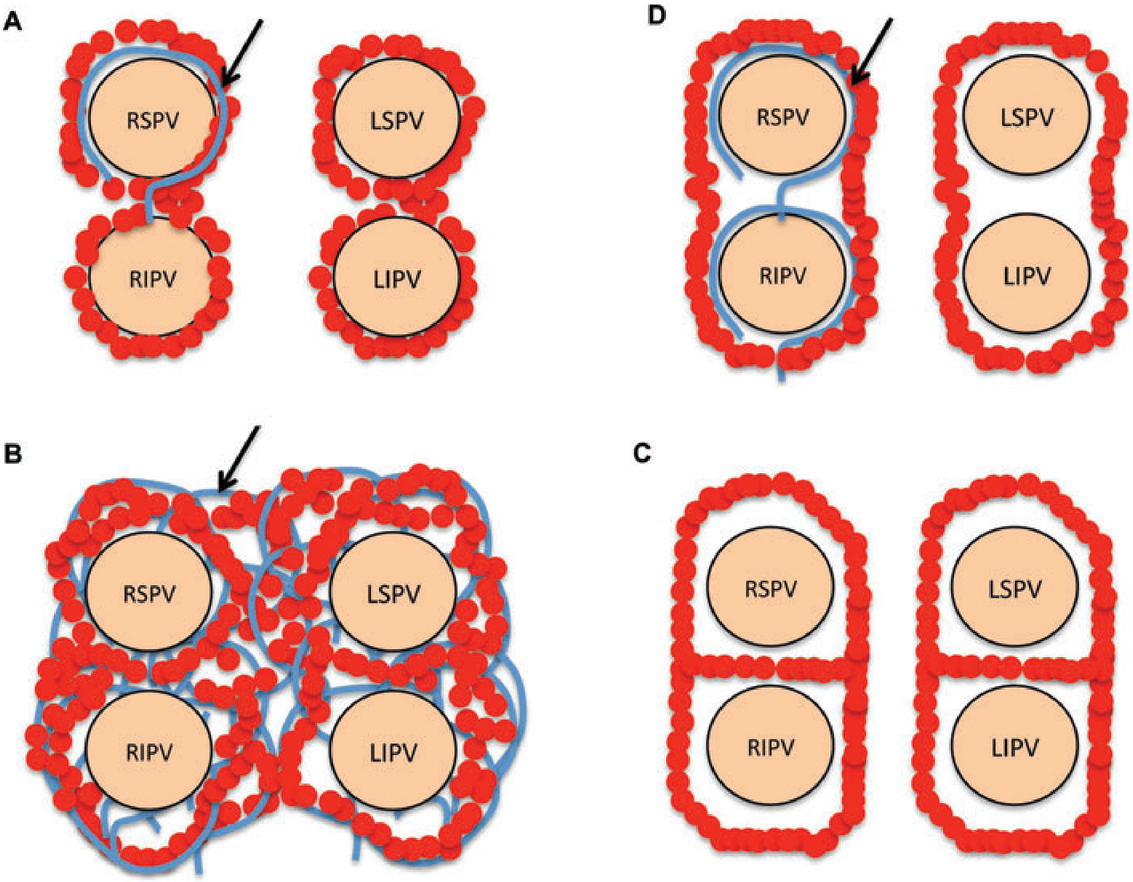


Figure 2. *(A) Segmental/ostial isolation: the isolation of PVs is performed at level of the ostium (black ring) and verified by means of a CMC (blue ring) sequentially positioned at each PV. The red dots correspond to the application of RF energy. The arrow indicates the CMC. (B) Circumferential/antral PV isolation: the isolation of PVs is performed at level of the antrum and the CMC is moved all around the PVs and the posterior wall of LA. (C) Circumferential PV ablation: the ablation is performed by using a 3D electroanatomical mapping and creating a circumferential lesion around each PV (1-2 cm outside the ostium); verification of PVs isolation by means of a CMC is not strictly required for this technique. (D) Double Lasso technique: the isolation of PVs is performed by means of continuous circular lesions around both ipsilateral PVs and verified by means of 2 CMCs placed within the superior and inferior Pvs. CMC = circular mapping catheter; LIPV = left inferior PV; LSPV = left superior PV; RIPV = right inferior PV; RSPV = right superior PV; PV = pulmonary vein.*

have included the use of cryothermy,[33-35] laser,[36,37] ultrasound,[38-40] and RF energy.[41-43] Typically these technologies have employed a noncompliant balloon and have suffered from inability to isolate the PVs proximally, particularly at the antrum, but instead achieve isolation more distally at the ostium of the PV or even within the PV itself.[44,45] This latter issue has been the "Achilles heel" of such balloon technologies, as the resulting lesion delivery at such a distal location has been associated with lower efficacy, by not addressing more proximal sites of triggers, and with an increase in complications such as PV stenosis and phrenic nerve damage. Other balloon-based technologies are under development that would employ a compliant balloon to address these shortcomings.[37]

Another new technology has been the development of *catheters with various lengths and shapes* of the effective ablation delivery region. With use of such catheters, delivery of arcs or lines of lesions might be facilitated.[46,47]

Robotic technologies have been developed for use for catheter navigation. Presently, 2 of such technologies are available.[48,49] One technology utilizes magnetic fields to navigate special magnetic catheters. The magnetic field can be manipulated at a remote workstation to direct the tip of the catheter. A significant advantage of the magnetic catheter is the physical property of being quite floppy, with virtually no ability to generate excessive contact force against the myocardium to prevent a risk of perforation. This allows for manipulation of the catheter without or at least with much reduced fluoroscopic guidance. A major limitation of this robotic technology is the inability to control additional catheters, such as the CMC and/or the ICE catheter. The use of this magnetic robotic technology for AF catheter ablation has been reported with comparable efficacy and safety to manual techniques.[50-52] Another robotic technology that has become available is a system that employs a deflectable sheath controlled at a remote workstation. The primary advantage of this system is the ability to use standard catheters rather than specialized catheters as with the magnetic robotic system. However, this system does not offer the safety of the magnetic catheters with regards to potential for excessive forces to the myocardium, so the risk of perforation remains an issue. Reports from centers with extensive experience has demonstrated comparable results to manual methods and reduced fluoroscopy times.[53,54]

Electrogram-Based Ablation or CFAEs Ablation

Different patterns of electrograms have been targeted during radiofrequency catheter ablation of AF.[21,55-64] Among these, CFAEs have been most widely studied. In the initial report by Nademanee *et al*., the definition of CFAE included: (1) atrial electrograms composed of 2 deflections or more, and/or perturbations of the baseline with continuous deflections of a prolonged activation complex over a 10-second recording period, and (2) atrial electrograms with very short cycle lengths ($\leq$120 ms) averaged over a 10-second recording period. Intraoperative mapping of AF has shown that CFAEs are found mostly in areas of slow conduction or at points where the wavelets turn around at the end of arcs of functional block. Such CFAEs have heterogeneous spatial and temporal distribution. Recent studies have attempted to target these CFAEs in order to terminate and prevent recurrence of AF.[55,56,61-63,65-67]

In the study by Nademanee *et al*., regarding 121 patients with AF (57 paroxysmal), CARTO mapping of both atria was performed during spontaneous or induced AF. CFAEs were identified using bipolar recordings filtered at 30 to 500 Hz and defined by the presence of voltage $\leq$ 0.15 mV.[55] RF ablation of the area with CFAEs was performed in an attempt to eliminate the CFAEs. According to this report, 92 (76%) of the 121 patients were free of arrhythmia at 1-year follow-up. However, other studies have shown conflicting results with some improvement or no improvement when ablation of CFAEs alone or in combination with PV isolation is performed, in patients undergoing AF ablation.[56,61-63,65-67] According to a recent meta-analysis, the addition of CFAE ablation to PV antral isolation increases the rate of sinus rhythm maintenance in patients with persistent and long-lasting persistent AF, but does not provide supplemental benefit in patients with paroxysmal AF.[67] Therefore, further randomized studies are needed to clarify the real value of CFAE ablation in patients with AF.

Linear Lesions

Linear lesions were used initially intraoperatively with the aim of preventing the multiple reentrant wavelets that sustain AF. It is not surprising that catheter-based ablation procedures pursued a similar strategy. The goal of linear lesions is the achievement of bidirectional conduction block. Despite the use of irrigated tip ablation catheters with 3D anatomical guidance, lesion creation remains challenging.[68]

Linear lesions have been reported to be associated with conversion of AF either directly to sinus rhythm or to atrial tachycardia (AT), further demonstrating that such lesions may at least in some patients deeply modify the substrate for AF.[69,70] Most of these ATs are macroreentrant and require linear lesions to be treated.[71] Such organized tachycardias may be observed during the index procedure or emerge upon follow-up. Although complete linear lesions can terminate such organized tachycardias, the development of a gap in conduction block along such lines has the potential for a proarrhythmic effect and can facilitate sustained reentry.[72]

For patients in whom atrial flutter has been previously recorded clinically as well as those in whom right atrial flutter is inducible after PV isolation, ablation of the right atrial cavo-tricuspid isthmus[73] may be appropriate but on long-term follow-up may be of limited added value beyond PV isolation alone.[74,75] Ablation of the posterolateral mitral isthmus (to the inferior pole of the left PV antrum) has been widely deployed in patients with persistent AF.[69,76,77] One limitation of the mitral isthmus ablation is that it can require supplemental radiofrequency applications in the distal CS with its intrinsic safety concerns before conduction block is achieved. A number of approaches have been proposed to overcome this requirement, including balloon occlusion of the CS to reduce the heat sink effect of the CS blood flow during endocardial ablation[78] and modification of the line to a more supero-lateral trajectory.

With wide area circumferential PV antral isolation approach, the distance between the contralateral encirclements is greatly reduced posteriorly. Thus, an LA roof line (which can be created sufficiently superiorly to minimize ablation adjacent to the esophagus) can be achieved with a short transverse lesion connecting the 2 encirclements. More recently the creation of a second transverse linear lesion between the inferior poles of the contralateral encirclements has been deployed in order to complete a box isolation of the posterior LA wall.[79] This latter technique has the advantage of isolating a large area of high frequency activity where triggers and drivers are more likely to occur than other parts of the atria. Supplemental linear ablation on the anterior wall of the LA appears to be of lesser potential impact.[80]

Catheter Ablation of Left Atrial GP

Autonomic influences in the heart are produced by the extrinsic (central) and intrinsic cardiac autonomic nervous systems. The intrinsic cardiac autonomic nervous system contains clusters of autonomic GP located in epicardial fat pads on the left and right atria (superior left GP, inferior left GP, anterior right GP, inferior right GP) and in the ligament of Marshall (Marshall tract GP).[81-83] In patients with AF, endocardial high-frequency stimulation (HFS, cycle length 50 ms, 12 Volt actual output, 10 ms pulse width) produces a positive vagal response (transient AV block during AF and hypotension), allowing the identification and localization of left atrial GP. These GP may represent a target of AF ablation.

For endocardial GP ablation, RF energy should be applied to each site exhibiting a positive vagal response to HFS.[83,84] HFS is repeated after each RF application. If a vagal response is still present, RF energy is reapplied until the vagal response is eliminated. Elimination of the vagal response to HFS at each GP generally requires 3-10 RF applications (usually 30-35-40 Watts for 30–40 seconds but less when close to the esophagus).

In a population of 63 patients with paroxysmal AF undergoing ablation of the left atrial GP followed by PV antrum isolation, GP ablation alone (prior to PV antrum isolation) decreased the occurrence of PV firing from 47 of 63 patients (75%) before GP ablation to only 9 of the 63 patients (14%) ($P < 0.01$) after GP ablation.[83] PV antrum isolation was then performed, which eliminated PV firing in the remaining 9 patients (0/63 patients). The description in this and earlier studies of the elimination of PV firing by PV isolation, without targeting the sites of firing,[85] may be explained by the interruption of the axons extending from the GP to the PV myocardium. A similar relationship is present between CFAE ablation[86] and GP ablation. GP ablation alone often eliminates the majority of CFAE, despite ablating a much smaller area than the overall CFAE area. CFAE ablation may eliminate much of the fractionation by ablating the axons without ablation of the GP cell bodies.

Ablation of AF Nests Guided by Real-Time Spectral Mapping in Sinus Rhythm

Pachon *et al*. have developed a system for real-time spectral mapping using fast Fourier transform in sinus rhythm.[86] This mapping strategy identifies sites in which the unfiltered, bipolar atrial electrograms contain unusually high frequencies, namely fibrillar myocardium or the so-called AF Nest. The investigators successfully targeted biatrial AF Nests, without intentional PV isolation, as a novel approach for AF ablation. Oh *et al*. compared CFAE sites and AF Nests in an animal model of vagally mediated AF and concluded that these sites did not share identical anatomical locations.[87] Typically for AF Nest ablation, RF delivery for 20–30 seconds abolishes the high-frequency potentials normalizing the spectrum. Arruda *et al*. evaluated the adjunctive role of AF Nest ablation to antral PV isolation and SVC isolation in a prospective randomized study. The adjunct of AF Nest ablation resulted in a 10% decrease of recurrence as compared to conventional antral PV isolation and superior vena cava isolation.[88]

Sequential Ablation Strategy

A stepwise approach has been recently developed in patients with long-lasting persistent AF with different sequences that target multiple atrial areas.[89] The endpoint of the sequential ablation strategy is termination of AF. This can be achieved by passing directly from AF either to sinus rhythm or, more commonly, to AT, which is then mapped and ablated. The first step consists in PV isolation using antral isolation. As only 12% of AF will stop at that stage, the second step is frequently needed. It requires ECG-guided ablation targeting continuous electrical activities, focal sources, areas with temporal gradient, etc. The last step uses linear lesions and is used in case of persisting AF/AT after the first 2 steps. The mitral isthmus line is deployed after the roof line as a last resort given the difficulties observed in achieving a complete block. Once sinus rhythm has been restored, PV isolation and linear lesions are checked for completeness and areas re-ablated if needed. It should be emphasized that this approach represents an extensive procedure associated with significant risks and requires careful and individualized risk–benefit assessment. However, it is associated with unprecedented success rate in long-lasting AF, particularly when AF termination is achieved during the index procedure.

Future Technologies

In order to improve permanent transmural lesion formation, *contact force sensing technology* (Biosense Webster and Endosense SA) is currently under clinical investigation. The contact force sensor integrates within the distal tip of a conventional mapping and ablation catheter, providing real-time catheter tip-to-tissue contact feedback. Preliminary results using the Endosense catheter demonstrate feasibility and safety in using this new technology for PV isolation.[90] Several ongoing studies will determine whether the addition of contact force measurement during AF ablation will result also in improved procedural outcome. An alternative means of contact force assessment utilizes *local impedance changes* between catheter tip and cardiac tissue. The software integrates with the Ensite NavX electroanatomical mapping system and initial animal and human studies have shown its clinical utility during mapping and ablation within the LA.[91,92]

TABLE 4

Key Points Regarding the Techniques and Technologies for AF Catheter Ablation

–PV isolation is the cornerstone of current AF catheter ablation techniques. A CMC is the most widespread and reliable method to assess effective PV isolation.

–PV isolation may be performed at different levels, but nowadays it is performed preferentially at level of PV antrum, to include in the lesion important anatomical structures for the initiation and maintenance of AF (LA posterior wall, GP, rotors, etc.).

–Nonparoxysmal AF patients necessitate a more extensive ablation protocol. Adjuvant ablation of the CFAEs increases the success rate of PV isolation in these patients.

–The incremental therapeutic value of other ablation strategies, such linear lesions, GP ablation, and stepwise approach remains to be established.

–New technologies (balloon-based, robotic, contact-force sensing technologies, etc.) are being developed with the principal aim of increasing the effectiveness and safety of catheter ablation of AF, while reducing the operator dependency.

The ability to register *real-time in-tissue temperature* during ablation could potentially facilitate better lesion formation. Using microwave radiometry, very early in-human data demonstrate a correlation between in-tissue temperature and lesion transmurality. Future studies are needed to assess the system's feasibility during AF ablation.

The *remote magnetic mapping and ablation system* by Magnetecs promises real-time catheter maneuverability within a magnetic field of 1.5 Tesla. The system uses 8 electrical magnets that can be switched off. Hence, no magnetic shielding of the examination room is needed. Studies are under way to test the system's mapping capabilities within humans.

The Amigo *robotic arm* by Catheter Robotics can be mounted on any conventional examination table and facilitates remote-controlled movement of mapping and ablation catheters. The system is available in Europe and can be integrated with any electroanatomical mapping system. Clinical data are limited with 1 trial currently recruiting patients to assess the system's ability to navigate and map within the human heart.

A new electroanatomical mapping system is currently being developed that uses a *basket-shaped mapping catheter* to facilitate acquisition of several thousand mapping points within several minutes. Initial clinical data indicate that the system is able to map complex left atrial arrhythmias in humans.

The key points regarding the techniques and technologies for AF catheter ablation are reported in Table 4.

Endpoints of Catheter Ablation for Atrial Fibrillation

The principal procedural endpoints used for catheter ablation of AF depend on the type of AF being treated. Endpoints include completion of a predetermined lesion set,[93] termination of AF during ablation,[89] and noninducibility of AF following ablation.[94,95] There is still debate surrounding the predictive value of such endpoints, in particular AF termination.

TABLE 5

Ablation Sites and Ablation Endpoints of the Different Techniques for Catheter Ablation of AF

Ablation Technique	Ablation Site	Ablation Endpoints
Segmental/ostial PV isolation	PV ostium	Complete elimination or dissociation of PV potentials assessed by a CMC
Circumferential PV isolation	1–2 cm outside PV ostium	Abatement of local bipolar voltage by 90% or <0.05 mV within encircled areas
Antral PV isolation	PV antrum	Complete elimination of PV potentials with isolation of all PVs and posterior wall of LA assessed by a CMC
CFAEs ablation	LA areas where CFAEs are recorded	Complete elimination of CFAEs Termination of AF Noninducibility of AF
Linear lesions	LA roof and mitral isthmus	Creation and demonstration of line of complete block
Autonomic GP ablation	GP located around PVs	Abolition of vagal reflexes induced by HFS
AF Nest ablation	Local high frequency activity or focal and centrifugal spread of activation or frequency areas	Abolition of these high sites with temporal gradient between 2 dipoles
Other structures and thoracic veins	CS, LA appendage, superior vena cava, persistent left superior vena cava, vein of Marshall	Complete elimination or dissociation of other structures or thoracic veins

In patients with paroxysmal AF, it is possible that the termination of AF during ablation is coincidental. In these patients noninducibility seems to be associated with an improved outcome.[95,96] However, there is no current consensus on the definition of noninducibility and the standardization of the induction protocol used. Furthermore, it is likely that the noninducibility of AF might identify a subgroup of patients who have less severe atrial disease and therefore more likely to have a successful outcome. For patients with persistent and long-lasting persistent AF, the procedural endpoint is also unclear. Although restoration of sinus rhythm by ablation, without the use of antiarrhythmic drugs or DC cardioversion, appears to be an intuitively ideal endpoint, this is not always achievable and results regarding clinical outcome are controversial.[97-99] Until more data are available, completion of a predetermined lesion set incorporating PV isolation remains the basic procedure.[100] Verification and completion of ablation linear lesion sets is fundamental to minimizing proarrhythmia and arrhythmia recurrence. The ablation endpoints of the principal ablation approaches previously discussed are summarized below and in Table 5.

PV Isolation

There is consensus that electrical PV isolation is the optimal endpoint for ablation targeting the LA–PV junction and is now generally incorporated as the initial lesion set in AF ablation strategies.[101,102] The most objective procedural endpoint is absence or dissociation of PV potentials recorded from a CMC positioned just inside the PV[28,29,103,104] (Table 5). Many consider the same endpoint of electrical PV isolation optimal for wide area circumferential PV ablation. However, reduction of local bipolar amplitude with low peak-to-peak bipolar potentials (≤ 0.1 mV) inside the encircled area as well as local endocardial activation time >30 ms between contiguous points lying in the same axial plane on the external and internal side of the line, are still suggested by some authors as a suitable endpoint in order to avoid the necessity for a CMC[26] (Table 5). Exit block into the LA can also be proven with pacing maneuvers from inside the PV, but this is not routinely applied. This is due to the technical difficulty of ensuring pacing capture of the muscle sleeves inside the vein without far-field capture of the left or right atrium.

The role of intravenous adenosine as an adjunct to prove permanent abolition of PV conduction has been suggested[105] and is part of an ongoing prospective study.[106] As an additional endpoint, nonexcitability of bilateral circumferential lines following PV isolation has been introduced.[107,108]

Electrogram-Based Ablation or CFAEs Ablation

Endpoints for ablation of sites of CFAEs include: (1) complete elimination of the areas with CFAEs, (2) conversion of AF to normal sinus rhythm for both paroxysmal AF and persistent/long-lasting persistent AF patients, (3) conversion of AF to an organized atrial tachyarrhythmia (AT or flutter), and (4) noninducibility of AF in paroxysmal AF patients[55,56,61-63,65-67] (Table 5).

The ablation typically begins at the sites where CFAEs have the shortest local A-A interval. Such sites are unfortunately ubiquitous in persistent AF. It is not known whether ablation of all such sites is necessary or if it is possible to target specific locations and thereby limit the extent of unnecessary ablation and resultant tissue damage. Irrespective of electrogram complexity, ablation all along some structures like the CS, LA appendage,[109] and septum may also have an impact on AF perpetuation.

Importantly, after "defragmentation" and prior ablation (PV isolation and eventually linear lesions), electrograms may become discrete or organized, allowing a dominant rate (frequency) and specific activation sequence to be identified. In such situations, parameters other than fragmentations may be used. Local high-frequency activity or focal and centrifugal spread of activation or sites with temporal gradient between 2 bipoles of conventional mapping catheter (representing local circuit, "rotor" or "AF nest") are potential targets for ablation.[110]

Linear Lesions

In patients with persistent or long-lasting persistent AF, the use of adjunctive linear ablation, mainly at the level of LA roof and mitral isthmus, has been associated with higher success rates.[95,111,112] The endpoint should be a complete line of linear lesions[76,77,113,114] because incomplete lesions are associated with recurrence of atrial arrhythmias.[72,115,116] The electrophysiological endpoint should therefore be demonstration of bidirectional line of block[76] (Table 5). A complete

LA roofline may be demonstrated by activation progressing in a caudal-cranial direction on the posterior wall during left appendage pacing.[77] A complete mitral isthmus line may be demonstrated by an inversion of CS activation sequence from distal–proximal to proximal–distal during pacing from the left appendage.[76]

Autonomic GP Ablation

Autonomic GP located around PV can be identified by HFS. HFS at these sites leads to induction of bradycardia or AV block due to increased vagal tone. Abolition of inducible vagal reflexes has been proposed as an endpoint of GP ablation[117] (Table 5). It is unclear whether GP should be specifically targeted given that these sites may be concomitantly ablated in the course of above-described ablation targets. Most centers still do not specifically target such GP, although these may be affected especially when extended ablation approaches are introduced.

CS and Other Thoracic Veins Ablation

Similar to triggers arising from the muscle sleeves surrounding the PVs, rapid atrial activity from the musculature of the CS may be a driver for persistent or long-lasting persistent AF. The same electrogram-based approach as discussed above can be applied to the CS.[118]

Other potential triggers, such as superior vena cava and persistent left superior vena cava,[119,120] can be electrically isolated by ablation technique and endpoints similar to PV isolation[121] (Table 5).

The key points regarding the endpoints of catheter ablation for AF are reported in Table 6.

Patient Management Pre-, During, and Postablation

Preablation Management

Anticoagulation

Effective anticoagulation therapy is often necessary before an ablation procedure for AF. The modalities and duration of preablation anticoagulation therapy are reported in detail later.

Other drugs

Drug treatment for nonarrhythmic indications is generally continued. There is no consensus with regard to discontinuing antiarrhythmic drugs (AADs), although to avoid confounding ablation effects with AADs effects, all AADs with the possible exception of amiodarone should be discontinued at least 4 half-lives in advance. However, if symptomatic arrhythmias demand, effective AADs may be continued.

Transesophageal echocardiogram

A preablation transesophageal echocardiogram (TEE) is used to rule out the presence of a LA thrombus, and should be considered a supplementary and backup strategy to continuous effective anticoagulation leading up to the ablation procedure. It should be performed shortly before the ablation procedure and without an intervening window in effective anticoagulation. In many EP laboratories, TEE is performed only in patients presenting with AF and off anticoagulation therapy.

Other imaging studies

Imaging to define the cardiac substrate could include establishing the presence and extent of coronary artery disease (if present) and left ventricular size and function. A transthoracic echocardiogram before the procedure is useful and allows measurement of chamber size and ejection fraction. LA size is an important determinant of rhythm outcome after ablation and may influence the selection of ablation strategies. The most widely used measure, single-plane dimension from the parasternal long-axis view, correlates modestly with LA volumes. Estimation of LA volume from multiple 2-D imaging planes or by volumetric analysis of MR or CT images may be preferable and more accurate. Evaluation of LA emptying and systolic function (ejection fraction) is not part of most standard imaging routines but may have an important role in evaluating the long-term impact of ablation on LA function.

An MR or contrast-enhanced spiral CT scan is obtained as a baseline both for comparison and for formulation of an ablation strategy with variable PV anatomy.[122] In some laboratories, the ablation is performed with MR or CT image integration. In such situations, both the underlying rhythm and ventricular rate at the time of acquisition are important in order to make effective use of the 3D images.[123] Preliminary data indicate that preprocedure delayed enhancement MR may be useful in predicting procedural outcome.[124]

Informed consent and preablation fasting

As for any ablation, an informed consent and appropriate preparation including at least 6 hours of fasting leading up to the procedure are necessary.

Management During Ablation

Sedation/anesthesia

Conscious sedation using midazolam combined with analgesia using fentanyl is used in ablation procedures of less complex arrhythmias and can also be applied during AF ablation. However, conscious sedation is often inadequate during AF ablation, due to long procedure times, pain during RF energy applications, and the need to limit patient motion during the procedure. Therefore, general anesthesia is widely used during AF ablation. *General anesthesia* may reduce the prevalence of PV reconnection during repeat ablation when compared with conscious sedation.[125] Alternatively, *deep sedation* during continuous infusion of propofol has evolved as a third sedation alternative. This strategy can achieve painless deep sedation without the need for intubation and general anesthesia, and can be guided by the electrophysiologist.[126]

Anticoagulation

The intensity of anticoagulation during the AF ablation is of critical importance and is described in chapter 6.

AADs/electrical cardioversion

Many investigators choose to perform the AF ablation procedure off AADs. The procedure can be performed during either sinus rhythm or AF. In selected cases, AADs may be administered intravenously when sinus rhythm is desired. Alternatively, electrical cardioversion can be applied when sinus rhythm is the preferred rhythm during specific parts of

TABLE 6

Key Points Regarding the Endpoints of Catheter Ablation for AF

–Primary targets of AF ablation are PVs and/or PV antrum.
–Primary goal is complete and permanent electrical isolation of PVs.
–Careful identification of PV ostia is essential to avoid ablation within the PVs.
–Ablation of focal extra-PV triggers (superior vena cava, vein of Marshall, CS, LA appendage) is recommended.
–In patients with paroxysmal AF, electrical isolation of the PVs is sufficient. In patients with persistent and long-lasting persistent AF, additional lesions are usually required (CFAEs ablation, linear lesions, GP ablation).
–For additional linear lesions (LA roof, mitral isthmus, anterior left septum), verification of line completeness demonstrated by bidirectional block is of fundamental importance to minimize arrhythmia recurrence.
–Ablation of the cavotricuspid isthmus is recommended only with history of typical atrial flutter or inducible cavotricuspid isthmus dependent atrial flutter.
–No consensus on other endpoints exists: use of intravenous isoproterenol to unmask focal extra-PV triggers, role of intravenous adenosine as an adjunct to prove permanent abolition of PV conduction, AF termination during ablation and AF inducibility postablation.

the procedure, e.g., verification of conduction block across linear ablation lines and confirmation of PV isolation.

Postprocedural Management

The immediate postprocedural management consists of continuing and maintaining anticoagulation, maintaining hemostasis at puncture sites, and supportive treatment. Vagal episodes remedied by fluid infusion and/or atropine are not uncommon; however, pericardial tamponade must be excluded in patients with postprocedural hypotension. Pericarditic discomfort may occur during the first 3–5 days, sometimes accompanied by a mild and self-limited febrile syndrome. Aspirin is usually sufficient treatment although uncommonly, continuing symptoms and a nonresolving pericardial effusion may require the administration of systemic steroids. The later occurrence (6–10 days postablation) of a febrile state with or without neurological symptoms should prompt suspicion of an atrio-esophageal fistula and lead to a contrast-enhanced spiral CT to exclude the diagnosis.

Many centers now perform AF ablation while continuing therapeutic anticoagulation with warfarin.[127] In this case, oral warfarin anticoagulation can simply be continued after ablation. For other practical aspects regarding anticoagulation after AF ablation, see later.

Rhythm outcome

Estimating the burden of AF, both symptomatic and asymptomatic, is the key to determining the outcome of the procedure. The ideal outcome would be a zero residual burden with no atrial flutter or AT. The absence of symptoms may not correspond to the stable restoration of sinus rhythm, probably due to ablation-induced denervation or because of the absence of symptoms at baseline. The accuracy of estimating AF burden depends chiefly upon the duration of ECG recording (Table 7).[128–135] Many laboratories use a clinical definition of successful ablation to mean the absence of symptomatic tachycardia, as well as the absence of documented AF during periodic follow-up visits as well as on periodic 24–48-hour Holter recordings, typically at 1, 3, and 6 months after the ablation. An event recorder may be used to evaluate symptoms not elucidated by the above tests. However, extending the duration of Holter tracings to 7 days has been shown to enhance the sensitivity of detecting recurrent AF.[136] Another approach has been to monitor periodic, even daily, transtelephonic ECG recordings supplemented by ECG transmission during symptomatic episodes, although the correlation to AF burden may be difficult to determine.[132] Finally, more and more implanted devices have sufficient memory and accurate arrhythmia recognition software to provide probably the most accurate measurement of AF burden possible, but of course only in a limited patient population.[137,138] From a clinical standpoint, when success is defined as the restoration of stable sinus rhythm, this assumes the elimination of (sustained) ATs as well, whether reentrant (flutters) or nonreentrant.

Owing to the difficulty of clinically measuring the AF burden, the temporal evolution of arrhythmias in ablated patients has not been clearly determined. Although some groups have re-ablated patients as soon as they develop recurrent AF, others have advocated waiting for 1–3 months with or without adding AADs treatment in the interim period. An early re-ablation may result (unnecessarily) in a higher incidence of local puncture site complications, a longer hospital stay, and the risks of an additional left-sided procedure. About 30–50% of patients with documented or symptomatic recurrences during the first 3 months after an AF ablation have no further AF or flutter even without additional ablation. However, early AF recurrences do portend a worse long-term outcome, and merit heightened awareness of later AF occurrences (see later).

AADs therapy

It has been demonstrated in a prospective randomized trial that treatment with AADs during the first 6 weeks after AF ablation reduces the incidence of clinically significant atrial arrhythmias and need for cardioversion or hospitalization for arrhythmia management.[139] However, systematic AADs therapy did not reduce late arrhythmia recurrence during longer-term follow-up in the same population.[140] Alternatively, AADs are stopped 4 half-lives before ablation and not restarted unless symptomatic or sustained recurrences occur. There are no guidelines for discontinuing AADs therapy after AF ablation. Depending upon the risk of recurrence and the accuracy of determining residual arrhythmias, trial of discontinuation may be offered after 3–6 arrhythmia-free months. According to a recent paper, transient use of small amounts of corticosteroids (prednisolone 0.5 mg/kg/day) shortly after ablation (first 3 days) may be effective and safe for preventing both immediate and late AF recurrences (14 months follow-up).[141] Other drugs such as *angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, statins,* and *polyunsaturated fatty acids* may potentially prevent AF by a variety of mechanisms, including anti-fibrotic, anti-inflammatory, and anti-oxidant effects. However, the efficacy of these drugs in reducing postablation arrhythmia recurrences has yet to be demonstrated.[142]

TABLE 7

Incidence of Asymptomatic AF in Postablation Patients

Authors	Total number of patients	Number of patients with asymptomatic AF (%)	ECG detection method
Oral *et al.*[128]	53	1 (2%)	Transtelephonic ECG monitoring
Hindricks *et al.*[129]	108	20 (18%)	7-day Holter monitoring
Senatore *et al.*[130]	72	8 (11%)	Transtelephonic ECG monitoring
Neumann *et al.*[131]	80	11 (14%)	External loop recorder
Vasamreddy *et al.*[132]	10	2 (20%)	Mobile continuous outpatient telemetry
Klemm *et al.*[133]	80	7 (9%)	Transtelephonic ECG monitoring
Verma *et al.*[134]	86	2 (2%)	Pacemaker/ICD memory
Steven *et al.*[135]	37	0 (0%)	Pacemaker/ICD memory

Note: Only the incidence of asymptomatic episodes is reported.

Late surveillance

Echocardiographic monitoring is useful to detect improvement in left ventricular function and assess reductions in LA size after ablation.[143,144] In the light of the high rates of symptomatic PV stenosis/occlusion in the early days of ablation targeting the PVs, routine MR or CT imaging was advocated at 3–6 months following the ablation. However, improvements in intra-procedural imaging as well as strategic changes in placing ablation lesions more remote from the PV ostia, has resulted in significant reductions in PV stenosis rates. Furthermore, about 80% of PV stenoses, including most single PV occlusions, are asymptomatic.[145] Consequently, routine imaging with MR or CT is often restricted to patients with suggestive symptoms. Finally, a significant risk of very late AF recurrence has been reported in several series.[146,147] It is therefore advisable to maintain periodic surveillance for arrhythmia recurrence at 6- or 12-month intervals, even in patients who are free of arrhythmias during the initial year following ablation.

The key points regarding patient management pre-, during, and postablation are reported in Table 8.

Periprocedural and Long-Term Anticoagulation

Stroke is by far the most serious adverse consequence of AF, and concern about stroke prevention pervades all decision making related to management of AF, including ablation. Although the primary motivation for PV isolation procedures is to reduce symptoms, nonetheless, stroke prevention needs to be considered before, during and after ablation procedures for AF.

Preablation Anticoagulation and TEE

Because AF ablation involves not only cardioversion in many patients and the introduction of foreign bodies into the left heart, but also the possibility of a lapse in anticoagulation during sheath removal, the importance of preprocedural anticoagulation is well accepted. However, there are many potential strategies and very little data to guide best practices.

Anticoagulation strategies prior to ablation procedures in high risk patients reflect guidelines for the care of patients with AF in general. Patients with CHADS2 scores of 2 or higher should be anticoagulated in any case, to an INR of 2–3 for at least 3 weeks prior to ablation; if warfarin is stopped prior to the procedure, enoxaparin or heparin may be used for "bridging." There is little consensus regarding the need for anticoagulation in low risk patients. Recent observational studies suggest that a strategy of performing ablation with a therapeutic INR may reduce the risk of ablation-related thromboembolism.[127,148,149] This strategy has the theoretical advantage of eliminating the lapse in anticoagulation during sheath removal, and has been shown to be associated with a low rate of bleeding complications and of periprocedural stroke. The impact of new oral anticoagulants has not been studied in this application.

Many centers routinely perform TEE prior to ablation to exclude the presence of thrombus in high risk patients, particularly in those with persistent AF. Other strategies to assess the presence of thrombus, such as CT angiography, or intra-procedural ICE, may be reasonable but have not been rigorously compared to TEE, which is the current gold standard. There is little consensus in low risk patients, or those with paroxysmal AF. A recent paper suggested that the incidence of intracardiac thrombus was low in ablation candidates (0.6%), but increased with increasing CHADS2 score, history of heart failure and left ventricular ejection fraction <35%.[150]

Anticoagulation During the Ablation Procedure

In the updated worldwide survey of catheter ablation for AF, a 0.94% incidence of stroke or TIA was reported,[151] however an 11–14% incidence of cerebral emboli were observed following catheter ablation in 2 recently published studies.[152,153] Major bleeding complications such as tamponade, hemothorax, and groin complications such as pseudoaneurysm or AV fistula totaled 2.3%.[151] Femoral hematomas are more common, up to 8%,[154] and may prolong hospitalization or produce a short period of disability. Achieving the lowest possible thromboembolic complication rate while maintaining an acceptably low bleeding complication rate is the goal of intra-procedural anticoagulation. Thrombus can form within sheaths or on guidewires and catheters, as observed by ICE, particularly in patients with persistent AF, dilated atria, and spontaneous echo contrast.[155] To prevent thrombus formation within the sheaths, it is common sense to flush them intermittently or use continuous irrigation, which may be more reliable. Since the capacity of the inner lumen for blood is larger without a catheter in place, it may be beneficial to leave catheters in sheaths while in the LA. Endocardial RF catheter ablation may disrupt endothelial integrity and expose a nidus of interstitial tissue, which may promote thrombus formation. Char may form on the electrodes of the ablation catheter if temperatures exceed 100°C

TABLE 8

Key Points Regarding Patient Management Pre-, During, and Postablation

Preablation
- –Effective anticoagulation often necessary. TEE recommended to rule out an LA thrombus in patients with persistent/long-lasting persistent AF and/or at high thromboembolic risk (see next chapter).
- –No consensus with regard to discontinuing AADs.
- –MR or CT scan important for comparison and for formulation of an ablation strategy with variable PV anatomy.

During Ablation
- –Conscious sedation, deep sedation, jet ventilation, and general anesthesia are alternative methods for patient sedation during AF ablation.
- –The intensity and the type of anticoagulation protocol are of key importance (see next chapter).

Postablation
- –Continuation and maintenance of anticoagulation crucial (see next chapter).
- –Ambulatory ECG monitoring with 1 of the different ECG detection methods strongly recommended in order to assess the correspondence between symptoms and arrhythmia and to discover asymptomatic episodes of AF.
- –No consensus exists for continuing/discontinuing AADs after AF ablation. The use of AADs in the first period after ablation reduces the recurrence rate of early arrhythmias but not the incidence of late arrhythmias.
- –The use of ACE inhibitors, statins, and PUFAs does not appear associated with a reduction of arrhythmia recurrences.
- –MR or CT imaging at 3–6 months not recommended routinely but only for patients with symptoms suggestive for PV stenosis.

at the electrode–tissue interface that may increase the risk of thrombus formation. A sudden impedance rise during RF energy delivery may indicate the development of char and should prompt withdrawal and inspection of the catheter tip. A catheter tip with open irrigation appears to reduce the risk of char and thrombus formation by cooling the electrode-tissue interface.[156]

Unfractionated heparin, delivered by weight/time-based nomograms and/or monitored by frequent measurement of activated clotting time (ACT), is typically given during the ablation procedure, even in the presence of a therapeutic INR (thrombus may form in the right atrium with similar frequency as it does in patients with an INR <2.0). Exchanging short vascular access sheaths for transseptal sheaths should be preceded by careful flushing and heparin delivery should be considered at this point rather than after transseptal puncture, particularly in patients with a higher risk of thromboembolism. The target intensity of anticoagulation is not standardized among experienced investigators, and may vary according to several factors, for example, patient age, type of ablation procedure, catheter used, and energy source. Observational studies have shown using ICE that the incidence of visualized thrombus markedly decreased with an increase in target ACT from 250–300 to >300 seconds.[155,157] Many experienced operators instruct their patients to maintain a therapeutic INR, as it may be easier to achieve and maintain target ACT values and may reduce the risk of stroke. The risk of major bleeding complications does not appear to increase using this strategy.[149,154] Additionally, management of cardiac tamponade appears to be equally safe in patients with a therapeutic INR, but reversal agents such as fresh frozen plasma or factor IX should be readily available during the procedure if a therapeutic INR is to be maintained.[158]

Postablation Anticoagulation

No universally accepted recommendations exist for anticoagulation therapy after successful ablation of AF. Due to the high risk of thromboembolism in the early postprocedural period,[159] in the many centers, warfarin therapy is started in all patients either the same evening of the ablation procedure or the next morning. In the initial period, LMWH (e.g., enoxaparin at a dosage of 0.5–1.0 mg/kg twice a day) is often given as bridging therapy by starting 3–4 hours after the ablation.[28,160] Less frequently, heparin is administered intravenously until the day after the procedure, starting about 3 hours after sheath removal at a rate of 1,000 IU/h.[160–162] Thereafter, LMWH is administrated until the INR is ≥ 2. Warfarin is usually continued for at least 3 months.

After this period the anticoagulation strategy is controversial. There have been several reports indicating that a low rate of stroke may occur in patients with successful ablation who do not receive anticoagulation.[159,162–166] However, these studies have 2 major limitations: (1) they are observational, retrospective, and not randomized; and (2) most enrolled few patients at high thromboembolic risk. The reasons for continuing anticoagulation after ablation mainly concern the risk of long-term recurrence[146,147,167–177] and in particular, the risk of asymptomatic recurrences.[128–135] Furthermore, it is generally accepted that there is a continuing risk of stroke in patients receiving AADs therapy even if it appears that therapy has eliminated AF recurrences. Therefore it would appear to be prudent at this point to recommend that long-term anticoagulation be continued in patients even after apparently successful ablation. The use of anticoagulation requires an assessment of stroke risk[178] and bleeding risk as well as patient values. Aspirin is generally considered a poor substitute for oral anticoagulation. New anticoagulants such as dabigatran, which is easier to use than warfarin, more effective and associated with fewer life-threatening bleeds make the decision to continue an anticoagulant after apparently successful ablation more attractive.[179]

The key points regarding periprocedural and long-term anticoagulation are reported in Table 9.

Peri-Procedural and Late Complications

Recognition of complications related to AF ablation can help minimize risk. Overall, the rate of major complications ranges from 0.8% to 5.2% in recent studies.[151,169,180–187] The incidence, causes, clinical presentation, diagnostic tools, preventive and therapeutic measures of each of these complications are summarized in Table 10. Death occurs, as a complication of AF ablation, in 1 of 1,000 patients.[188] The most frequent causes of death are cardiac tamponade, stroke, and atrio-esophageal fistula.[189]

TABLE 9

Key Points Regarding Periprocedural and Long-Term Anticoagulation

Preablation
–In patients at moderate to high risk of stroke, anticoagulation with a Vitamin K antagonist (INR 2-3, target 2.5) or a new anticoagulant is recommended for 3 weeks prior to ablation. For patients at low risk of stroke, the need for this is unknown.
–TEE or other methods to exclude intracardiac thrombus prior to ablation is recommended in patients with persistent AF or other high-risk characteristics.
–If INR has been therapeutic every week for the 4 weeks preceding the ablation, the TEE could be avoided.
During Ablation
–Heparin administration should be initiated at the time of the exchange of short vascular sheaths for transseptal sheaths, and no later than immediately after transseptal puncture is safely accomplished.
–Heparin should be administered as an initial bolus dose of 100–140 IU/kg followed by an infusion of 15–18 IU/kg/hour and/or by additional boluses. For patients with an INR range of 2.0–3.5, the initial bolus dose should be reduced to 80 IU/kg.
–The ACT target should be 350–400 seconds based on limited data. The ACT target does not differ in patients with and without a therapeutic INR.
–Heparin infusion is discontinued in all patients after removal of catheters from the LA. Protamine infusion may be administered (dose 30–50 mg) or ACT allowed to decrease below 250 seconds prior to sheath removal to minimize the potential for femoral hematoma formation.
–Ablation on therapeutic coumadin could be considered.
Postablation
–Oral anticoagulation should be started after ablation and continued for at least 3 months in all patients.
–Oral anticoagulation should be continued indefinitely in most patients who are at moderate or high risk of stroke (based on a risk stratification system such as CHADS$_2$ or CHA$_2$DS$_2$-VASc). This recommendation is based on a known risk of AF recurrence, and a lack of randomized, prospectively obtained trial data indicating the safety of anticoagulation discontinuation.

Pericardial Effusion/Cardiac Tamponade

A risk of 1.3% for cardiac tamponade has been reported in the last worldwide survey on AF ablation outcome.[151]

Clinical manifestations of acute tamponade include hypotension, tachycardia, paradoxical pulse, jugular venous distension, and shock.

Monitoring with ICE or TEE and direct visualization of the transseptal puncture may help minimize risk.[190] Cautious LA catheter manipulation and careful titration of RF power delivery seems to reduce direct LA trauma and tissue boiling with endocardial rupture.

Most large effusions can be drained with a percutaneous technique with documentation of the absence of ongoing bleeding. Occasionally, open-heart surgery, including cardio-pulmonary bypass may be required particularly when ongoing bleeding after initial drainage is evident and substantive.[191]

Recently, cases of delayed cardiac tamponade (i.e., occurring after discharge from the EP lab or from hospital) have been reported, sometimes preceded by evidence of pericarditis.[192]

Thromboembolic Events

The prevalence of thromboembolism during or after AF ablation has been reported to vary from 0% to 1.1% in different studies.[151,180,183,184,187] For the possible causes, prevention and therapy of this complication see the previous section on periprocedural and long-term anticoagulation.

PV Stenosis

With the evolution of PV isolation techniques and ablation at the PV ostium or even more proximal at the antral level, the incidence of severe PV stenosis has decreased to 0–0.5%.[151,180,183,184,186,187] However, PV stenosis may be underreported because most of the patients remain asymptomatic and postablation imaging is no longer routine at most centers. In the updated worldwide AF ablation registry, the rate of PV stenosis requiring intervention was 0.29%.[151]

The clinical manifestation of PV stenosis may be quite insidious. Many people are asymptomatic if only single PV stenosis is present even when marked (>70%).[193] The most frequent symptoms of PV stenosis are cough, dyspnea, hemoptysis, or recurrent and drug-resistant pneumonia.[194–196] Symptoms may develop both early and/or late after the procedure with most patients presenting within 2–6 months.[194]

To reduce the risk of PV stenosis when RF-ablation is performed near the PV ostium, the anatomy should be clearly defined using angiography of the PVs, ICE, or 3D mapping systems with image integration of preprocedure acquired MR or CT imaging. Avoidance of lesion placement within venous structures is critical.[194] Cryo-energy was promoted to eliminate the risk of PV stenosis.[33–35] However, the first cases of PV stenosis after cryo-balloon PV isolation have been reported recently.[197]

Significant (>70%) PV stenosis in symptomatic patients should be treated by angioplasty and/or stenting.[198] Angioplasty is associated with high restenosis rate of 45%.[198,199] PV stenting with bare metal stents with a size of ≥ 10 mm[200,201] or drug-eluting stents[202] seem to reduce the restenosis rate. Because of the disappointing surgical results for congenital stenosis, surgery should be considered the treatment of last resort. Whether patients with 1 PV stenosis and no or minimal clinical symptoms should be treated is not yet known. Anticoagulation is typically maintained if severe stenosis is present to prevent acute thrombosis.

Phrenic Nerve Injury

The estimated incidence of phrenic nerve injury is between 0.1% and 0.48%.[203,204] The right phrenic nerve is vulnerable to collateral injury during energy delivery at or close to right superior PV and superior vena cava.[205] The left phrenic nerve is susceptible to damage when lesions are applied in the vicinity of the LA appendage.[206]

Phrenic nerve injury appears to be clinically silent in many patients (22–50%),[203,204] with the majority of the remaining patients presenting with mild symptoms such as dyspnea, cough, and weakness. However, some patients develop more severe lung complications such as pneumonia, atelectasis, pleural effusion, and respiratory failure. Surgical plication of the paralyzed right diaphragm may be required. The

TABLE 10

Complications of AF Ablation

Complication	Incidence	Cause	Clinical Presentation	Diagnostic Tools	Prevention	Therapy
Cardiac tamponade	0.0–2.9%	TSP Linear lesions High RF power	Chest pain Tachycardia Dyspnea Abrupt hypotension/shock	TTE	ICE-guided procedure Power limitation Avoidance of RF delivery in CS	Pericardiocentesis Surgical drainage
TEs	0.0–1.1%	Use of number of sheaths/catheters in the arterial system Wide disruption of LA endocardial surface	Neurological deficits Acute ischemia of different organs depending on the site of TEs	Head CT/MR imaging Different tools	Intermittent flush or continuous irrigations of the sheaths Intravenous heparin administration with an ACT targeted of 250–400 Use of open irrigated tip catheters	Different according to the organ site of the TEs
PV stenosis	0.0–0.5%	RF delivery inside PVs	Cough Dyspnea Hemoptysis Recurrent/drug-resistant pneumonia	TEE V/Q lung scan CT/MR imaging	Use of imaging techniques Impedance measurements Titration of energy delivery	Anticoagulation Angioplasty/stenting Surgery
PN injury	0.1–0.5%	RF delivery at sites in close proximity to right/left PN (RSPV, SVC, etc.)	Dyspnea Cough Weakness Unilateral diaphragmatic paralysis	Fluoroscopy	Avoidance of energy application at sites of high-output pacing-induced diaphragmatic contraction	No therapy (spontaneous recovery)
Atrioesophageal fistula	0.03–0.25%	RF delivery at posterior wall of LA	Fever Malaise Dysphagia Hematemesis/melena Neurological deficits Intermittent cardiac ischemia Septic shock	CT/MR imaging	Monitoring of esophageal location/temperature Avoidance of micro bubble formation Low-energy delivery for short duration	Surgical correction Stenting of the esophagus
Periesophageal vagal injury	1.0%	Injury of periesophageal vagal plexus	Abdominal bloating Discomfort Pain	Gastroscopy andupper gastrointestinal investigation	Esophageal temperature monitoring Power titration and limitation at posterior LA	Endoscopic intrapyloric botulinum toxic injection

Continued.

TABLE 10

Continued.

Complication	Incidence	Cause	Clinical Presentation	Diagnostic Tools	Prevention	Therapy
Vascular complications (groin hematoma, pseudoaneurysm, AV fistula, retroperitoneal bleeding)	0.2–2.5%	Use of numerous venous catheters Routine use of femoral arterial line Intense use of anticoagulation	Local symptoms/signs Anemia	Echography	Procedure performance on oral anticoagulation Use of ultrasound-guided access Use of micropuncture kits Avoidance of large sheaths Adequate vascular compression	Transfusion if necessary Echo-guided manual compression Thrombin injection Surgical intervention
Acute circumflex artery occlusion	0.002%	RF delivery in the distal part of CS	Chest pain ST-segment elevation	ECG Coronary angiography	More posterior placement of mitral isthmus linear lesions Power limitation	Standard therapy of acute coronary artery occlusion
Air emboli	?	Sheaths/catheters exchanges Aspiration/irrigation/ continuous infusion of sheaths	Symptoms/signs of acute myocardial ischemia Neurological manifestations	ECG/coronary angiography Head CT/MR imaging	Proper attention to the technique	Standard therapy of air emboli Hyperbaric oxygen
Catheter entrapment in the MV	0.01%	Inadvertent positioning of the CMC into the ventricle	No specific symptoms/signs	TTE	Posterior TSP Clockwise catheter rotation when leaving transseptal sheath	Gentle catheter manipulation Advancement of sheath over the catheter into the ventricle Surgical extraction
Left AFL/tachycardia	3–40%	Reconnection of previously isolated PVs Slow conduction induced by incomplete linear lesions	Palpitations	ECG	Complete PV isolation Avoidance of linear lesions Documentation of bidirectional block in case of linear lesions	AA drugs Redo ablation

ACT = activated clotting time; AFL = atrial flutter; AV = arterio-venous; CMC = circular mapping catheter; CS = coronary sinus; CT = computed tomography; ICE = intracardiac echocardiography; LA = left atrium; MR = magnetic resonance; MV = mitral valve; PN = phrenic nerve; PVs = pulmonary vein(s); RF = radiofrequency; RSPV = right superior PV; SVC = superior vena cava; TEE = transesophageal echocardiography; TEs = thromboembolisms; TSP = transseptal puncture; TTE = transthoracic echocardiography.

diagnosis of phrenic nerve injury can be confirmed by fluoroscopy demonstrating a positive "sniff test" and the presence of unilateral diaphragmatic paralysis.

Despite the low prevalence and apparent benign course in most patients, prevention of persistent phrenic nerve injury is possible by identification of phrenic nerve location with high-output pacing ($\geq$30 mA, 2 ms).[203,204,207,208] Such a maneuver is recommended before energy delivery at or near the anterior aspect of right superior PV, the superior vena cava, and the LA appendage roof and, in the case of diaphragmatic contraction, ablation should be avoided. Other methods have recently been reported to allow RF delivery in regions where phrenic nerve injury would be expected. Applying an intra-pericardial balloon[209,210] and progressive infusion of air and saline in the pericardial space[211] to separate the phrenic nerve from the epicardial surface has allowed successful ablation without phrenic nerve injury. Another option, with greater inherent risk, includes close monitoring of the diaphragmatic excursion with immediate offset of ablation upon its reduction or if hiccups develop.

Atrio-Esophageal Fistula

Atrio-esophageal fistula formation is a rare but nearly universally fatal complication of AF ablation. A nationwide survey reported an incidence of 6 cases in 20,425 LA procedures (0.03%) with 5 deaths.[212] The mean time to presentation of this complication is 12.3 days[213] but it has been described as late as 41 days.[214]

Because of the high risk of death,[212,213] atrio-esophageal fistula, when occurs, requires rapid and accurate recognition and diagnosis. Fever, malaise, leukocytosis, dysphagia, hematemesis, and neurological symptoms in patients with a recent catheter ablation procedure should raise suspicion of atrio-esophageal fistula. If a fistula is suspected, it is important that endoscopy is avoided because insufflation of the esophagus can cause massive air emboli through the fistula leading to stroke and myocardial infarction.[213,215–218] Currently, imaging techniques such as MR or CT are used to diagnose an atrio-esophageal fistula. CT of the chest or head revealing intravascular air should immediately suggest the possible diagnosis.

Monitoring of esophageal location/temperature and low-energy short-duration delivery on the posterior LA are all means utilized to minimize risk of the atrio-esophageal fistula during AF ablation.[219] However, until now there are no data that clearly favors an approach on another.

Although mortality of atrio-esophageal fistula is very high, previously published reports documented survival following rapid surgical correction or esophageal stenting.[220,221]

Periesophageal Vagal Injury

An unusual extracardiac complication of AF ablation characterized by abdominal bloating and discomfort occurring within a few hours to 2 days after the procedure has been described.[222] The incidence of such adverse event was 1% in a series of 367 patients.[222] This rare complication is probably due to LA RF energy delivery affecting the periesophageal vagal plexus. Upper gastrointestinal investigation showed a pyloric spasm, gastric hypomotility, and a markedly prolonged gastric emptying time. To avoid this complication, the authors suggested using esophageal temperature monitoring and avoiding the ablation of LA endocardium directly overlying the esophagus.

Vascular Complications

Vascular complications including femoral artero-venous fistula, pseudo-aneurysm, and large hematomas are common after AF ablation (0.2–2.5%).[151,180–187] These complications are due to the numerous vascular access sites required for the procedure and high intensity anticoagulation during and following the procedure. The prevalence of pseudo-aneurysm ranges from 0% to 1.0% and the prevalence of AV fistula from 0% to 0.97% in large series.[151,180,182–185,187] Suggestions for limiting vascular complications include use of smaller gauge needles for venous access, avoid femoral arterial access, perform procedure on warfarin anticoagulation to avoid the need for "bridging" anticoagulation, decreasing number of sheaths in 1 vein, use of micropuncture kits, and use of ultrasound guided access in obese patients.[223,224]

Treatment of pseudoaneurysm depends on the size and complexity and can include surgical repair but most are treated with ultrasound guided compression and thrombin injection.[225,226] Treatment of AV fistula is also dependent on the size and complexity and includes simple observation, ultrasound guided compression, endovascular stent and surgery, but most can be treated with simple observation.[227]

Acute Coronary Artery Injury

Linear lesions deployed in the mitral isthmus can create coronary circumflex injury. Fortunately, the incidence of this complication is very low (0.002% in a large clinical experience with 71% of the study group having RF energy delivered in the CS).[228]

Assessing the location of the circumflex coronary vessel and its proximity to the planned ablation sites although not routinely performed should be considered with careful power titration as appropriate.

Air Emboli

Air emboli may enter the arterial system during transseptal puncture, sheath/catheter exchanges, aspiration, irrigation, intravenous medication administration or continuous infusion of sheaths.[229–231]

An air embolus often travels to the right coronary artery and mimics typical clinical presentations of acute inferior myocardial wall ischemia. Air emboli may also travel to cerebral circulation and may lead to severe neurological manifestations.

Air emboli are best prevented by proper attention to catheter and sheath technique. Caution should be exercised when exchanging the sheaths and catheters. Air filters can be used to minimize the risk of a large air embolus. If sheaths are continuously irrigated throughout the procedure, automatic pumps capable of detecting air in the tubing should be considered.

Air embolus to the coronary arteries often resolves within several minutes without major complications and residual myocardial injury. If the signs of an embolus persist, coronary angiography and, if necessary, aspiration of air from within the coronary artery should be considered. Treatment of large cerebral air emboli with prompt hyperbaric oxygen may have clinical value.[232]

Catheter Entrapment in the Mitral Valve or PV

The original worldwide survey on AF ablation on 7,154 patients reported an incidence of 0.01% of valve damage due to catheter entrapment in the mitral valve apparatus.[233] The CMC is at particular risk for entrapment within the mitral apparatus.[234]

Several recommendations can be made to reduce the risk. First, the CMC should be positioned in the posterior LA during transseptal catheterization. Second, the catheter should be torqued in a clockwise direction when leaving the transseptal sheath. These first 2 tips have allowed for safe catheter manipulation and successful ablation even in the setting of prior mitral surgery and prosthetic mitral valve.[235,236] Third, it is recommended to advance the catheter and/or the sheath over the catheter when mitral valve entrapment is observed.[237] Finally, early surgical extraction should be strongly considered before forceful manual extraction.[238]

Rarely the CMC can get entrapped in the PV with the potential risk of laceration and intrapulmonary bleeding.[239]

Organized Left ATs After AF Ablation

Organized left ATs are common after AF ablation with a reported incidence of 1.2–40% (Table 11).[72,76,96,115,116,240-255] The variability in the frequency of occurrence and the mechanism of the tachycardia appears to be clearly dependent on the type of ablation procedure used and the extent of the underlying atrial disease.[247,251,252,256,257] Centers utilizing circumferential PV ablation combined with additional linear lesions in the LA, targeting of CFAEs and other more extensive LA ablation report a higher prevalence of macro-reentrant atypical flutters and an overall incidence of organized left ATs that is more than 5–10 times that observed with only PV isolation.[72,76,96,115,116,240-252,256,257] This is especially true if no attempt is made to establish/confirm a line of bidirectional block or anchor clusters of more extensive LA ablation to anatomic obstacles.[145,258,259]

The macro-reentrant circuit of atypical flutter typically moves around a large anatomic barrier such as the mitral annulus or ipsilateral PVs and typically incorporates a zone of slow conduction created by gaps in LA linear lesions.[260,261] Occasionally circuits can occur around the fossa ovalis, from the CS musculature and adjacent LA or involve smaller circuits around anatomic barriers related to prior surgical or catheter-based lesions.[262,263] Centers that utilize PV isolation have predominantly localized reentrant left ATs originating from reconnected PVs.[244,246,253,257]

Patients with organized left ATs are frequently very symptomatic because they tend to demonstrate 2:1 AV conduction and a faster ventricular rate than observed in response to AF. Despite the general poor response to medical therapy and frequent recurrence after cardioversion, attempts to temporize are still recommended when the arrhythmia is observed early postablation. This is especially true given the fact that up to 50% of these tachycardias appear to resolve spontaneously during the "healing phase" postablation.[116]

Depending on the underlying mechanism, the ablation strategy may require isolation of the reconnected PV segment (for focal or local re-entrant tachycardias of PV origin) or may involve targeting the zone of slow conduction or a well-defined anatomic isthmus for macro-reentrant flutter.[72,244,257] It is routine to re-isolate PVs even if the mechanism of the LA flutter is macro-reentry to minimize the risk of manifest AF and recurrent LA flutter if lines of block do not hold long term. Overall, ablation is quite effective for these postablation left ATs with reported long-term success in excess of 80%.[72]

Adverse Impact on Atrial Contractility

Reverse remodeling of the left cardiac chambers with improvement in function has been reported after successful RF catheter ablation of paroxysmal and persistent AF.[27,143,144,264-273] However, the consequences of RF ablation on the LA contractility are still somewhat inconsistent based on published reports.

A recent meta-analysis, including 17 studies and 869 patients, assessed the effects of AF catheter ablation on LA size, volume, and function. Independent of the technique applied there was a significant decrease in LA diameters and volumes during follow-up in patients without AF recurrence but not in those with AF recurrence. LA ejection fraction and LA active emptying fraction did not decrease in patients without AF recurrence, whereas they decreased in those with AF recurrence.[272]

It appears that the effects of RF ablation on LA function are dependent on the extent of ablation and time they are assessed. Extensive ablation during PV antral isolation causes initial impairment in atrial function; however, the positive remodeling that occurs with rhythm restoration in patients with a high burden of AF typically outweighs negative effects of ablation.[270,271]

It is important to recognize that studies performed till now have used different protocols to evaluate the LA size, have included different patient populations, and incorporated different ablation techniques. These limitations suggest that more investigation and standardization is required in this important area.

It is also noteworthy that, very recently, a new syndrome, so-called "stiff LA syndrome," has been described as possible complication of AF ablation.[274] The syndrome, although rare (incidence of 1.4%), is clinically significant and characterized by dyspnea, congestive heart failure, LA diastolic dysfunction, and new-onset pulmonary hypertension.[274]

Radiation Exposure During Catheter Ablation of AF

Catheter ablation of AF frequently requires a long fluoroscopy time. Although single ablation procedure brings a very low cancer risk, repeated procedures are usually associated with a measurable risk increase. Consequently, every effort should be made to abate total radiation time during AF ablation.[275-279]

Very low frame rate pulsed fluoroscopy systems have become the norm to minimize radiation exposure during ablation procedure. Limiting cine-angiography, avoidance of magnification and changing the angulation of fluoroscopic equipment are other helpful measures to reduce fluoroscopy time. Electro-anatomic and remote navigation systems that facilitate catheter placement and stability further help to reduce radiation exposure.[280-282] Operator exposure can also be reduced by use of appropriate lead shielding.[283]

Skin radiation "burns," with proper operating equipment, are currently extremely rare as a result of AF ablation.[284,285]

The key points regarding periprocedural and late complications are reported in Table 12.

TABLE 11

Iatrogenic Postatrial Fribrillation Ablation LAT/FL: Literature Data

Author	Number of Patients	LAT/FL (%)	Time to LAT/FL (mo)	Mean TCL (ms)	Macroreentry	Focus	Acute Success (%)	Chronic Success (%)	Mean Follow-Up (mo)
Kanagaratnam *et al.*[240]	71	14 (20)	NR	NR	5/5†	0	100	100	NR
Villacastin *et al.*[241]	30	2 (6.6)	2	240	2	0	100	100	6.5
Oral *et al.*[242]	80	1 (1.2)	NR	NR	1	0	100	100	NR
Ernst *et al.*[243]	88	6 (7.0)	NR	NR	6	0	100	100	NR
Gerstenfeld *et al.*[244]	341	10 (3.4)	5.7 ± 2.8‡	253 ± 33	1	8	100	100	6.7 ± 2.3
Mesas *et al.*[115]	276	13 (4.7)	2.6 ± 1.6‡	275 ± 25	11	3	100	87	2.5 ± 1.2
Pappone *et al.*[245]	560	39 (7.0)§	2.4/2.9	NR	31	8	100	100	6.3/8.2
Jaïs *et al.*[76]	100	12 (12)	NR	NR	9	3	100	87¶	12
Oral *et al.*[96]	100	21 (21)	NR	NR	NR	NR	NR	NR	NR
Ouyang *et al.*[246]	100	21 (21)	0.21	206	17	2	100	100	5.8 ± 1.8
Cummings *et al.*[247]	737	23 (3.1)	NR	NR	23	0	100	61	16.5 ± 2.9
Hocini *et al.*[248]	20	4 (20)	4 ± 1‡	NR	4	0	100	100	NR
Chugh *et al.*[116]	349	85 (24)	1.5 ± 2.0	238 ± 35	28/28†	0	88	82	7.5 ± 4
Shah *et al.*[249]	207	16 (8)	2.3 ± 2.0	271 ± 45	15/15†	0	93	87	21 ± 11
Daoud *et al.*[251]	112	28 (25)	1.0 ± 0.5	NR	9/9†	0	94	NR	NR
Deisenhofer *et al.*[250]	67	21 (31)	3.2 ± 3.1	264 ± 41	16/16†	0	89	38	10.4 ± 6.7
Chae *et al.*[252]	800	78 (10)	NR	256 ± 49	137/155	18/155	86	77	13 ± 10
Sawhnet *et al.*[253]	66	8 (12)	9.8 ± 4.9†‡	NR	9/9	0	100	83	NR
Rostock *et al.*[254]	320	128 (40)	NR†‡	270 ± 40	44/61†	17/61†	93	82	21 ± 4
Chang *et al.*[255]	452	87 (19)	NR†‡	NR	84/120	36/120	90	97	21 ± 16

Adapted from Raviele A, Themistoclakis S, Rossillo A, Bonso A. Iatrogenic postatrial fibrillation ablation left atrial tachycardia/flutter: How to prevent and treat it? J Cardiovasc Electrophysiol 2005;16:298-301.[72]

†Only a limited number of the total population of patients with LAT/FL underwent repeat ablation procedure.

‡Time to LAT/FL ablation.

§28 (10%) in the 280 patients who were randomized to circumferential ablation alone, and 11 (3.9%) in the 280 patients who were randomized to circumferential plus linear lesions ablation.

¶Regards both AF and LAT/FL.

TABLE 12

Key Points Regarding Periprocedural and Late Complications

–Recognition of common and unique complications related to AF ablation can minimize the risk and optimize the outcome of ablation procedure.

–In order to reduce the risk, operators must be familiar with risk factors, clinical signs, and symptoms of early as well as delayed occurring complications.

–The rate of major complications of AF ablation ranges from 0.8% to 5.2% according to the ablation strategy used, lesion extension, patient characteristics, and center experience.

–Death occurs, as complication of AF, in 1 of 1,000 patients.

–The most common complications of AF ablation are vascular lesions, cardiac tamponade, and thromboembolic events. Other complications (e.g., atrio-esophageal fistula), although rare, may be very serious and life-threatening.

Short- and Long-Term Efficacy of Catheter Ablation for AF

Since the Venice Chart International Consensus Document in 2007,[1] more data have become available describing the acute, mid/long-term and very long-term efficacy of catheter ablation for AF. In order to define the success rates of any given procedure, there must be a consistent approach to the technique, a well-accepted method of follow-up, and a strict definition of success. Fortunately, over the last few years, a fairly good agreement has been reached on all the above-mentioned criteria. For most studies in patients with paroxysmal AF, PV isolation is considered a sufficient endpoint for ablation. Additional linear ablation and/or targeting of CFAEs has largely been reserved for patients with more persistent AF. Most studies have conformed to the HRS/EHRA/ECAS Expert Consensus Statement recommendations that follow-up postablation should be a minimum of 12 months with ECGs and 24-hour Holter monitors at least every 3 months.[101] Finally, the definition of success has become more standardized. For the most part, early recurrences occurring within the first 3 months after the procedure are discounted as being due to inflammatory changes and/or incomplete healing of the lesion sets, part of the so-called "blanking period." Recurrences after 3 months have been defined as episodes of AF lasting >30 seconds for reporting purposes, although the relevance of such short episodes of AF is not known.[101]

Acute Efficacy of AF Ablation

Acute recurrences of AF are not uncommon within the first 2–3 months postablation. Studies suggest that the incidence of early AF recurrence ranges from 35% to 50%.[286–288] These studies also show that most patients who go on to have late recurrence have usually had recurrence within the first 3 months. However, as many as 50% of patients who have early recurrences will not continue to have AF in the longer term.[286,287] While most studies use a 3-month blanking, as recommended by the HRS/EHRA/ECAS Expert Consensus Statement, other data have suggested that 2 months may be long enough.[289] Many studies have also used temporary AADs therapy during the blanking period to prevent early recurrences, supported by the 5A trial.[139]

Mid- to Long-Term Efficacy of AF Ablation

In patients with paroxysmal AF and minimal structural heart disease, consistent success rates for catheter ablation can be achieved. In these patients, the success rate at 1 year off AADs is 60–75% after single procedure and 65–90% after multiple procedures.[151,290] A number of recent systematic reviews have been published comparing the efficacy of catheter ablation of AF to AADs therapy.[291-294] The technique used in these studies was a PV isolation technique with little to no adjuvant ablation performed. The results of all of these reviews showed superiority of RF ablation over AADs therapy with a success rate of 75.7–77%.[291,294] A single repeat ablation procedure was required in 10–25% of patients, increasing the chance of off-drug success by an additional 5–15%.[295] The results of single prospective randomized trials published after the first Venice Chart International Consensus Document were similar.[296-302] In the 4A study, Jais *et al.* showed an 89% success rate at 1 year with catheter ablation (mean 1.8 ± 0.8 procedures) compared to 23% success for AADs ($P < 0.001$; $n = 112$).[300] In a large, multicenter, randomized trial with RF ablation and an intensive postablation monitoring regimen, Wilber *et al.* reported a 66% single-procedure success rate at 1 year compared with only 16% with AADs ($P < 0.001$; $n = 167$).[301] Finally, in the STOP-AF trial, which utilized cryo-ablation balloon technology for PV isolation, 245 patients were enrolled and the ablation group had a 69.9% success rate at 1 year (after 1 or more procedures) compared with only 7.3% success rate with AADs ($P < 0.001$).[302]

Very Long-Term Efficacy of AF Ablation

Data on very long-term outcomes from AF ablation, beyond 1 year, are more limited and largely restricted to single-center experiences (Table 13).[146,147,167-177] A few studies have shown that outcome of AF ablation beyond 1 year is preserved. Weerasooriya *et al.* described 1 high-volume center's experience over 5 years of follow-up in both paroxysmal (63%) and persistent AF patients, showing that the majority of recurrences occur within 6 months of the ablation procedure. Success rates at 1, 2, and 5 years were 87%, 81%, and 63%, respectively, with a median of 2 procedures per patient.[176] Other authors reported similar results.[167,169,172,177] Risk factors for very late recurrence appear to be nonparoxysmal AF, valvular heart disease, cardiomyopathy, and advanced age.[176] Other studies, however, have published less optimistic results.[146,147,168] Wokhlu *et al.* reported that the risk of recurrence increased in absolute terms by 12% in paroxysmal patients and 20% in persistent patients from year 1 to year 2.5.[147] Bertaglia *et al.* published that the actuarial atrial arrhythmia recurrence rate was 13.0% at 2 years, 21.8% at 3 years, 35.0% at 4 years, 46.8% at 5 years, and 54.6% at 6 years.[146] However, in both of these studies, the initial success rates were substantially lower than those reported in the previous section. Perhaps a difference in ablation technique is resulting in a higher late recurrence rate. Furthermore, although recurrences may be common, performing an additional procedure may still provide very long-term success, as described by Sawhney *et al.*[170]

Efficacy in Nonparoxysmal AF

In general, the success rate of AF ablation is lower in patients with persistent or long-lasting persistent AF compared to paroxysmal AF.[303] Many studies show success rates of 40–70% in nonparoxysmal AF and many have suggested the need for supplemental substrate modification in addition to PV isolation.[35] In a recently published meta-analysis of ablation in persistent AF, the pooled, single procedure, drug-free success rate was only 44% in 211 patients who underwent wide antral PV isolation alone.[303] With repeat procedures and concomitant AADs therapy, the success rates increase to 59% and 77%, respectively. Addition of adjuvant ablation may further improve outcome. The drug-free, 1 procedure success rate of PV isolation + linear ablation ranges from 48% to 57%,[303] which is better than that of PV isolation alone. Similarly, the success rate of PV isolation + CFAEs is higher than that of PV isolation alone: 51% with 1 procedure and 77% with 2 procedures.[63,66,304]

TABLE 13

Very Long-Term Efficacy of AF Ablation

Authors	Patients (No.)	Follow-Up (Months)	Recurrences After Single Procedure (%)		Recurrences After Repeat Procedures (%)
Shah *et al.*[167]	264†	28 ± 12	8.7%		3%
Katritsis *et al.*[168]	35	42 ± 6	79%		34%
Bhargava *et al.*[169]	1,404	57 ± 17	27%		10%
Sawhney *et al.*[170]	71	63 ± 5	44%		16%
Bertaglia *et al.*[146]	177†	49 ± 13		42%	
Wokhlu *et al.*[147]	774	36 ± 23			36%
Miyazaki *et al.*[172]	574	27 ± 14		34%	16%
Tzou *et al.*[173]	123†	60		29%	
Ouyang *et al.*[174]	161	54	53%		20%
Medi *et al.*[175]	100	39 ± 10	51%		18%
Weerasooriya *et al.*[176]	100	60	71%		37%
Pappone *et al.*[177]	99	48		27%	

†Patients free of arrhythmic recurrences at 1-year follow-up.

TABLE 14

Key Points Regarding the Short and Long-Term Efficacy of Catheter Ablation for AF

–Early recurrences of AF are not uncommon during the first 2–3 months postablation (35–50%). These arrhythmias tend to disappear after the initial period in 50% of the cases and not necessarily express procedural failure.

–AF ablation is an effective therapy over the mid/long term. In the first year following ablation, the success rate after multiple procedures is 65–90% for paroxysmal AF and 40–70% for nonparoxysmal AF.

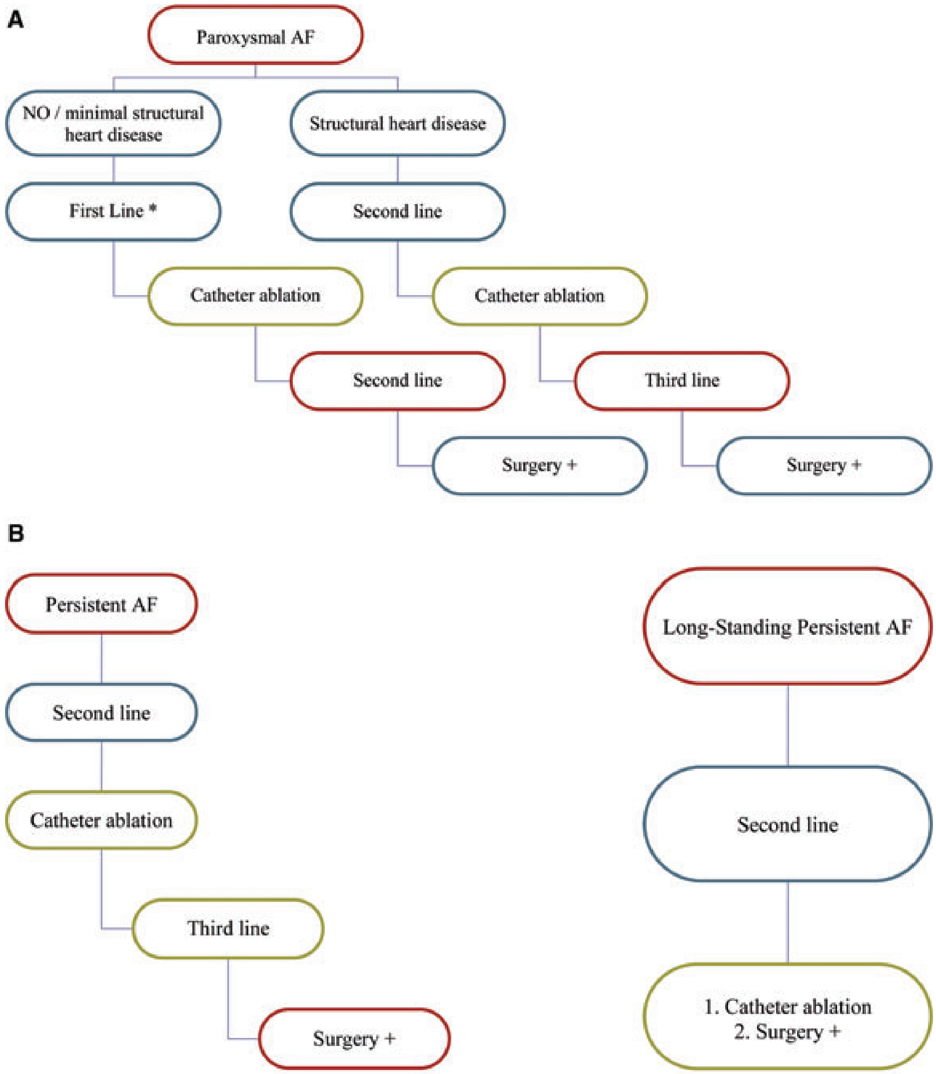
–Outcome for AF ablation seems to be preserved also beyond 1 year with only few very late recurrences; additional data, however, are required to this regard to confirm the robustness of the therapy.

–Prospective randomized trials conducted in a limited number of patients with paroxysmal AF have systematically shown that AF ablation is superior to AADs therapy in controlling AF; however, whether this translates into reduced morbidity and mortality remains to be assessed.

–Clinical factors predictive of procedural failure include nonparoxysmal AF, advanced age, hypertension, diabetes, sleep apnea syndrome, LA enlargement, LA scarring, and structural heart disease, such as cardiomyopathy or valvular heart disease.

Mechanisms of AF Ablation Failure

Studies have shown that the mechanism for long-term recurrence is linked to the recovery of electrical conduction between the PVs and the LA both in patients with paroxysmal and nonparoxysmal AF.[305] Recurrence, particularly atrial flutters, may also be related to incomplete scars created by the initial ablation.[253] Re-isolation of the PVs is quite often effective in treating recurrent AF or atrial flutters.[247] However, performance of additional ablation may be required, such as linear ablation or ablation of CFAEs, particularly in nonparoxysmal AF.[306] The mechanism of very late recurrences beyond 1 year may also involve development



*** Selected patients (See text)**
+ first line may be considered if the patient is undergoing cardiac surgery

Figure 3. *Indications to catheter ablation of AF. (A) Patients with paroxysmal AF. (B) Patients with persistent AF and long-lasting persistent AF.*

of non-PV triggers, either outside of the PV antra in the LA, or even within the CS and right atrium.[172,307]

A number of clinical factors predict late failure of AF ablation. In particular, LA scarring may be the strongest predictor of procedural failure.[124,308] Other risk factors include significant LA enlargement, advanced age, nonparoxysmal AF, and structural heart disease, such as cardiomyopathy or valvular heart disease.[147,176] Diabetes, hypertension, and sleep apnea syndrome have also been reported as risk factors for late recurrence.[146,287,309]

The key points regarding the short- and long-term efficacy of catheter ablation for AF are reported in Table 14.

Indications to Catheter Ablation of AF and Cost-Effectiveness

Indications to Catheter Ablation of AF

Several studies from high-volume centers have demonstrated the efficacy of catheter ablation for AF, mainly in patients with paroxysmal AF.[113,169,170,174,296-301,310,311] Therefore, catheter ablation of *paroxysmal AF* in symptomatic patients is an established indication in experienced centers after failure of AADs therapy (*second-line therapy*) (Fig. 3A) and LA size and left ventricular function are important to define the class of recommendation according to latest US guidelines for the management of patients with AF.[312,313] Class I, level of evidence A, is now recommended for patients with normal or mildly dilated LA and normal or mildly reduced left ventricular function without severe pulmonary disease.[313] Class IIa, level of evidence A, is recommended for patients with dilated LA or reduced left ventricular function and class IIb is recommended for patients with significant LA enlargement or significant LV dysfunction.[313] Ablation of *persistent AF* is feasible as *second-line therapy* after failure of medical treatment (Class IIa, level of evidence A) (Fig. 2B),[313] but there is no real consensus since the procedure is more complex with a lower success rate. For these reasons, catheter ablation of persistent AF requires a more accurate selection of patients and, particularly among patients with *long-standing persistent AF*, multiple interventions are frequently necessary to increase the success rate.[169] Thus, more data are needed to determine the most suitable candidates with long-standing AF for ablation (Fig. 3B). A new

Class I *first-line indication* for catheter ablation of AF is proposed for selected patients with very symptomatic *paroxysmal AF* (Fig. 3A).[296] This approach will require an accurate selection of candidates that includes patient preference for nonpharmacologic therapy, the absence (lone AF) or the presence of "minimal" structural heart disease, relatively frequent AF, e.g., >2 episodes/month, and with operators that are very experienced. For these highly selected patients the ablative procedure may be performed at an earlier stage of the disease[296,311] to avoid or limit arrhythmia progression to more persistent forms,[311] which is associated with lower success rate and with an increased need for repeat procedures.

Cost-Effectiveness

Whereas several studies have reported the costs of AF ablation, limited information is available on cost-effectiveness of the procedure.[314-320] The issue is further complicated by the fact that cost-effectiveness of AF ablation is influenced by several factors, the most relevant of whom being the type of AF, the clinical characteristics of patient population, the duration of the follow-up, the intensity of ECG monitoring, the success and complication rates of the procedure, the experience of the ablation centers, the costs of ablation tools and drug therapy and the differences in resource utilization.[321,322] In general, cost-effectiveness is better in patients with paroxysmal AF, with no or minimal heart disease, highly symptomatic with higher $CHADS_2$ score, treated in high-volume centers and followed for a sufficiently long period of time.[321,322] Under these conditions, the initial higher costs of ablation procedure are usually offset by the subsequent higher costs of AADs within a period of time ranging from 2 to 5 years or more.[314,318] In a recent study, the incremental cost-effectiveness ratio for AF ablation versus AADS was 51.431 $ per quality-adjusted life-year.[319] This suggests that AF ablation is a reasonably cost-effective therapy.

The key points regarding indications and cost-effectiveness of catheter ablation of AF are reported in Table 15.

TABLE 15

Key Points Regarding Indications and Cost-Effectiveness of Catheter Ablation of AF

Paroxysmal AF
- –As second-line therapy, after failure of AADs, catheter ablation is an established indication in symptomatic patients. The class of recommendation depends on LA size and left ventricular function.
- –As first-line therapy, catheter ablation may be indicated in a very selected group of highly symptomatic patients with no or minimal heart disease and relatively frequent episodes of AF.

Persistent/Long-Lasting Persistent AF
- –As second-line therapy, after failure of AADs, catheter ablation is feasible in symptomatic patients, but the selection has to be accurate because the procedure is more complex and associated with lower success rate and higher need for repeat interventions.

Cost-Effectiveness
- –Catheter ablation of AF is a reasonably cost-effective therapy provided that the selection of patients is appropriate.

Clinical Trials on AF/Future Perspectives

Available randomized studies of AF comparing catheter ablation and AADs have essentially focused on recurrences of AF, either clinically or electrocardiographically, and only to a lesser extent on measurements of quality of life.[296-302] Moreover, in these studies, no attempts were made to evaluate the effect on hospitalization, long-term survival, and thromboembolic complications, as the number of patients included was too small and the follow-up too short. The scientific evidence is also insufficient for drawing definitive conclusions about the cost-effectiveness of the AF ablation therapy, since its long-term effects are still uncertain. Therefore, further large randomized trials are needed to better clarify the real impact of AF ablation on these clinically relevant issues. Several ongoing trials have been planned to this regard.[323] Some (e.g., CABANA, EAST, and CASTLE-AF) are focused on mortality, hospitalization and stroke, others (e.g., RAAFT-2 and MANTRA-PAF) will test the effectiveness of catheter ablation early in the treatment of AF, and some more will assess the role of AF ablation in patients with heart failure (e.g., AATAC-HF, AMICA and ARC-HF) or with persistent and long-standing persistent AF (e.g., SARA).[323-326] The results of these trials will further improve our understanding of the clinical value of AF ablation.

The key points regarding clinical trials on AF/future perspectives are reported in Table 16.

TABLE 16

Key Points Regarding Clinical Trials on AF/Future Perspectives

- –Multiple randomized trials have demonstrated a superiority of AF ablation over AADs therapy in patients with drug-refractory symptomatic paroxysmal AF. Catheter ablation significantly reduces AF recurrences and hospitalizations, and improves quality of life.
- –The effects of catheter ablation on hard endpoints such as mortality or thromboembolic events remain to be established.
- –Ongoing trials are evaluating effectiveness of catheter ablation in broader patient populations, such as patients with nonparoxysmal AF and left ventricular dysfunction, as well as the effects of ablation on hard endpoints such as mortality.

Surgical Approach/Ablation of AF

Historical Aspects and Surgical Ablation Technologies

The surgical ablation era for the treatment of AF began in the early 1980s. In 1987, the Cox-Maze (C-M) procedure was introduced and then progressively modified over time.[327] The last version, the C-M III procedure, proved to be highly effective in eliminating AF with 97% of the patients free from symptomatic AF at a mean late follow-up of 5.4 ± 2.9 years.[328] However, it was technically difficult, highly invasive, and associated with significant risks. With the introduction of ablation devices in the last decades, only a small number of cardiac surgeons still perform the cut-and-sew operation today. Ablation devices have transformed the field of AF surgery by decreasing procedural difficulty and operative time, thus allowing for an application to a broader patient population and for the development of minimally invasive techniques.[329] Many devices using different energy sources have been proposed and employed for surgical treatment of AF. They include RF (unipolar and bipolar), cryo-ablation (nitrous oxide and argon-based technology), and high intensity frequency ultrasound devices. Each ablation technology has its own advantages and disadvantages. It is imperative for surgeons to develop a complete understanding of the effects of each specific ablation technology on atrial hemodynamic, function, and electrophysiology. This will allow for more appropriate use of devices in the operating room.

Surgical Techniques and Outcome

There are a myriad of different surgical ablation procedures that are presently performed. They can be grouped into 4 broad categories: the C-M procedure, PV isolation alone, PV isolation with left atrial lesion sets, and hybrid approach.

C-M procedure

The original cut-and-sew C-M III procedure is only rarely performed today. At most centers, the surgical incisions have been replaced with lines of ablation using a variety of energy sources. The most widely adopted variation has been the C-M IV procedure, which utilizes bipolar RF energy to replace most of the surgical incisions.[330] This RF ablation-assisted procedure incorporates most of the lesions of the C-M III and is performed on cardiopulmonary bypass. The operation can be done either through a median sternotomy or a less-invasive right mini-thoracotomy.[331] The PVs are isolated with the bipolar clamps on the beating heart. It is imperative to document entrance and/or exit block at the time of surgery. In a large C-M IV series, the freedom from AF was 89% and the freedom from AF off AADs was 78% at 1 year, in the entire population of patients.[332] In patients undergoing a stand-alone C-M IV procedure for lone AF, the results were even better with a freedom from AF of 90% and freedom from AF off AADs of 84% at 2 years with no intraoperative mortality and no postoperative strokes.[333] There was no difference in success rates for patients with paroxysmal AF compared to those with persistent or long-lasting persistent AF. Similar results have been obtained using cryoablation or high intensity frequency ultrasound.

PV isolation alone

The PVs have been isolated either separately or as a large box lesion incorporating the posterior LA. This procedure may be performed through thoroscopy with a minimally invasive surgical approach[334] and may be associated with GP ablation. In a recent study using this technique, the success rate at 1 year was 65% with a low incidence of postoperative complications.[335] However, a number of studies support the contention that PV isolation alone or associated to autonomic denervation[335,336] is inadequate for persistent and long-lasting persistent AF due to the substrate changes induced by electrical remodeling.

Expanded lesion sets

When connection lines to the mitral annulus are added, the success rates are more satisfactory and comparable to those of the cut and sew maze. Jeanmart and colleagues reported an AF-free rate of 69.7% with an endocardial box lesion plus a connecting line to the mitral annulus.[337] However, incorporation of the mitral valve isthmus can be challenging. To overcome this problem and to replicate the LA lesions of the C-M III, the Dallas lesion set was developed.[338] With this approach the connection to the mitral valve is made to the anterior annulus at the left fibrous trigone.[339] The other lesions include a line from the right superior PV to the left superior PV and a line from the left superior PV to the base of the amputated LA appendage.[340] In a multicenter registry, including 124 patients treated with the Dallas lesion set, a high success rate was measured: 63% in a group that had previously undergone catheter ablation (n = 21) and 86% in patients who had not been ablated before (unpublished data provided by Edgerton JR).

Hybrid approach

Further frontiers include the use of hybrid approach, combining the strengths of epicardial and endocardial ablation.[341] Lesions are more likely to be transmural when burning inside and outside simultaneously. The potential for improved outcomes through hybrid ablation also derives from combining expertise levels. The demonstration of the efficacy of this approach awaits the completion of currently underway trials.

Indications

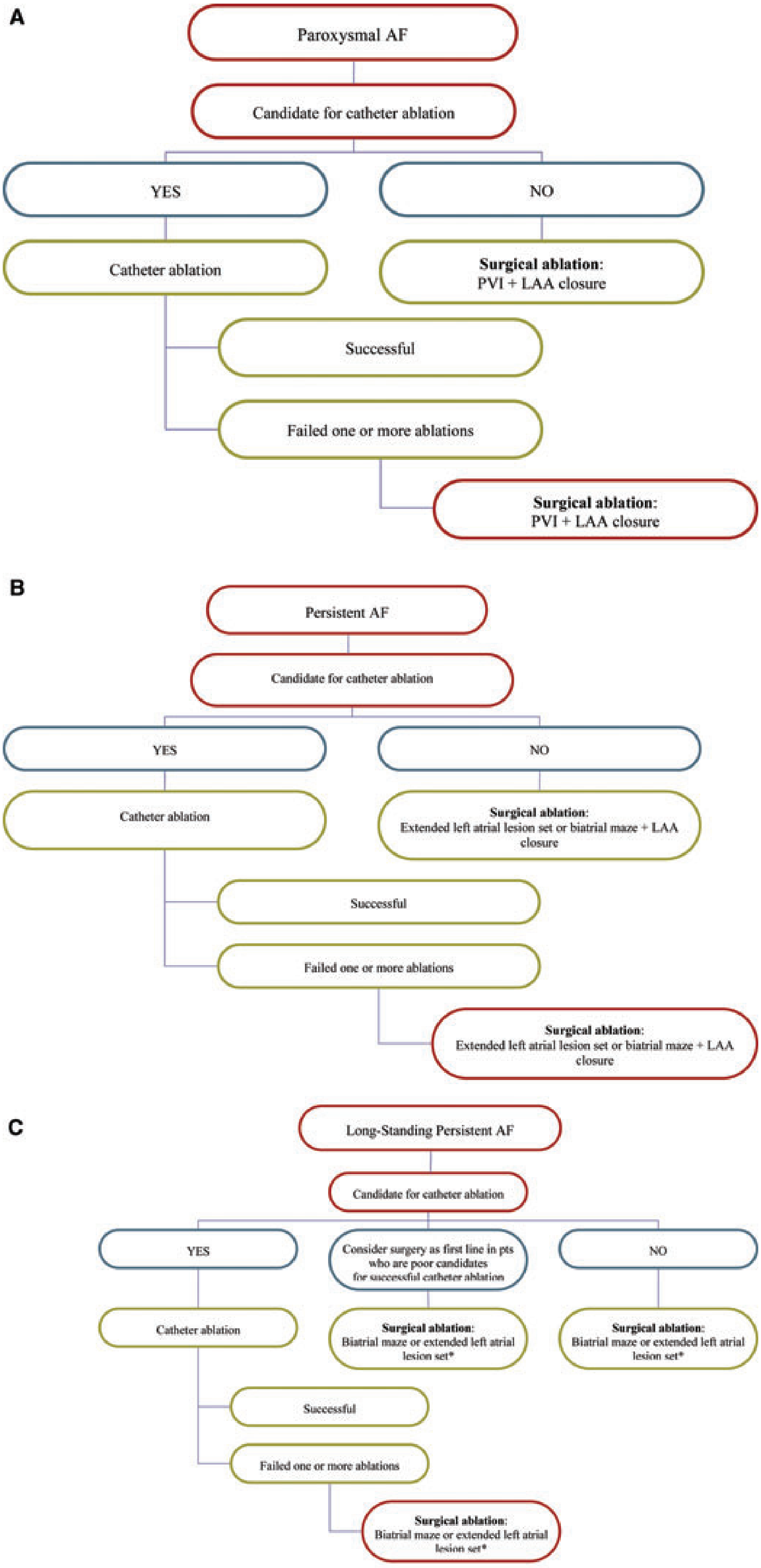
The current indications for surgical ablation as defined in the HRS/EHRA/ECAS expert consensus statement[101] on AF ablation include: (1) all symptomatic patients with documented AF undergoing other cardiac surgical procedures; and (2) selected asymptomatic patients with AF undergoing cardiac surgery in which the ablation can be performed with minimal risk in experienced centers. Moreover, surgical ablation is indicated, as stand-alone procedure, in symptomatic patients who either prefer a surgical approach, have failed 1 or more attempts at catheter ablation or are not candidates for catheter ablation (Fig. 4). However, there are other relative indications for surgery, in particular for a stand-alone procedure, that were not included in the HRS/EHRA/ECAS expert consensus statement that should be taken into consideration as first-line therapy in lieu of less invasive catheter ablation. The following are examples: (1) AF patients who develop a contraindication to long-term anticoagulation and have a high risk for stroke ($CHADS_2$ score ≥ 2) are excellent candidates for surgery. The C-M procedure both eliminates AF in most of these patients, and also amputates the LA appendage. The stroke rate following the procedure off anticoagulation has been remarkably low, even in patients with high $CHADS_2$ scores;[342] (2) surgical treatment for AF also should be considered in patients with long-lasting AF who have suffered a cerebrovascular accident despite adequate anticoagulation. These patients are at high risk for repeat neurological events. In a series of over 200 patients with a stand-alone C-M procedure there was only 1 late stroke, and over 80% of patients were off anticoagulation at last follow-up;[343,344] (3) finally, symptomatic AF patients with a clot in the LA appendage who have failed medical therapy are not candidates for catheter ablation and should be referred for surgical ablation.

The key points regarding surgical approach/ablation are reported in Table 17.

Hospital Equipment and Facilities, Personnel, Training Requirements, and Competences

Hospital Equipment, Facilities, and Technological Requirements

Centers involved in AF ablation procedures should be equipped with state-of-the-art equipment. These should include the following:



*** extended left atrial lesion set - only in experienced centres with established AF team.**

Figure 4. *Indications to surgical ablation of AF. (A) Patients with paroxysmal AF. (B) Patients with persistent AF. (C) Patients with long-lasting AF.*

TABLE 17

Key Points Regarding Surgical Approach/Ablation of AF

–Surgical techniques for AF include Cox-Maze procedure, PV isolation alone, PV isolation with LA lesion sets, and hybrid approach.
–The original "cut and sew" Cox-Maze procedure is only performed rarely today. At most centers the surgical incisions have been replaced with lines of AF ablation using a variety of energy sources (especially bipolar RF).
–The surgical procedures can be done either through sternotomy or through thoracoscopy with a minimally invasive surgical approach.
–Success rates of surgical AF ablation vary between 65% and 90% during follow-up. This great range can be attributed to many factors including type of AF, patient characteristics, the use of different ablation devices and energy sources, differing lesion sets, and surgeon experience.
–Surgical AF ablation is indicated in all symptomatic patients as well as in selected asymptomatic patients with documented AF who undergo other cardiac surgical procedures.
–Surgical AF ablation is also indicated, as stand-alone procedure, in symptomatic patients with AF who either prefer a surgical approach, have failed 1 or more attempts at or are not candidates to catheter ablation.

- Sedation, anesthesia and resuscitation equipment, including pericardiocentesis materials, biphasic defibrillator, and a mechanical ventilator.
- Up-to-date ECG, blood pressure, oxygen saturation, and ACT monitoring equipment.
- Modern catheterization laboratories, including X-ray systems allowing dose-reduction and image optimization and staff protection.
- A multichannel recording system (at least a 16-channel recording system) and a multi-programmable stimulator.
- 3D electro-anatomical mapping: at least 1 system.
- RF power generators and/or cryoablation console.
- Cardiac imaging techniques, including at least transthoracic echocardiography and TEE and preferably also a multislice-CT scanner or MR scanner.
- Intracardiac echocardiography (recommended but not mandatory).

Other equipments, such as magnetic and robotic navigation systems and single-shot device systems, are promising but their impact and superiority compared to the conventional approach of AF ablation is unclear and remains speculative.

Training and Knowledge

Indications and patient selection

The physician (i.e., electrophysiologist) should be competent in counseling patients and evaluating the potential risks and benefits of catheter ablation and should be able to direct current recommendations to the specific needs of individual patients.

Anatomical knowledge

The detailed knowledge of cardiac anatomy with specific attention to LA and its adjacent structures is highly required for performing the technical aspects of transseptal puncture, cannulation of the LA and navigation and to avoid or reduce the risk of procedure-related complications.

Interpretation of electrograms/knowledge in basic EP studies

Every electrophysiologist performing catheter ablation of AF must have achieved a proficiency in the ECG and intracavitary electrograms interpretation. Recognition of PV potentials both at baseline and during CS pacing and when PV electrical disconnection is achieved remains the cornerstone of the ablation procedure. Correct identification and interpretation of CFAEs is also important, because these potentials may be a target for ablation in patients with persistent and long-lasting persistent AF.

TABLE 18

Basic Technical Skills to be Proficient for an Atrial Fibrillation Procedure

–Vascular access and cannulation.
–Fluoroscopy system use and familiarity with fluoroscopic projections and landmarks.
–Catheter manipulation and positioning.
–Set up and understanding of the electrophysiology system, including the intracardiac recording system, the electrical stimulator, and the 3D electro-anatomical system.
–Knowledge on materials and systems to manage complications (defibrillator, pericardiocentesis kit, etc.)

Knowledge of 3D mapping systems

An electrophysiologist who performs AF ablation procedures must be familiar with the handling and interpretation, as well as with the limitations of different 3D mapping systems. Therefore trainees should be able to perform and interpret the different types of electrophysiological analysis like activation mapping for the treatment of left-atrial macroreentrant tachycardia, voltage mapping for substrate guided ablation approaches and purely anatomical maps for conventional AF ablation procedures.

Technical competence

Technical competence and skills in catheter, sheath and guide wire manipulation are required.

Basic technical skills

Basic technical skills to be proficient for an atrial fibrillation procedure are listed in Table 18.

Transseptal puncture

A good knowledge of transseptal puncture techniques is mandatory for all electrophysiologists involved in PV isolation and other left-sided procedures.

Competence in performing basic EP studies and ablation procedures

The European Heart Rhythm Association (EHRA) presently recommends receiving formal training for at least 1 year in conventional electrophysiology procedures and simpler ablations before being involved in AF ablation procedures.[345] Following this first year, the trainee should receive formal training for at least another year in more complex procedures, 1 of them being AF ablation. According to this scientific organization the trainee should be directly involved in a minimum number of 150 ablation procedures (35 to be performed as the primary operator) and 10 transseptal catheterizations (5 to be performed as the primary operator) at the end of this 2-year period.[345] The American Accreditation Council of Graduate Medical Education (ACGME) recommends involvement in a minimum of 75 catheter ablation procedures.[346] However, these requirements are the basis to be trained in ablation procedures in general and

TABLE 19

Key Points Regarding Hospital Equipment and Facilities, Personnel, Training Requirements and Competences

–Centers involved in AF ablation procedures should be equipped with state-of-the-art equipment.
–The physicians should be competent in counseling patients and evaluating the potential risks and benefits of catheter ablation on individual basis.
–Every electrophysiologist performing AF catheter ablation should have a detailed anatomical knowledge of LA and its adjacent structures, must have achieved a proficiency in the ECG and intracavitary electrograms interpretation, and must be familiar with the handling and interpretation of different 3D mapping systems.
–Moreover, technical competence and skills in catheter, sheath, and guide wire are required.
–Although no scientific organization has established precise criteria, participation in at least 30–50 mentored AF ablations and 10 transseptal punctures is considered the minimum requirement to be considered trained for AF ablation.

possibly more practical experience, especially in transseptal catheterization, should be required to be fully competent to perform AF ablation procedures as independent operator and to manage potential complications, such as macroreentrant left AT.[101] To date, no scientific organization has established a minimum number of AF procedures to be performed as primary operator in order to be considered fully trained for this task. The American College of Cardiology and the American Heart Association recommend participation in 30 to 50 mentored AF ablations.[347] The former committee also recommends involvement in 10 transseptal punctures.[347] Anyhow, some reports suggested that results improved in centers with experience in more than 100 AF ablations.[233]

Management of Complications

Trainees must be familiar with risk factors, clinical signs, and symptoms of potential early as well as delayed occurring complications. Backup of an experienced physician with skills in emergency needle pericardiocentesis is necessary and training in pericardiocentesis definitely necessary. Awareness of risks of conscious sedation (including hypoventilation, aspiration, and respiratory arrest) as well as management of those should be trained.

Follow-Up

Trainees must be familiar with the principles of adequate rhythm monitoring following AF catheter ablation with clinical trials necessitating more intense AF monitoring than in clinical practice.[101,348] The trainee must be familiar with indications and contraindications for cardioversion, concomitant AADs use and timing of repeat ablation. Furthermore the use of anticoagulation regimes must be set in the right context with adequate risk-benefit evaluation of thromboembolic and bleeding risks.

The key points regarding hospital equipment and facilities, personnel, training requirements and competences are reported in Table 19.

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Appendix

Venice Chart Co-Chairmen

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Anatomy of structures relevant to atrial fibrillation ablation

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Techniques and technologies for atrial fibrillation catheter ablation

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