2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Patient Selection, Procedural Techniques, Patient Management and Follow-up, Definitions, Endpoints, and Research Trial Design

A report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society

Hugh Calkins, MD, FACC, FHRS, FAHA; Karl Heinz Kuck, MD, FESC; Riccardo Cappato, MD, FESC; Josep Brugada, MD, FESC; A. John Camm, MD, PhD; Shih-Ann Chen, MD, FHRS[§]; Harry J.G. Crijns, MD, PhD, FESC; Ralph J. Damiano, Jr., MD[^]; D. Wyn Davies, MD, FHRS; John DiMarco, MD, PhD, FACC, FHRS; James Edgerton, MD, FACC, FACS, FACCP[^]; Kenneth Ellenbogen, MD, FHRS; Michael D. Ezekowitz, MD; David E. Haines, MD, FHRS; Michel Haissaguerre, MD; Gerhard Hindricks, MD; Yoshito Iesaka, MD[§]; Warren Jackman, MD, FHRS; Jose Jalife, MD, FHRS; Pierre Jais, MD; Jonathan Kalman, MD[§]; David Keane, MD; Young-Hoon Kim, MD, PhD[§]; Paulus Kirchhof, MD; George Klein, MD; Hans Kottkamp, MD; Koichiro Kumagai, MD, PhD[§]; Bruce D. Lindsay, MD, FHRS[∞]; Moussa Mansour, MD; Francis E. Marchlinski, MD; Patrick M. McCarthy, MD[^]; J. Lluis Mont, MD, FESC; Fred Morady, MD; Koonlawee Nademanee, MD; Hiroshi Nakagawa, MD, PhD, Andrea Natale, MD, FHRS[i]; Stanley Nattel, MD; Douglas L. Packer, MD, FHRS; Carlo Pappone, MD, PhD; Eric Prystowsky, MD, FHRS; Antonio Raviele, MD, FESC; Vivek Reddy, MD; Jeremy N. Ruskin, MD; Richard J. Shemin, MD[^]; Hsuan-Ming Tsao, MD[§]; David Wilber, MD

[^]*STS Representative*
[§]*APHRS Representative*
[i]*ACC Representative*
[∞]*AHA Representative*

TASK FORCE MEMBERS:
Chairs:
Hugh Calkins, MD, FACC, FHRS, FAHA, Chair, Johns Hopkins Hospital, Maryland, USA
Karl Heinz Kuck, MD, FESC, Co-Chair, Allgemeines Krankenhaus St. Georg, Hamburg, GERMANY
Riccardo Cappato, MD, FESC, Co-Chair, Arrhythmia and EP Center, IRCCS Policlinico San Donato, Milan, ITALY

Section Chairs:
Atrial Fibrillation: Definitions, Mechanisms, and Rationale for Ablation—Shih-Ann Chen, MD, FHRS, Taipei Veterans General Hospital, TAIWAN

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Indications for Ablation and Patient Selection—Eric N. Prystowsky, MD, FHRS, The Care Group, LLC, Indiana, USA
Techniques and Endpoints for Atrial Fibrillation—Karl Heinz Kuck, MD, FESC, Allgemeines Krankenhaus St. Georg, Hamburg, GERMANY
Technologies and Tools—Andrea Natale, MD, FHRS, Texas Cardiac Arrhythmia Institute at St. David's Medical Center, Texas, USA
Other Technical Aspects—David E. Haines, MD, FHRS, Chair, William Beaumont Hospital, Michigan, USA
Follow-up Considerations and Definitions for Success—Francis E. Marchlinski, MD, Hospital of the University of Pennsylvania, Pennsylvania, USA
Outcomes and Efficacy of Catheter Ablation of Atrial Fibrillation—Hugh Calkins, MD, FACC, FHRS, FAHA, Johns Hopkins Hospital, Maryland, USA
Complications of Atrial Fibrillation Ablation: Definitions, Incidence, Prevention and Management—D. Wyn Davies, MD, FHRS, St. Mary's Hospital, Imperial College Healthcare NHS Trust, London, UNITED KINGDOM
Training Requirements and Competencies—Bruce D. Lindsay, MD, FHRS, Cleveland Clinic Foundation, Ohio, USA
Surgical Ablation of Atrial Fibrillation—Ralph Damiano, Jr., MD, Washington University School of Medicine, Missouri, USA
Clinical Trial Considerations—Douglas L. Packer, MD, FHRS, Mayo Foundation, Minnesota, USA

Co-Authors:
Josep Brugada, MD, FESC, Hospital Clinic, University of Barcelona, SPAIN
A. John Camm, MD, PhD, St. George's University of London, London, UNITED KINGDOM
Harry J.G. Crijns, MD, PhD, FESC, University Hospital Maastricht, THE NETHERLANDS
John DiMarco, MD, University of Virginia Health System, Virginia, USA
James Edgerton, MD, FACC, FACS, FACCP, The Heart Hospital Baylor Plano and Cardiopulmonary Research, Science, and Technology Institute, Texas, USA
Kenneth Ellenbogen, MD, Virginia Commonwealth University, Virginia, USA
Michael D. Ezekowitz, MD, Jefferson Medical College, Pennsylvania, USA
Michel Haissaguerre, MD, Université De Bordeaux, Hôpital Cardiologique, FRANCE
Gerhard Hindricks, MD, University of Leipzig, Leipzig, GERMANY
Yoshito Iesaka, MD, Tsuchiura Kyodo Hospital, JAPAN
Warren M. Jackman, MD, FHRS, University of Oklahoma Health Science Center, Oklahoma, USA
Pierre Jais, MD, Université De Bordeaux, Hôpital Cardiologique, FRANCE
Jose Jalife, MD, University of Michigan, Michigan, USA
Jonathan Kalman, MD, Royal Melbourne Hospital, Melbourne, AUSTRALIA
David Keane, MD, St. Vincent's University Hospital, Dublin, IRELAND
Young-Hoon Kim, MD, PhD, Korea University Medical Center, Seoul, KOREA
Paulus Kirchhof, MD, University of Birmingham Centre for Cardiovascular Sciences, Birmingham, UNITED KINGDOM, and Department of Cardiology, University of Münster, Münster, GERMANY
George Klein, University Hospital, London, Ontario, CANADA
Hans Kottkamp, MD, FESC, Clinic Hirslanden Zurich, SWITZERLAND
Koichiro Kumagai, MD, PhD, Fukuoka Sanno Hospital, JAPAN
Moussa Mansour, MD, Massachusetts General Hospital, Massachusetts, USA
Francis Marchlinski, MD, Hospital of the University of Pennsylvania, Ohio, USA
Patrick McCarthy, MD, Northwestern Memorial Hospital, Illinois, USA
J. Lluis Mont, MD, FESC Hospital Clinic, University of Barcelona, SPAIN

Fred Morady, MD, University of Michigan Health System, Michigan, USA
Koonlawee Nademanee, MD, Pacific Rim EP Research Institute Center, California, USA
Hiroshi Nakagawa, MD, PhD, University of Oklahoma Health Sciences Center, Oklahoma, USA
Stanley Nattel, MD, Montreal Heart Institute, Quebec, CANADA
Carlo Pappone, MD, PhD, Maria Cecilia Hospital, Cotignola, ITALY
Antonio Raviele, MD, FESC, Umberto I Hospital, Venice, ITALY
Vivek Reddy, MD, Mount Sinai School of Medicine, New York, USA
Jeremy N. Ruskin, MD, Massachusetts General Hospital, Massachusetts, USA
Richard J. Shemin, MD, David Geffen School of Medicine at UCLA, California, USA
Hsuan-Ming Tsao, MD, National Yang Ming University Hospital, TAIWAN
David Wilber, MD, FHRS, Loyola University Medical Center, Illinois, USA

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1. Introduction

During the past decade, catheter ablation of atrial fibrillation (AF) has evolved rapidly from an investigational procedure to its current status as a commonly performed ablation procedure in many major hospitals throughout the world. Surgical ablation of AF, using either standard or minimally

invasive techniques, is also performed in many major hospitals throughout the world.

In 2007, an initial Consensus Statement on Catheter and Surgical AF Ablation was developed as a joint effort of the Heart Rhythm Society, the European Heart Rhythm Association, and the European Cardiac Arrhythmia Society.[e1] The 2007 document was also developed in collaboration with the Society of Thoracic Surgeons and the American College of Cardiology. Since the publication of the 2007 document, there has been much learned about AF ablation, and the indications for these procedures have changed. Therefore the purpose of this 2012 Consensus Statement is to provide a state-of-the-art review of the field of catheter and surgical ablation of AF and to report the findings of a Task Force, convened by the Heart Rhythm Society, the European Heart Rhythm Association, and the European Cardiac Arrhythmia Society and charged with defining the indications, techniques, and outcomes of this procedure. Included within this document are recommendations pertinent to the design of clinical trials in the field of AF ablation, including definitions relevant to this topic.

This statement summarizes the opinion of the Task Force members based on an extensive literature review as well as their own experience. It is directed to all health care professionals who are involved in the care of patients with AF, particularly those who are undergoing, or are being considered for, catheter or surgical ablation procedures for AF. This statement is not intended to recommend or promote catheter ablation of AF. Rather the ultimate judgment regarding care of a particular patient must be made by the health care provider and patient in light of all the circumstances presented by that patient.

In writing a "consensus" document, it is recognized that consensus does not mean that there was complete agreement among all Task Force members. Surveys of the entire Task Force were used to identify areas of consensus and also to develop recommendations concerning the indications for catheter and surgical AF ablation. The grading system for indication level of class of evidence was adapted based on that used by the American College of Cardiology and the American Heart Association.[e2] However, it is important to state that this document is not a guideline. The indications for catheter and surgical ablation of AF are presented with a class and grade of recommendation to be consistent with what the reader is used to seeing in guideline statements. A Class I recommendation means that the benefits of the AF ablation procedure markedly exceed the risks, and that AF ablation should be performed. A Class IIa recommendation means that the benefits of an AF ablation procedure exceed the risks, and that it is reasonable to perform AF ablation. A Class IIb recommendation means that the benefit of AF ablation is greater or equal to the risks, and that AF ablation may be considered. A Class III recommendation means that AF ablation is of no proven benefit and is not recommended.

The committee reviewed and ranked evidence supporting current recommendations with the weight of evidence ranked as Level A if the data were derived from multiple randomized clinical trials or meta-analyses (of selected studies) or selected meta-analyses. The committee ranked available evidence as Level B when data were derived from a single randomized trial or nonrandomized studies. Evidence was ranked as Level C when the primary source of the recommendation was consensus opinion, case studies, or standard of care. For certain conditions for which inadequate data are available, recommendations are based on expert consensus and clinical experience and ranked as Level C.

The main objective of this document is to improve patient care by providing a foundation of knowledge for those involved with catheter ablation of AF. It is recognized that this field continues to evolve rapidly. As this document was being prepared, further clinical trials of catheter and surgical ablation of AF were underway.

The Task Force writing group was composed of experts representing seven organizations: the American College of Cardiology (ACC), the American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), the European Cardiac Arrhythmia Society (ECAS), the European Heart Rhythm Association (EHRA), the Society of Thoracic Surgeons (STS), and the Heart Rhythm Society (HRS). All members of the Task Force, as well as peer reviewers of the document, were asked to provide disclosure statements for all relationships that might be perceived as real or potential conflicts of interest. These tables are shown at the end of this document. Despite a large number of authors, the participation of several societies and professional organizations, and the attempts of the group to reflect the current knowledge in the field adequately, this document is not intended as a guideline. Rather, the group would like to refer to the current guidelines on AF management[e3,e4] for the purpose of guiding overall AF management strategies. This Consensus Document is specifically focused on catheter and surgical ablation of AF, which we recognize is relevant for only a small portion of the population affected by AF.

2. Atrial fibrillation: definitions, mechanisms, and rationale for ablation

2.1. Definitions

AF is a common supraventricular arrhythmia that is characterized by chaotic contraction of the atrium. An electrocardiogram (ECG) recording is necessary to diagnose AF. Any arrhythmia that has the ECG characteristics of AF and lasts sufficiently long for a 12-lead ECG to be recorded, or at least 30 seconds on a rhythm strip, should be considered an AF episode.[e1,e3] The diagnosis requires an ECG or rhythm strip demonstrating: 1) "absolutely" irregular RR intervals (in the absence of complete AV block), 2) no distinct P waves on the surface ECG, and 3) an atrial cycle length (when visible) that is usually variable and less than 200 ms.[e3] Although there are several classification systems for AF, for this consensus document, we have adopted in large part the classification system that was developed by the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation and the ESC 2010 Guidelines for the Management of Atrial Fibrillation.[e2,e3,e5] We recommend that this classification system be used for future studies of catheter and surgical ablation of AF.

Every patient who presents with AF for the first time is considered to have first diagnosed AF, irrespective of the duration of

Table 1 Types and classification of atrial fibrillation**

Atrial Fibrillation Episode	An atrial fibrillation episode is defined as AF that is documented by ECG monitoring and has a duration of at least 30 seconds, or if less than 30 seconds, is present continuously throughout the ECG monitoring tracing. The presence of subsequent episodes of AF requires that sinus rhythm be documented by ECG monitoring between AF episodes.
Paroxysmal AF*	Paroxysmal AF is defined as recurrent AF (≥2 episodes) that terminates spontaneously within 7 days. Episodes of AF of ≤ 48 hours' duration that are terminated with electrical or pharmacologic cardioversion should also be classified as paroxysmal AF episodes.
Persistent AF*	Persistent AF is defined as continuous AF that is sustained beyond seven days. Episodes of AF in which a decision is made to electrically or pharmacologically cardiovert the patient after ≥ 48 hours of AF, but prior to 7 days, should also be classified as persistent AF episodes.
Longstanding Persistent AF	Longstanding persistent AF is defined as continuous AF of greater than 12 months' duration.
Permanent AF	The term permanent AF is not appropriate in the context of patients undergoing catheter or surgical ablation of AF, as it refers to a group of patients for which a decision has been made not to restore or maintain sinus rhythm by any means, including catheter or surgical ablation. If a patient previously classified as having permanent AF is to undergo catheter or surgical ablation, the AF should be reclassified.

**It is recognized that patients may have both paroxysmal and persistent AF. A patient's AF type should be defined as the most frequent type of AF experienced within six months of an ablation procedure.* Continuous AF is AF that is documented to be present on all ECG monitoring performed during a defined period of time.
**We recommend that the term "chronic AF" not be used in the context of patients undergoing ablation of AF as it is ambiguous, and there is no standardized definition of this term.

the arrhythmia. Paroxysmal AF is defined as recurrent AF (≥2 episodes) that terminates spontaneously within 7 days (Table 1). Persistent AF is defined as recurrent AF that is sustained for ≥7 days. In addition, we recommend that patients with continuous AF who undergo cardioversion within 7 days be classified as having paroxysmal AF if the cardioversion is performed within 48 hours of AF onset, and persistent AF if the cardioversion is performed more than 48 hours after AF onset. A third category of AF is "longstanding persistent AF" that is defined as continuous AF of greater than one-year's duration. The term permanent AF is defined as AF in which the presence of the AF is accepted by the patient (and physician). Within the context of any rhythm control strategy, including catheter ablation, the term permanent AF is not meaningful. The term permanent AF represents a joint decision by the patient and a physician to cease further attempts to restore and/or maintain sinus rhythm at a particular point in time. It is important, therefore, to recognize that the term "permanent AF" represents a therapeutic attitude on the part of a patient and the physician rather than any inherent pathophysiological attribute of the AF. Such decisions may change as symptoms, the efficacy of therapeutic interventions, and patient and physician preferences evolve. If after reevaluation, a rhythm control strategy is recommended, the AF should be redesignated as paroxysmal, persistent, or longstanding persistent AF.[e2] Silent AF is defined as asymptomatic AF often diagnosed by an opportune ECG or rhythm strip. Any of the above mentioned types of AF may be silent (ie, asymptomatic). It is recognized that a particular patient may have AF episodes that fall into one or more of these categories.[e2] It is recommended that patients be categorized by their most frequent pattern of AF during the six months prior to performance of an ablation procedure.

It is recognized by the consensus Task Force that these definitions of AF are very broad, and that when describing a population of patients undergoing AF ablation, additional details should be provided. This is especially important when considering the category of persistent AF and longstanding persistent AF. Pathophysiologically oriented classifications of AF, such as recently proposed, and reporting of concomitant cardiovascular diseases will help in this regard.[e6] Investigators are urged to specify the duration of time patients have spent in continuous AF prior to an ablation procedure, and also to specify whether patients undergoing AF ablation have previously failed pharmacologic therapy, electrical cardioversion, and/or catheter ablation. Shown in Table 1 are a series of definitions for types of AF that can be used for future trials of AF ablation and also in the literature to help standardize reporting of patient populations and outcomes.

2.2. Mechanisms of atrial fibrillation

For many years, three major schools of thought competed to explain the mechanism(s) of AF: multiple random propagating wavelets, focal electrical discharges, and localized reentrant activity with fibrillatory conduction.[e7–e11] Considerable progress has been made in defining the mechanisms of initiation and perpetuation of AF.[e12–e14] Perhaps the most striking breakthrough was the recognition that, in a subset of patients, AF was triggered by a rapidly firing focus and could be "cured" with a localized catheter ablation procedure.[e12,e13] This landmark observation compelled the arrhythmia community to refocus its attention on the pulmonary veins (PVs) and the posterior wall of the left atrium (LA), as well as the autonomic innervation in that region (Figure 1). It also reinforced the concept that the development of AF requires a "trigger" and an anatomic or functional substrate capable of both initiation and perpetuation of AF.

In this section of the document, a contemporary understanding of the mechanisms of AF is summarized. As illustrated in Figure 2, some authors[e15–e17] have proposed that, in the presence of an appropriate heterogeneous AF substrate, a focal trigger can result in sustained high frequency reentrant AF drivers (rotors). The waves that emerge from the rotors un-

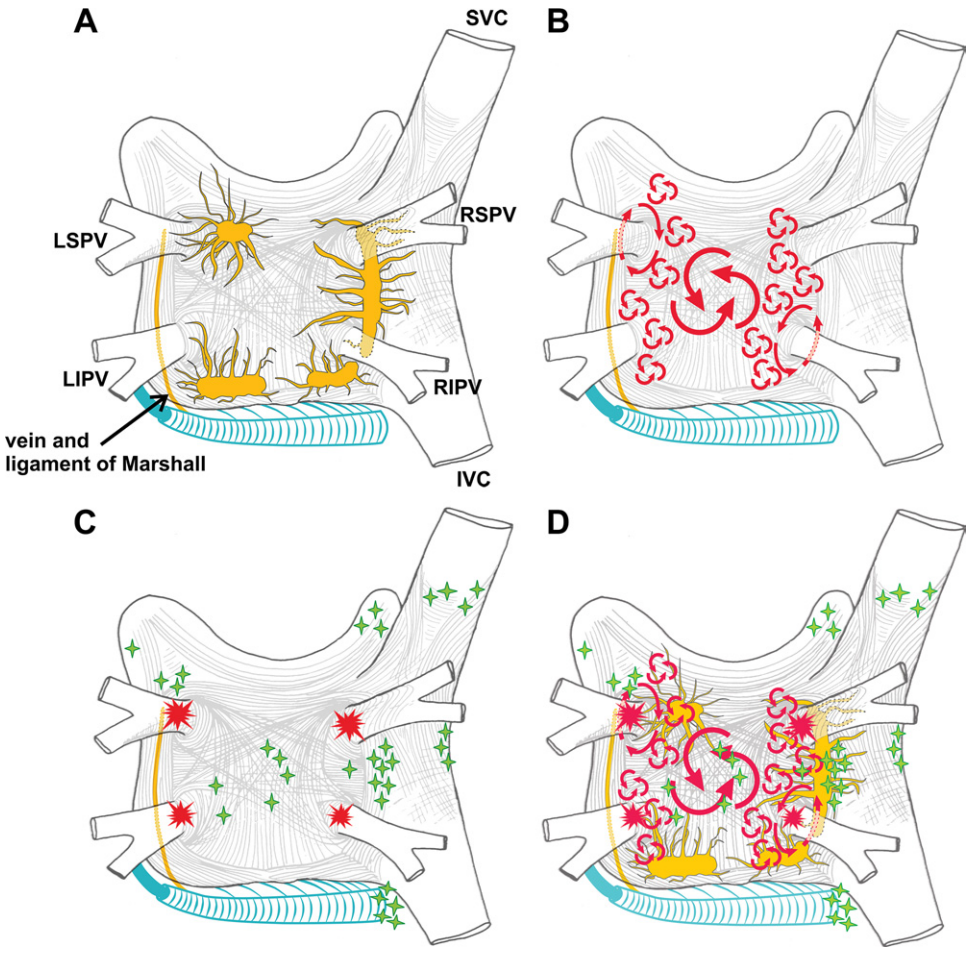

Figure 1 Structure and mechanisms of atrial fibrillation. **A:** Schematic drawing of the left and right atria as viewed from the posterior. The extension of muscular fibers onto the PVs can be appreciated. Shown in *yellow* are the five major left atrial autonomic ganglionic plexi (GP) and axons (superior left GP, inferior left GP, anterior right GP, inferior right GP, and ligament of Marshall). Shown in *blue* is the coronary sinus, which is enveloped by muscular fibers that have connections to the atria. Also shown in *blue* is the vein and ligament of Marshall, which travels from the coronary sinus to the region between the left superior PV and the left atrial appendage. **B:** The large and small reentrant wavelets that play a role in initiating and sustaining AF. **C:** The common locations of PV *(red)* and also the common sites of origin of non-PV triggers (shown in *green).* **D:** Composite of the anatomic and arrhythmic mechanisms of AF. (Adapted from Circulation,[e28] Am J Cardiol,[e735] Tex Heart Inst J.[e736])

dergo spatially distributed fragmentation and give rise to fibrillatory conduction.[e7,e8,e18–21] Evidence suggests that when high frequency atrial activation is maintained for at least 24 hours, ion channel remodeling changes the electrophysiologic substrate,[e8,e19,e21] promoting sustained reentry and increasing the activity of triggers, further contributing to AF permanence. Sustained high rates in the atrium and/or the presence of heart disease are associated with structural remodeling of the atria and alter the substrate even further[e21] and help to perpetuate AF. AF can also be the result of preexisting atrial disease. Although much has been learned about the mechanisms of AF, they remain incompletely understood. Because of this, it is not yet possible to precisely tailor an ablation strategy to a particular AF mechanism in the great majority of AF patients.

2.3. Multiple wavelet hypothesis

Until the mid to late 1980s, the multiple wavelet hypothesis for AF was widely accepted as the dominant AF mechanism.[e22] This hypothesis was developed by Moe and colleagues and subsequently confirmed by experimental work.[e23] According to this hypothesis, AF results from the presence of multiple independent wavelets occurring simultaneously and propagating randomly throughout the left and right atria. This model suggests that the number of wavelets at any point in time depends on the atrial conduction velocity, refractory period, and excitable mass. Perpetuation of AF requires the presence of a minimum number of coexisting wavelets and is favored by slowed conduction, shortened refractory periods, and increased atrial mass. Enhanced spatial dispersion of refractoriness promotes perpetuation by heterogeneous conduction delay and block. It is notable that the development of the surgical Maze procedure was predicated on this model of AF and the concept that maintenance of AF needs a critical number of circulating wavelets, each of which requires a critical excitable mass of atrial tissue.[e24] However, experimental and clinical results suggest that, while AF maintenance by randomly propagating wavelets may occur in some cases, atrial refractory periods and cycle lengths do not seem to distribute

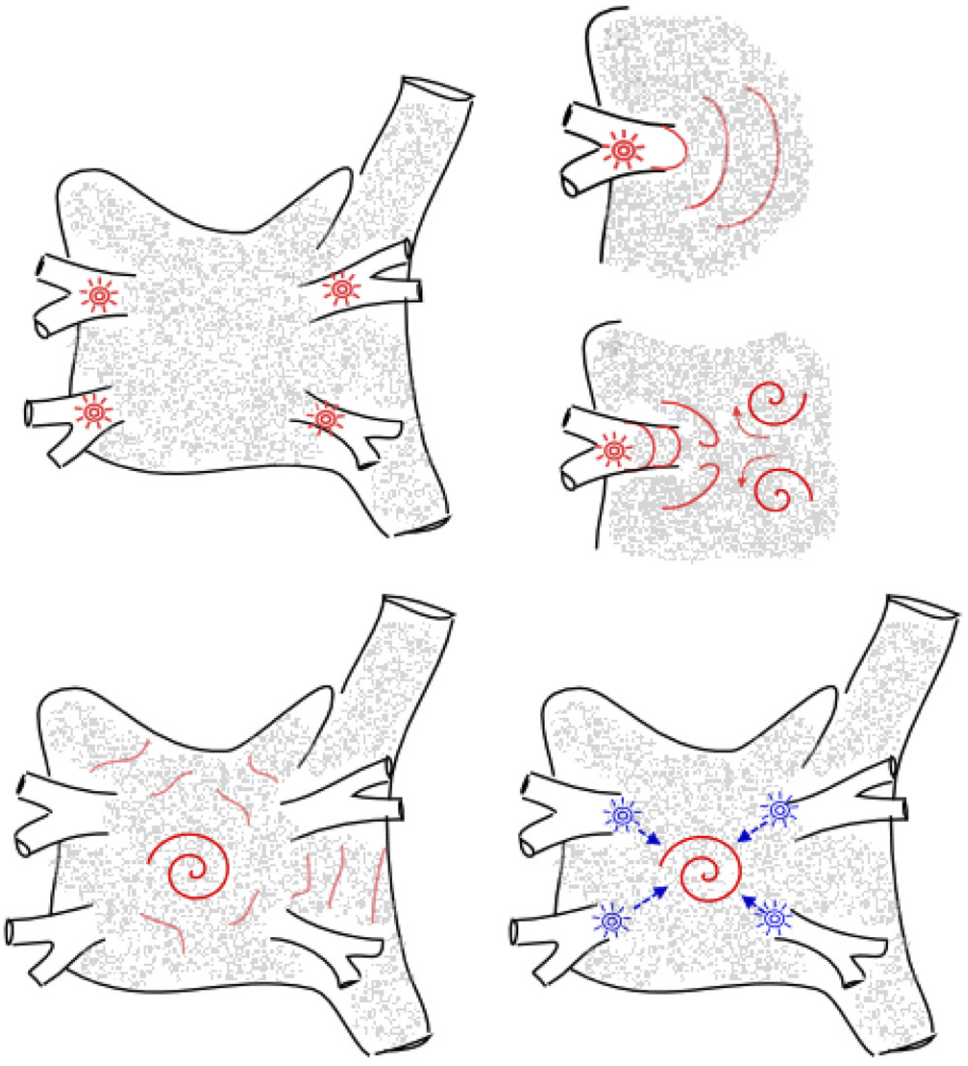

Figure 2 Focal triggers leading to initiation of reentry. Schematic drawing that illustrates the manner in which focal triggers lead to initiation of reentry (rotors). Eventually, atrial remodeling leads to additional focal triggers and perpetuation of reentry.

randomly. Rather, as demonstrated in the atria of the dog, atrial fibrillation cycle length (AFCL) is significantly shorter in the LA compared with the right atrium, and an area in the posterior LA is consistently found to have the shorter AFCL.[e25]

2.4. Focal triggers

Haissaguerre and colleagues are credited with making the landmark observation that AF is often triggered by a focal source, and that ablation of that focal trigger can eliminate AF.[e12–e14] This observation was reported in a series of three manuscripts. An initial series of three patients who underwent successful catheter ablation of AF was published in 1994.[e12] In each of these patients, AF was determined to arise from a "focal source." The successful treatment of these three patients with catheter ablation suggested that in some patients, AF may result from a focal trigger and that ablation of this trigger could eliminate AF. It is notable that prior research in an animal model had demonstrated that AF could be induced by local administration of aconitine that triggered a rapid focal atrial tachycardia (AT).[e26] This type of "focal AF" also was shown to be cured by isolation of the site of the aconitine-induced focal AT from the remainder of the atria. In a subsequent report on 45 patients with frequent drug-refractory episodes of AF, Haissaguerre and colleagues[e27] found that a purely right-sided linear ablation approach resulted in an extremely low long-term success rate. These investigators also found that linear lesions were often arrhythmogenic due to gaps in the ablation lines, and that many patients were ultimately cured with ablation of a single rapidly firing ectopic focus. These ectopic foci were found at the orifices of the left or right superior PVs or near the superior vena cava (SVC). The latter observation led these investigators to systematically attempt cure of paroxysmal AF by mapping and ablating individual foci of ectopic activity.[e12–e14] Many of these foci were found well into the PVs, outside of the cardiac silhouette, where myocardial sleeves are known to extend.[e14] These observations of the importance of a focal trigger in the development of AF have

been confirmed by others. Thus, it is now well established that the PVs appear to be a crucial source of triggers that initiate AF.

2.5. Electrophysiology of the pulmonary veins

Nathan and Eliakim[e28] are credited with first drawing attention to the presence of sleeves of cardiac tissue that extend onto the PVs (Figure 1). However, investigation of the anatomic and electrophysiologic properties of the PVs remained limited, until the importance of PV triggers in the development of AF was appreciated. There is now general agreement that myocardial muscle fibers extend from the LA into all the PVs for 1 to 3 cm; the thickness of the muscular sleeve is highest at the proximal ends (1–1.5 mm) and then gradually decreases distally.[e11,e29,e30]

PV focal firing may trigger AF or act as a rapid driver to maintain the arrhythmia. The mechanisms of this focal firing are incompletely understood. The location of the precursors of the conduction system is defined, during embryological development of the heart, by the looping process of the heart tube.[e31,e32] Cell markers common to precursors of specialized conduction tissue derived from the heart tube have been found within myocardial sleeves.[e33] The presence of P cells, transitional cells, and Purkinje cells has been demonstrated in human PVs.[e34,e35] PV-sleeve cardiomyocytes have discrete ion channel and action potential properties that predispose them to arrhythmogenesis.[e34,e35] They have small background I_{K1}, which could favor spontaneous automaticity,[e34] as could their reduced coupling to atrial tissue, a property common to pacemaking structures.[e36] Other work shows susceptibility to Ca^{2+}-dependent arrhythmia mechanisms,[e37] possibly due to cells of melanocyte origin.[e38] Isolated cardiomyocytes from rabbit and canine PVs show abnormal automaticity and triggered activity during manipulations that enhance Ca^{2+}-loading.[e37–e39] These properties may explain the electrical activity within the PVs that is commonly observed after electrical disconnection of the PVs from the atrium.[e40]

Other studies have provided evidence to suggest that the PVs and the posterior LA are also preferred sites for reentrant arrhythmias.[e16,e41] One important factor may be the shorter action potential duration of the PVs versus atrium[e34] due to larger delayed-rectifier K^+-currents and smaller inward Ca^{2+}-currents in PV.[e39,e42] In addition, PVs demonstrate conduction abnormalities that promote reentry due to abrupt changes in fiber orientation as well as Na^+-channel inactivation by reduced resting potentials due to small I_{K1}.[e34,e41] Yet another study examined the impact of increasing atrial pressure on PV activation, finding that as LA pressure was increased above 10 cm H_2O, the LA–PV junction became the source of dominant rotors.[e43] These observations help explain the clinical link between AF and increased atrial pressure. Several clinical studies have reported shorter refractory periods inside PVs compared to the LA, decremental conduction inside PVs, and easy induction of PV reentry with premature stimulation from the PVs. Accordingly, rapid reentrant activity with entrainment phenomenon have been described inside PVs after successful pulmonary vein isolation (PVI).[e44,e45] Electrophysiologic evaluation of the PVs using a multielectrode basket catheter has revealed effective refractory period heterogeneity and anisotropic conduction properties within the PV and at the PV–LA junction, which can provide a substrate for reentry.[e46] The response of PV activity to adenosine administration in patients with paroxysmal AF is more consistent with a reentrant than a focal ectopic type of mechanism.[e47,e48] In addition, dominant-frequency analysis points to an evolution of mechanisms in AF patients, with PV sources becoming less predominant as AF becomes more persistent and atrial remodeling progresses.[e44] There is considerable evidence for a role of autonomic regulation in AF occurrence, and the location of autonomic ganglia close to the PVs suggests a contribution of their specific innervation to PV arrhythmogenesis and the beneficial effects of PV ablation procedures.[e49,e50]

2.6. Frequency gradients in atrial fibrillation organization

A number of experimental and clinical studies have appeared over the last several years demonstrating the importance of the local atrial activation rate (cycle length) in the maintenance of AF,[e47,e49,e51–e54] the role of atrial remodeling in the perpetuation of AF,[e19–e21] the importance of wavebreak and reentry in the posterior LA,[e53,e55] and the existence of a hierarchical organization and left-to-right gradients of the electrical excitation frequency.[e47,e48,e51,e52,e54] In addition, optical mapping studies in animals have confirmed that the turbulent electrical activity seen by electrogram (EGM) recordings of the atria during AF may in some cases be explained by fibrillatory conduction from a single or a small number of rapidly spinning sources in the LA.[e16,e56] At the subcellular level, the high density of autonomic plexi and nerves on the posterior wall of the LA and its greater density of inward rectifier potassium channels[e57] provide a reasonable explanation for the shorter refractory periods in that region and for the hierarchical distribution of dominant frequency gradients that characterize AF. It was recently demonstrated that in sinus rhythm there are intra-atrial heterogeneities in the repolarizing currents. Chronic AF decreases I_{To1} and I_{Kur} differentially in each atrium and increases I_{Ks} in both atria, an effect that further promotes reentry and likely contributes to the perpetuation of the arrhythmia.

The above studies offer mechanistic rationale for the empiric observation by clinical electrophysiologists that the LA is the region that seems to harbor the AF sources in the majority of patients. They also afford an explanation for the need for circumferential and linear ablation, as well as other anatomic approaches that not only include the PVs but also a large portion of the LA. Inclusion of the atrial myocardium in ablation strategies is particularly important in patients with persistent AF, who in fact represent the vast majority of patients presenting with this arrhythmia. Recent data in persistent AF patients provide compelling evidence

that the sources are in fact reentrant and located outside of the PVs. Other studies in patients have used power spectral analysis and mapping to localize dominant frequency sites of activation.[e48] They demonstrated that in paroxysmal AF patients, the PV ostial region does harbor the highest frequency sites, and AF can be terminated successfully by targeting radiofrequency (RF) ablation to those sites in up to 87% of patients.[e48,e58] However, in longstanding persistent AF patients, it is rare to find dominant frequency sites at the PV region, and this agrees well with the relatively poor success rate of RF ablation in such patients. The data suggest that in patients with longstanding persistent AF, atrial remodeling somehow augments the number of AF drivers and shifts their location away from the PV/ostial region.

2.7. Cardiac autonomic nervous system and triggered spontaneous pulmonary vein firing

Autonomic input to the atria arises from both the central autonomic nervous system (pre-ganglionic) and the intrinsic cardiac autonomic nervous system (ANS).[e59,e60] The intrinsic cardiac ANS includes clusters of ganglia, known as autonomic ganglionated plexi (GP), located in specific epicardial fat pads and within the ligament of Marshall. The GP receive input from the central (extrinsic) ANS and contain afferent neurons, post-ganglionic efferent parasympathetic and sympathetic neurons, and numerous interconnecting neurons that provide communication within and between the GP. In animal models, stimulating the vagosympathetic trunk ("vagus nerve") allows AF to sustain but requires pacing or other stimuli to initiate AF.[e61,e62] In contrast, stimulating the GP produces repetitive short bursts of rapid, irregular firing in the adjacent PV, initiating sustained AF.[e63] The focal firing in the PVs has a pause-dependent initiation pattern and produces EGMs that are very similar to the pattern of firing recorded in the PVs of patients with paroxysmal AF.[e64] Focal firing in the PVs by GP stimulation requires both sympathetic and parasympathetic activity.[e65–e67] Parasympathetic stimulation shortens the action potential duration (and effective refractory period) in atrial and PV myocytes, and sympathetic stimulation increases calcium loading and automaticity. Combined, they cause pause-induced early after depolarizations (EADs) and triggered activity in PV and atrial myocytes. The mechanism of triggered firing may relate to the combination of a very short action potential duration and increased calcium release during systole, leading to high intracellular calcium during and after repolarization. These observations suggest that the high calcium concentration may activate the sodium/calcium exchanger, leading to a net inward current, EADs and triggered firing.[e62,e65,e68] Compared to atrial myocytes, PV myocytes have a shorter action potential duration and greater sensitivity to autonomic stimulation, which may explain the predominance of focal firing in PVs in patients with paroxysmal AF and the interruption of focal firing by ablation of the autonomic GP.[e69] Interruption of nerves from the GP to the PVs may explain, at least in part, the frequent elimination of focal firing within the PVs produced by PVI procedures.[e70,e71] These findings suggest that interruption of nerves from the GP may have a role in the success of PVI procedures and may explain the success of early ablation studies targeting only the GP in patients with paroxysmal AF.[e70,e71] Regeneration of those axons may contribute to late recurrence of AF after PVI.[e72,e73] Ablation of the nerve cell bodies, by targeting the GP, may permanently denervate the PVs. The addition of GP ablation to PVI appears to be synergistic, because each of these procedures is currently incomplete: all GP tissue cannot be localized for ablation by the current endocardial stimulation techniques; and PVI procedures are frequently associated with late reconnection to the atrium.[e74,e75]

A relationship has been observed between autonomic GP activity and complex fractionated atrial EGMs (CFAEs). The location of the GP can be identified as sites associated with transient AV block during high frequency electrical stimulation (HFS, 20 Hz).[e76,e77] The GP are consistently located within areas of CFAEs.[e78] Stimulating the GP by HFS or the injection of acetylcholine into a fat pad containing a GP produces CFAEs in the same area as recorded during AF.[e76,e78–e80] Sequential ablation of multiple (four or more) GP in animal models and in patients with paroxysmal or persistent AF reduces or eliminates all CFAEs, and decreases or eliminates the inducibility of AF.[e79–e81] AF persisting after GP ablation typically shows more organized atrial EGMs with longer cycle lengths.[e80] These changes in EGM patterns with sequential ablation of GP are similar to the progressive slowing and organization of EGMs during the stepwise ablation technique performed in patients with longstanding persistent AF.[e81–e84] The relationship between CFAE and GP activity may also explain the varied success reported for CFAE ablation. Studies describing high success with CFAE ablation show ablation sites concentrated in areas close to the GP,[e82] while studies describing poor success generally show a widespread pattern of ablation sites.[e84] The latter studies may have inadvertently targeted the peripheral CFAE sites, leaving the GP largely intact.

Several recent observations in animal models may have an influence on AF therapy in the future. GP activity may play a role in the electrical remodeling produced by rapid atrial pacing. Shortening of the refractory period in the atria and PVs and the inducibility of AF produced in short-term models of rapid atrial pacing are facilitated by GP stimulation and blocked by GP ablation.[e85,e86]

Another recent finding is the inhibition of GP activity and PV firing by low-level stimulation of the vagosympathetic trunk.[e87] A loss of responsiveness of the GP to central vagal stimulation in older patients may help to explain the striking increase in the prevalence of AF in elderly people. Therapeutic implications include the possibility that chronic low-level stimulation of the vagosympathetic trunk may help suppress AF in patients with paroxysmal AF. Although these data suggest a potentially important role of the autonomic nervous system in the development of AF, as well as

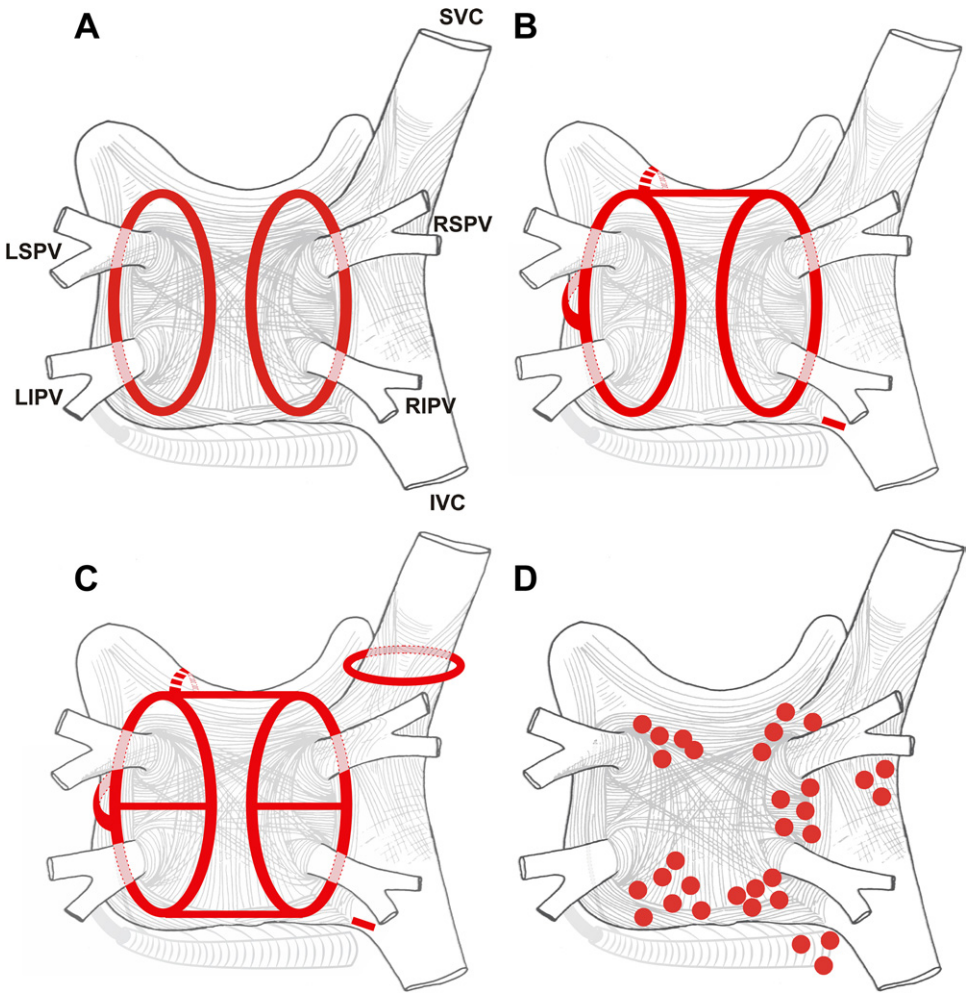

Figure 3 Schematic of common lesion sets employed in AF ablation. **A:** The circumferential ablation lesions that are created in a circumferential fashion around the right and the left PVs. The primary endpoint of this ablation strategy is the electrical isolation of the PV musculature. **B:** Some of the most common sites of linear ablation lesions. These include a "roof line" connecting the lesions encircling the left and/or right PVs, a "mitral isthmus" line connecting the mitral valve and the lesion encircling the left PVs at the level of the left inferior PV, and an anterior linear lesion connecting either the "roof line" or the left or right circumferential lesion to the mitral annulus anteriorly. A linear lesion created at the cavotricuspid isthmus is also show. This lesion is generally placed in patients who have experienced cavotricuspid isthmus dependent atrial flutter clinically or have it induced during EP testing. **C:** Similar to 3B but also shows additional linear ablation lesions between the superior and inferior PVs resulting in a figure of 8 lesion set as well as a posterior inferior line allowing for electrical isolation of the posterior left atrial wall. An encircling lesion of the superior vena cava (SVC) directed at electrical isolation of the SVC is also shown. SVC isolation is performed if focal firing from the SVC can be demonstrated. A subset of operators empirically isolates the SVC. **D:** Some of the most common sites of ablation lesions when complex fractionated electrograms are targeted (these sites are also close to the autonomic GP). (Adapted from Circulation,[e28] Am J Cardiol,[e735] Tex Heart Inst J.[e736])

a role of autonomic modulation in the treatment of AF, it is important to recognize that definitive proof is lacking, as it is not possible to ablate autonomic ganglia without also ablating atrial myocardium.

2.8. Electrophysiologic basis for catheter ablation of atrial fibrillation

It is well accepted that the development of AF requires both a trigger and a susceptible substrate. The goals of AF ablation procedures are to prevent AF by either eliminating the trigger that initiates AF or altering the arrhythmogenic substrate. The most commonly employed ablation strategy today, which involves the electrical isolation of the PVs by creation of circumferential lesions around the right and the left PV ostia, probably impacts both the trigger and substrate of AF (Figure 3).[e88–e91] In particular, this approach seeks to electrically isolate the PVs, which are the most common site of triggers for AF. Other less common trigger sites for AF, including the vein and ligament of Marshall and the posterior LA wall, are also encompassed by this lesion set. The circumferential lesions may also alter the arrhythmogenic substrate by elimination of tissue located near the atrial–PV junction that provides a substrate for reentrant circuits that may generate or perpetuate AF, and/or by reduction of the mass of atrial tissue needed to sustain reentry. The circumferential lesion set may interrupt sympathetic and parasympathetic innervation from the autonomic ganglia that have been identified as potential triggers for AF (Figure 1).[e92] Extensive atrial remodeling poses a

particular challenge for the ablation of longstanding persistent AF.[e93,e94]

Recurrences of all types of AF following an initially successful AF ablation procedure result from PV reconnection. It is extremely unusual to find no evidence of return of PV conduction at the time of repeat AF ablation procedures.[e95] CFAEs are widely targeted in attempts to suppress the AF-maintaining substrate, but clinical results have varied widely.[e96] Detailed mechanistic analyses of CFAE generation promise to develop new methods by which they can be used to identify AF drivers.[e74] There is increasing recognition of the importance of atrial autonomic ganglia in AF maintenance and the value of targeting them in AF ablation procedures.[e97] Atrial fibrotic remodeling plays an important role in AF pathophysiology; recent work suggests that noninvasive assessment of atrial fibrosis may be predictive of the outcome of AF ablation procedures.[e98]

2.9. Rationale for eliminating atrial fibrillation with ablation

There are several hypothetical reasons to perform ablation procedures for treatment of AF. These include improvement in quality of life (QOL), decreased stroke risk, decreased heart failure risk, and improved survival. In this section of the document, these issues will be explored in more detail. However, it is important to recognize that the primary justification for an AF ablation procedure at this time is the presence of symptomatic AF, with a goal of improving a patient's quality of life. Although each of the other reasons to perform AF ablation identified above may be correct, they have not been systematically evaluated as part of a large randomized clinical trial and are therefore unproven.

Several epidemiologic studies have shown strong associations between AF and increased risk of cerebral thromboembolism, development of heart failure, and increased mortality.[e99–e101] It is well known that AF causes hemodynamic abnormalities including a decrease in stroke volume, increased LA pressure and volume, shortened diastolic ventricular filling period, AV valvular regurgitation, and an irregular and often rapid ventricular rate.[e102] AF with a rapid ventricular response can also cause reversible left ventricular (LV) systolic dysfunction. Persistence of AF leads to anatomic and electrical remodeling of the LA that may facilitate persistence of AF. Most importantly, many patients, even those with good rate control, experience symptoms during AF.

There have been multiple randomized clinical trials performed that address the question of whether rhythm control is more beneficial than rate control for AF patients.[e103–e105] These studies have not demonstrated that sinus rhythm restoration is associated with better survival. In all trials, antiarrhythmic drugs were used for rhythm control. The Pharmacological Intervention in AF (PIAF) trial first demonstrated that rate control was not inferior to rhythm control in the improvement of symptoms and quality of life.[e106] An additional study reported similar findings.[e104] The Strategies of Treatment of AF (STAF) trial showed no significant difference in the primary endpoints of death, systemic emboli, and cardiopulmonary resuscitation between the two strategies.[e103] Another recent study demonstrated an improvement in quality of life and exercise performance at 12 months' follow-up in a series of patients with persistent AF.[e107] In the AF Follow-up Investigation of Rhythm Management (AFFIRM) trial, in which 4,060 AF patients with high risk for stroke and death were randomized to either rhythm control or rate control, there were no significant differences in all-cause death between the two strategies.[e105] However, a post-hoc on-treatment analysis of the AFFIRM study revealed that the presence of sinus rhythm was associated with a significant reduction in mortality, whereas the use of antiarrhythmic drugs increased mortality by 49%,[e108] suggesting that the beneficial effect of sinus rhythm restoration on survival might be offset by the adverse effects of antiarrhythmic drugs. Previously, the Danish Investigations of Arrhythmia and Mortality on Dofetilide (DIAMOND) study also showed the presence of sinus rhythm was associated with improved survival.[e109] It must be noted, however, that this was a retrospective analysis, and the improvement in survival may have resulted from factors other than the presence of sinus rhythm. In contrast, a recent study demonstrated that a rhythm control strategy, or the presence of sinus rhythm, is not associated with better outcomes in congestive heart failure patients with AF.[e110]

These clinical trials clearly show that the strategy of using antiarrhythmic drugs to maintain sinus rhythm does not achieve the potential goals of sinus rhythm mentioned above. However, there are signals in these data to suggest that sinus rhythm may be preferred over rate control if it could be achieved by a method other than drug therapy. One study compared the efficacy and safety of circumferential PV ablation with antiarrhythmic drug treatment in a large number of patients with long-term follow-up and showed that ablation therapy significantly improved the morbidity and mortality of AF patients.[e90] Because this was a single-center study, without audit of the raw data, and not a prospective randomized study, these findings must be considered very preliminary. Several recent small randomized trials in patients with paroxysmal AF demonstrated that catheter ablation was superior to antiarrhythmic therapy in the prevention of recurrent AF.[e111–e113] A limitation of these studies is that most patients had previously failed treatment with at least one antiarrhythmic medication. There are several published studies that have reported a low risk of stroke in patients who discontinue systemic anticoagulation several months or more following AF ablation.[e114–e117] These findings need to be interpreted with caution, however, because AF can recur early or late after AF ablation and recurrences are more likely to be asymptomatic following, as compared with prior to, AF ablation. In addition, patients' stroke risk profile often increases as they age and pick up additional comorbidities such as hypertension. Thus there

are some data to suggest that there are benefits to sinus rhythm obtained by ablation techniques over rate control. However, large prospective multicenter randomized clinical trials will be needed to definitively determine whether sinus rhythm achieved with ablation techniques lowers morbidity and mortality as compared with rate control alone or treatment with antiarrhythmic therapy. The ongoing Catheter Ablation vs. Antiarrhythmic Drug Therapy for AF (CABANA) study will provide important information as it investigates whether catheter ablation is superior to medical therapy in patients with AF who are at increased stroke risk.[e118]

2.10. Mechanisms of recurrence following catheter or surgical AF ablation

It is now well established that both catheter and surgical ablation of AF are associated with an important risk of late recurrence of AF.[e72,e73,e119–e127] Although the highest risk of recurrence is during the first 6 to 12 months following ablation, there is no follow-up duration at which point patients are no longer at risk of a "new" late recurrence of AF. Although the precise mechanisms of these late recurrences have not been defined completely, electrical reconnection of one or more PVs is an almost universal finding among patients who return for a second AF ablation procedure following an initial catheter or surgical ablation procedure. Because of this observation, most of the EP community feels that the dominant mechanism of recurrence of AF is electrical reconnection of the PVs. Additional evidence supporting this mechanism is the extremely low rate of late AF following double lung transplantation in which permanent PVI is achieved.[e128] There are several other potential mechanisms of late recurrence of AF that should be considered. First, it is possible that some late recurrences of AF result from non-PV arrhythmogenic foci that were not identified and targeted during an initial ablation procedure. Second, it is possible that late recurrences of AF are a result of postablation modulation in autonomic innervations of the heart and PVs.[e62–e77] And finally, it is possible that ongoing electrical and structural remodeling of the atria as a result of aging, heart failure, inflammation, and other comorbidities such as diabetes[e129–e136] leads to progressive atrial electrical instability. Evidence to support the latter hypothesis is derived in part by the studies reporting that patients with comorbid conditions such as sleep apnea, hypertension (HTN), and hypercholesterolemia, as well as those with a history of persistent AF, are at highest risk of late recurrence.[e135,137–e139]

2.11. Demographic profile of AF patients and risk factors for development of AF

There are multiple conditions known as "risk factors for AF" that play an etiologic role through diverse mechanisms.[e6] Some of them, like HTN,[e135,e139] obesity,[e140–e142] endurance sport training,[e143,e144] obstructive sleep apnea,[e140–e142] and alcohol consumption,[e145] are modifiable and therefore, in theory, strictly controlling them may prevent arrhythmia or modify postablation evolution. On the other hand, factors such as genetic disorders,[e146,e147] age,[e137,e148,e149] sex,[e137] or tall stature[e44,e146,e150] can be identified but not prevented or treated. To individualize treatment, it is important to establish the most likely contributors to AF in each patient. Atrial size, a relevant marker of risk for AF and for postablation recurrences of the disease, is a common pathway for the action of most of the identified risk factors.

The well-known and more prevalent risk factors are age, male sex, HTN, diabetes mellitus, hyperthyroidism, and structural heart disease. Aging is a key risk factor[e136–e138] that probably acts through age-related fibrosis. HTN is associated with increased risk for AF even if apparently well controlled.[e138,e139,e148] Structural heart disease, regardless of cause, is also a major contributor to AF, and mitral valve disease and hypertrophic cardiomyopathy produce severe atrial disease. In addition, systolic or diastolic dysfunction and heart failure of any etiology predispose to AF, probably through volume and/or pressure overload of the atrium.[e151,e152] Diabetes mellitus and hyperthyroidism are well recognized and independent risk factors for AF; even when well-controlled, AF may recur.[e141,e153] AF risk factors have also been shown to be of value in predicting progression of paroxysmal to persistent AF. Risk factors that have been identified as independent predictors of AF recurrence include heart failure, age, previous transient ischemic attack or stroke, chronic obstructive pulmonary disease, and hypertension. Based on this analysis, the HATCH score was developed to help predict those at highest risk of AF progression.[e154]

In recent years, new risk factors have been described that may contribute to the marked, increased prevalence of AF, which is not fully explained by the aging of the population.[e141,e143,e147,e150,e155–e167] Obesity has proven to be associated with a higher risk of AF in several population-based studies. Tall stature also is associated with an increased risk, and may explain the sex-based difference in AF prevalence: AF is more prevalent in men than in women. The prevalence of AF is also increased in individuals with a long history of endurance training, perhaps, as suggested in an animal model, through training-related hypertrophy, atrial dilatation, fibrosis, or perhaps by training induced alterations in autonomic tone. However, moderate exercise may decrease the prevalence, perhaps by controlling other risk factors such as HTN and obesity. Obstructive sleep apnea also has been associated with AF. Whether this represents an independent factor or acts through its association with obesity and HTN remains to be elucidated, but it seems to increase the risk of recurrences after AF ablation. Finally, in a small percentage of patients, AF is due to hereditary genetic causes as discussed in the following paragraph.

2.12. Genetics of AF: relevance to AF

The descendants of individuals with AF are at increased risk of developing AF, even after considering established risk factors for AF.[e157,e158,e160,e168,e169] Recent studies suggest that lone AF may be a traditional monogenic syndrome

with reduced penetrance, and multiple genetic loci have been described in families with Mendelian forms of AF. However, not all[e160] the responsible genes have been identified.[e170,e171] Gain-of-function mutations in *KCNE2*[e172] and *KCNJ2*,[e173] encoding the inward rectifier potassium current (I_{K1}), have been associated with familial AF in two Chinese families. Similar studies have associated familial AF with various other genes, including those genes coding the α subunit of the $K_v1.5$ channel responsible for I_{Kur} *(KCNA5);* the gap junctional protein connexin40 *(GJA5);* SUR2A, the adenosine triphosphate (ATP) regulatory subunit of the cardiac K_{ATP} channel *(ABCC9);* and *KCNE5,* which co-associates with *KCNQ1* to form the I_{Ks} channel.[e174–e177] Rare forms of familial AF are caused by mutations in one or more subunits of potassium, sodium, and calcium ion channel genes, as well as in a nuclear pore[e178] anchoring protein and natriuretic peptide gene[e173,e179–e183] and also have been associated with inherited channelopathies such as Brugada, Long QT, Short QT syndromes, and cardiomyopathies.[e172,e175,e178–e184]

Genetic linkage analyses have identified AF loci on chromosomes 10q22-24,[e170] 6q14-16,[e171] 5p13,[e185] and 11p15.5.[e182] In the case of 11p15.5, the genetic defect involved heterozygous missense mutations in *KCNQ1,* resulting in gain-of function of the *KCNQ1-KCNE1* and *KCNQ1-KCNE2* ion channels conducting the slowly activating delayed rectifier current, I_{Ks}.[e186] Genetic predisposition to AF has gained notoriety also thanks to genomic wide association studies (GWAS)[e187–e191] that have identified at least two genetic variants on chromosome 4q25 associated with AF, although the mechanism of action for these variants remains unknown. One of such variants is located near the developmental left–right asymmetry homeobox gene Pitx2, which implicates this gene and its signaling pathways in prevention of atrial arrhythmias.[e191]

It is reasonable to suggest that investigating in detail the underlying bases of these and other characteristics of the LA that differentiate it from the right atrium may greatly advance therapy by helping to explain the mechanisms of the genesis and perpetuation of chronic AF.

3. Indications for catheter and surgical ablation of atrial fibrillation

The 2007 HRS/EHRA/ESC Expert Consensus Document on Catheter and Surgical Ablation of Atrial Fibrillation recommended that the primary indication for catheter AF ablation is the presence of symptomatic AF, refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication.[e1] The 2007 Task Force also recognized that in rare clinical situations, it may be appropriate to perform catheter ablation of AF as first line therapy. Since publication of this document five years ago, a large body of literature, including multiple prospective randomized clinical trials, has confirmed the safety and efficacy of catheter ablation of AF. The substantial body of literature defining the safety and efficacy of catheter ablation of AF is summarized in Section 8 of this document. Similarly, the body of literature defining the safety and efficacy of surgical ablation of AF either performed in conjunction with another cardiac surgical procedure or performed as a stand-alone procedure is summarized in Section 11 of this document.

Shown in Table 2 of this document are the Consensus Indications for Catheter and Surgical Ablation of AF. As outlined in the introduction section of this document, these indications are stratified as Class I, Class IIa, Class IIb, and Class III indications. The evidence supporting these indications is graded as Level A through C. In making these recommendations, the Task Force considered the body of literature that has been published, which has defined the safety and efficacy of catheter and surgical ablation of AF. Both the number of clinical trials and the quality of these trials were considered. In considering the class of indications recommended by this Task Force, it is important to keep several points in mind. First, these classes of indications only define the indications for catheter and surgical ablation of AF when performed by an electrophysiologist or surgeon who has received appropriate training and/or has a certain level of experience and is performing the procedure in an experienced center (see section 10). Catheter and surgical ablation of AF are highly complex procedures, and a careful assessment of benefit and risk must be considered for each patient. Second, these indications stratify patients only based on the type of AF and whether the procedure is being performed prior to or following a trial of one or more Class 1 or 3 antiarrhythmic medications. As detailed in Section 8, there are many additional clinical and imaging based variables that can be used to further define the efficacy and risk of ablation in a given patient. Some of the variables that can be used to define patients in whom a lower success rate or a higher complication rate can be expected include the presence of concomitant heart disease, obesity/sleep apnea, left atrial size, and the duration of time a patient has been in continuous AF. Each of these variables needs to be considered when discussing the risks and benefits of AF ablation with a particular patient. Third, it is key to consider patient preference. Some patients are reluctant to consider a major procedure or operation and have a strong preference for a pharmacologic approach. In these patients, trials of additional antiarrhythmic agents and amiodarone may be preferred to catheter ablation. On the other hand, some patients prefer a nonpharmacologic approach. Fourth, it is also important to recognize that in some patients, AF is a slowly progressive condition and that patients early in the course of their AF disease may do well with only infrequent episodes for many years to come and/or may be responsive to well-tolerated antiarrhythmic drug therapy. And finally, it is important to bear in mind that a decision to perform catheter or surgical AF ablation should only be performed after a patient carefully considers the risks, benefits, and alternatives to the procedure.

As demonstrated in a large number of published studies, the primary clinical benefit from catheter ablation of AF is an improvement in quality of life resulting from elimination of arrhythmia-related symptoms such as pal-

Table 2 Consensus indications for catheter and surgical ablation of AF

Indications for catheter ablation of AF	Class	Level
Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication		
Paroxysmal: Catheter ablation is recommended*	I	A
Persistent: Catheter ablation is reasonable	IIa	B
Longstanding Persistent: Catheter ablation may be considered	IIb	B
Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent		
Paroxysmal: Catheter ablation is reasonable	IIa	B
Persistent: Catheter ablation may be considered	IIb	C
Longstanding Persistent: Catheter ablation may be considered	IIb	C
Indications for concomitant surgical ablation of AF		
Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication		
Paroxysmal: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Longstanding Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent		
Paroxysmal: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications	IIa	C
Longstanding Persistent: Surgical ablation may be considered for patients undergoing surgery for other indications	IIb	C
Indications for stand alone surgical ablation of AF		
Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication		
Paroxysmal: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach	IIb	C
Paroxysmal: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation	IIb	C
Persistent: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach	IIb	C
Persistent: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation	IIb	C
Longstanding Persistent: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach	IIb	C
Longstanding Persistent: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation	IIb	C
Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent		
Paroxysmal: Stand alone surgical ablation is not recommended	III	C
Persistent: Stand alone surgical ablation is not recommended	III	C
Longstanding Persistent: Stand alone surgical ablation is not recommended	III	C

**Catheter ablation of symptomatic paroxysmal AF is considered a Class 1 indication only when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced center.*

pitations, fatigue, or effort intolerance (see section 8). Thus, the primary selection criterion for catheter ablation should be the presence of symptomatic AF. As noted above, there are many other considerations in patient selection other than type of AF alone. In clinical practice, many patients with AF may be asymptomatic but seek catheter ablation as an alternative to long-term anticoagulation with warfarin or other drugs with similar efficacy. Although retrospective studies have demonstrated that discontinuation of warfarin therapy after catheter ablation may be safe over medium-term follow-up in some subsets of patients, this has never been confirmed by a large prospective randomized clinical trial and therefore remains unproven.[e116,e117,e191,e192] Furthermore, it is well recognized that symptomatic and/or asymptomatic AF may recur during long-term follow-up after an AF ablation procedure.[e72,e73,e119,e122,e124,e126,e127] It is for these reasons that this Task Force recommends that discontinuation of warfarin or equivalent therapies postablation is not recommended in patients who have a high stroke risk as determined by the $CHADS_2$ or CHA_2DS_2VASc score.[e193] Either aspirin or warfarin is appropriate for patients who do not have a high stroke risk. If anticoagulation withdrawal is being considered, additional ECG monitoring may be required, and a detailed discussion of risk versus benefit should be entertained. A patient's desire to eliminate the need for long-term anticoagulation by itself should not be considered an appropriate selection criterion. In arriving at this recommendation, the Task Force recognizes that patients who have undergone catheter ablation of AF represent a new and previously unstudied population of patients. Clinical trials therefore are needed to define the stroke risk of this patient population and to determine whether the risk factors identified

in the $CHADS_2$ or CHA_2DS_2VASc or other scoring systems apply to these patients.

4. Techniques and endpoints for atrial fibrillation ablation

4.1. Historical considerations

Cox and colleagues are credited with developing and demonstrating the efficacy of surgical ablation of AF.[e24,e194] Subsequent surgeons evaluated the efficacy of surgical approaches that limit the lesion set to PVI.[e195,e196] The final iteration of the procedure developed by Cox, which is referred to as the Maze-III procedure, was based on a model of AF in which maintenance of the arrhythmia was shown to require maintenance of a critical number of circulating wavelets of reentry. The Maze-III procedure was designed to abort or block all possible anatomical reentrant circuits in both atria. The success of the Maze-III procedure in the early 1990s led some interventional cardiac electrophysiologists to attempt to reproduce the procedure with RF catheter lesions using a transvenous approach. Swartz and colleagues[e197] reported recreation of the Maze-I lesion set in a small series of patients using specially designed sheaths and standard RF catheters. Although the efficacy was modest, the complication rate was high, and the procedure and fluoroscopy times were long. This demonstration of a proof of concept led others to try to improve the catheter-based procedure. Although a large number of investigators attempted to replicate the surgical Maze procedure through the use of either three-dimensional (3D) mapping systems or the use of multipolar ablation electrode catheters, these clinical trials had limited success.[e27,e198–e203] Based on these observations and the rapid advances in ablation of AF targeting initiating focal triggers, electrophysiologists lost interest in catheter based linear ablation for AF ablation.

4.2. Ablation approaches targeting the pulmonary veins

The identification of triggers that initiate AF within the PVs led to prevention of AF recurrence by catheter ablation at the site of origin of the trigger.[e12–e14,e204] Direct catheter ablation of the triggers was limited by the infrequency with which AF initiation could be reproducibly triggered and also by the difficulty of precise mapping within the 3D venous structures. To overcome these limitations, an ablation approach was introduced by Haissaguerre and colleagues[e204] that was designed to electrically isolate the PV myocardium. This segmental PVI technique involved the sequential identification and ablation of the PV ostium close to the earliest sites of activation of the PV musculature. An ablation strategy of encircling the PVs with RF lesions guided by 3D electroanatomical mapping was subsequently developed by Pappone and colleagues.[e203,e205]

The recognition of PV stenosis as a complication of RF delivery within a PV, as well as the recognition that sites of AF initiation and/or maintenance were frequently located within the PV antrum, resulted in a shift in ablation strategies to target the atrial tissue located in the antrum rather than the PV itself.[e88,e206] Ablation at these sites was either performed segmentally, guided by a circular mapping catheter[e204,e207] positioned close to the PV ostium, the so-called "segmental PV ablation," or by wider continuous circumferential ablation lesions created to surround the right or left PVs,[e203,e205,e208] the so-called "wide area circumferential ablation" or WACA. The circumferential ablation/isolation line was either guided by 3D electroanatomic mapping,[e89,e205,e209] by fluoroscopy,[e210] or by intracardiac echocardiography (ICE).[e88,e211] Although previous studies comparing these two different procedures reported contradictory data,[e212,e213] a randomized study showed that isolation of a large circumferential area around both ipsilateral PVs with verification of conduction block is a more effective treatment of AF than segmental isolation.[e214] The endpoint for this procedure was amplitude reduction within the ablated area,[e205,e209] elimination (or dissociation) of the PV potentials recorded from either one or two circular mapping catheters or a basket catheter within the ipsilateral PVs,[e88,e89,e210,e212,e213,e215] and/or exit block from the PV.[e216]

Elimination (or dissociation) of the PV potentials recorded from a circular multipolar electrode catheter is the primary endpoint for PV ablation procedures targeting the PVs for 75% of Task Force members. In contrast, only 10% of Task Force members rely on exit block as an endpoint for the ablation procedure. In a recent randomized study, the use of a circular catheter to guide and to confirm PVI obtained better results than single catheter mapping.[e217] Consistent with the results of this study, a single catheter approach to AF ablation, without employing a circular multipolar electrode catheter as an ablation endpoint, was used by less than 10% of Task Force members. Although some studies have reported that an ATP challenge can identify dormant PV conduction and that ablation based on this approach reduces AF recurrence after PVI,[e218–e220] less than one fourth of the Task Force members employ this technique as a routine clinical tool.

4.3. Ablation approaches not targeting the pulmonary veins

4.3.1. Linear ablation

Circumferential isolation of PVs has become the standard therapy for paroxysmal AF. However, due to the high recurrence rate observed in patients with persistent and long-standing persistent AF with PVI alone, continued efforts are underway to identify additive strategies to improve outcome. One of these strategies is to create additional linear lesions in the LA similar to those advocated with the Cox-Maze-III, and others (Figure 3).[e221–e224] The most common sites are the LA "roof" connecting the superior aspects of the left and right upper PVI lesions, the region of tissue between the mitral valve and the left inferior PV (the mitral isthmus), and anteriorly between the roof line near the left or right circumferential lesion and the mitral annulus (Figure 3).[e221] A prior randomized, prospective trial of catheter ablation of paroxysmal AF comparing segmental PVI ver-

sus circumferential PV ablation (CPVA) plus left atrial (LA) linear ablation (CPVA-LALA) at the LA roof and myocardial infarction showed that significantly more patients had LA flutter in the CPVA-LALA group,[e225] suggesting that additional ablation lines should not be performed in cases of paroxysmal AF. The role of additional lines in cases of persistent AF remains controversial.[e226] Routine isolation of the posterior wall does not seem to achieve better results in a prospective randomized study.[e227] On the other hand, it has been widely demonstrated that incomplete block across the ablation lines can be responsible for AT recurrence.[e228–e230] Therefore, if additional linear lesions are applied, line completeness should be demonstrated by mapping or pacing maneuvers.

In patients with long-lasting persistent AF, the stepwise approach has been proposed.[e231] The strategy starts by pulmonary isolation, following by ablation of CFAE, looking for reversion to sinus rhythm or AT. If this endpoint is not achieved, additional linear lesions are deployed.[e82,e231,e232] However, other studies did not find any correlation between acute termination of AF and better long-term outcome.[e233] Ablation of the cavotricuspid isthmus is recommended by the Task Force, based on consensus opinion, in patients with a history of typical atrial flutter or inducible cavotricuspid isthmus dependent atrial flutter.[e234]

4.3.2. Non-PV triggers

Non-PV triggers initiating AF can be identified in up to one-third of unselected patients referred for catheter ablation for paroxysmal AF.[e14,e45,e235–e238] Supraventricular tachycardias such as AV nodal reentry or accessory pathway-mediated atrioventricular reciprocating tachycardia may also be identified in up to 4% of unselected patients referred for AF ablation and may serve as a triggering mechanism for AF.[e239] Non-PV triggers can be provoked in patients with both paroxysmal and more persistent forms of AF.[e237] In selected patients, elimination of only the non-PV triggers has resulted in elimination of AF.[e45,e239,e240] The sites of origin for non-PV atrial triggers include the posterior wall of the LA, the SVC, the inferior vena cava, the crista terminalis, the fossa ovalis, the coronary sinus (CS), behind the Eustachian ridge, along the ligament of Marshall, and adjacent to the AV valve annuli (Figure 1).[e45,e236–e238,e240,e241] Furthermore, reentrant circuits maintaining AF may be located within the right and left atria.[e242] Provocative maneuvers such as the administration of isoproterenol in incremental doses of up to 20 mcg/min, and/or cardioversion of induced and spontaneous AF, can aid in the identification of PV and non-PV triggers.

4.3.3. Ablation of complex fractionated atrial electrograms

Areas with CFAEs have been reported to potentially represent AF substrate sites and became target sites for AF ablation.[e82,e92,e243,e244] CFAEs are EGMs with highly fractionated potentials or with a very short cycle length (<120 ms). CFAEs usually are low-voltage multiple potential signals between 0.06 and 0.25 mV. The primary endpoints during RF ablation of AF using this approach are either complete elimination of the areas with CFAEs, conversion of AF to sinus rhythm (either directly or first to an AT), and/or noninducibility of AF. For patients with paroxysmal AF, the endpoint of the ablation procedure using this approach is noninducibility of AF. For patients with persistent AF, the endpoint of ablation with this approach is AF termination. This endpoint was found to be associated with improved outcome.[e232] When the areas with CFAEs are completely eliminated but the arrhythmias continue as organized atrial flutter or AT, the atrial tachyarrhythmias are mapped and ablated. In patients with longstanding persistent AF, a step-wise approach to ablation has been reported to successfully convert AF to either sinus rhythm or AT in greater than 80% of patients.[e231,e245] An endpoint of noninducibility of AF has never been evaluated.[e246]

One of the limitations of targeting CFAEs with ablation has been the extensive amount of ablation needed. As a result some strategies for differentiating "active" from "passive" have been described. These include pharmacologic interventions, the use of monophasic action potential, limiting ablation to areas of continuous electrical activity, and activation mapping of AF.[e247–e250] It is important to recognize that improved outcomes with CFAE ablation in patients with persistent AF have not been uniformly reported and that the scientific basis of CFAE ablation is not universally accepted.

Fifty percent of Task Force members routinely employ CFAE-based ablation as part of an initial ablation procedure in patients with longstanding persistent AF. Fifty percent of those that perform CFAE based ablation use AF termination as the desired endpoint of their procedure.

4.3.4. Ablation of ganglionated plexi

Adding GP to other ablation targets may improve ablation success.[e70,e74,e91,e92] The four major LA GP (superior left GP, inferior left GP, anterior right GP, and inferior right GP) are located in epicardial fat pads at the border of the PV antrum, and can be localized at the time of ablation using endocardial high frequency stimulation (HFS) (Figure 1). For ablation, RF current can be applied endocardially at each site of positive vagal response to HFS. HFS is repeated and additional RF applications can be applied until the vagal response to HFS is eliminated. When considering ablation of GP, it is important to recognize that it is currently not possible to selectively ablate GPs without ablating atrial myocardium.

4.4. Task force consensus

Shown in Table 3 are the areas of consensus on ablation techniques that were identified by the Task Force. The Task Force recommends that ablation strategies that target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures and that complete electrical isolation of all PVs should be the goal. Please refer to Table 3 for a review of the consensus recommendations.

Table 3 Recommendations regarding ablation technique

- Ablation strategies that target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures.
- If the PVs are targeted, electrical isolation should be the goal.
- Achievement of electrical isolation requires, at a minimum, assessment and demonstration of entrance block into the PV.
- Monitoring for PV reconduction for 20 minutes following initial PV isolation should be considered.
- For surgical PV isolation, entrance and/or exit block should be demonstrated.
- Careful identification of the PV ostia is mandatory to avoid ablation within the PVs.
- If a focal trigger is identified outside a PV at the time of an AF ablation procedure, ablation of that focal trigger should be considered.
- If additional linear lesions are applied, operators should consider using mapping and pacing maneuvers to assess for line completeness.
- Ablation of the cavotricuspid isthmus is recommended in patients with a history of typical atrial flutter or inducible cavotricuspid isthmus dependent atrial flutter.
- If patients with longstanding persistent AF are approached, operators should consider more extensive ablation based on linear lesions or complex fractionated electrograms.
- It is recommended that RF power be reduced when creating lesions along the posterior wall near the esophagus.

5. Technologies and tools

In this section, we provide an update on a large number of technologies and tools that are employed for AF ablation procedures. It is important to recognize that this is not a comprehensive listing and that new technologies, tools, and approaches are being developed. It is also important to recognize that RF energy is by far the dominant energy source that has been used for catheter ablation of AF. Cryoablation has more recently been developed as a tool for AF ablation procedures. Other energy sources and tools are in various stages of development and/or clinical investigation.

5.1. Energy sources—radiofrequency energy

The presumed basis of successful AF ablation is production of myocardial lesions that block the propagation of AF wave fronts from a rapidly firing triggering source or modification of the arrhythmogenic substrate responsible for reentry. Successful ablation depends upon achieving lesions that are reliably transmural.[e251,e252] The conventional approach employed by cardiac electrophysiologists to reach the goal of AF ablation is RF energy delivery by way of a transvenous electrode catheter.

RF energy achieves myocardial ablation by the conduction of alternating electrical current through myocardial tissue, a resistive medium. The tissue resistivity results in dissipation of RF energy as heat, and the heat then conducts passively to deeper tissue layers. Most tissues exposed to temperatures of 50°C or higher for more than several seconds will show irreversible coagulation necrosis, and evolve into non-conducting myocardial scar.[e253] High power delivery and good electrode–tissue contact promote the formation of larger lesions and improve procedure efficacy. High power delivery can be achieved with large-tip or cooled-tip catheters.[e254,e255] Optimal catheter–tissue contact is achieved by a combination of steerable catheter selection, guide sheath manipulation, and skill of the operator. Significant complications can occur during AF ablation if high RF power is administered in an uncontrolled fashion. The increased risk of AF ablation compared to ablation of other arrhythmias may be attributable to the great surface area of tissue ablated, the large cumulative energy delivery, the risk of systemic thromboembolism, and the close location of structures susceptible to collateral injury, such as phrenic nerve,[e256] PVs,[e257] and esophagus.[e258] Thrombus and char can be minimized by limiting power and/or target temperature,[e259] by monitoring the production of steam microbubbles at the catheter tip with ICE,[e260–e262] and by cooling the electrode–tissue interface with saline irrigated tips.[e263] Intramural steam pops can be reduced by limiting power and the electrode–tissue contact pressure, which is greater when the catheter is oriented perpendicular to the atrial wall.

Early reports of catheter ablation of AF employed conventional 4-mm or 5-mm tip ablation catheters. Lesions were created with point-to-point application of RF energy or with continuous RF energy application while the catheter was dragged across the myocardium. The majority of the members of the Task Force now employ irrigated tip catheters. Comparative trials of irrigated tip and large tip RF technologies versus conventional RF electrodes have demonstrated increased efficacy and decreased procedure duration in the ablation of atrial flutter,[e264–e266] but only limited trials of large tip and open irrigation catheters have been performed in patients undergoing AF ablation. Despite the widespread adoption of irrigated RF ablation catheters, there is no definitive proof that these catheters reduce complications or improve outcomes when used for ablation of AF. Increased efficacy is observed with higher power applications of RF energy.[e267]

Various techniques have been proposed to minimize collateral injury. Temperature sensors at the electrode catheter tip can provide gross feedback of surface temperature, but because of passive convective cooling from circulating blood flow, or active cooling in a cooled tip catheter, the peak tissue temperatures are sometimes millimeters below the endocardial surface. Three-fourths of the Task Force routinely decrease RF power when ablating in the posterior LA. Limiting power will limit collateral injury but at the expense of reliably transmural lesions. ICE has been employed to monitor lesion formation. If the tissue shows evidence of increased echogenicity, or if small gas bubbles are observed, then power should be reduced or terminated.[e260–e262] It is important to note, however, that the presence of gas bubbles cannot be used to monitor lesion formation when an open irrigated catheter is used for ablation. The time to steady-state tissue temperatures during RF cath-

eter ablation is approximately 60–90 seconds.[e253] Therefore, limiting lesion duration may result in smaller ablative lesions.

5.2. Contact force sensing catheters and systems

A constant challenge in catheter ablation is optimizing electrode–tissue contact. With excellent contact, energy coupling to tissue is optimized and less energy is dissipated into the circulating blood pool. Thus, more predictable and reliable lesions can be created with excellent catheter contact to the endocardium. Attempts have been made to monitor catheter contact to the endocardium with imaging, predominantly intracardiac echocardiography. However, the technology now exists to directly measure the force exerted at the catheter tip or to estimate contact force based on local impedance.[e268–e272] It is hypothesized that monitoring electrode–tissue contact will improve efficacy of transmural lesion formation and improve procedure success. It is also hypothesized that monitoring electrode–tissue contact will reduce the rate of complications, particularly cardiac tamponade.

5.3. Energy sources—cryoablation energy

Cryothermal energy is an alternative energy source that has been used for decades by cardiac surgeons for treatment of cardiac arrhythmias. More recently, a number of point-by-point and balloon-based cryoablation systems have been developed for endocardial use.[e273–e277] Endocardial cryoablation catheters were employed initially for treatment of supraventricular arrhythmias, especially those near the AV node, and subsequently were used for AF ablation using a segmental PV isolation strategy.[e273–e275,e277] Although this point-by-point cryoablation approach proved to be associated with a low complication rate, the procedures were lengthy, and the long-term efficacy was limited. This early work ultimately paved the way for the development of a cryoablation balloon ablation catheter.[e276]

Cryoablation systems work by delivering liquid nitrous oxide under pressure through the catheter to its tip or within the balloon, where it changes to gas, resulting in cooling of surrounding tissue. This gas is then carried back through the reciprocating vacuum lumen. The mechanism of tissue injury results from tissue freezing with a creation of ice crystals within the cell that disrupts cell membranes and interrupts both cellular metabolism and any electrical activity in that cell. In addition, interruption of micro-vascular perfusion may interrupt blood flow, similarly producing cell death.

Achieving optimal cryoablation lesions is critically dependent upon regional blood flow around the tip of the catheter or balloon. As with RF energy, good tissue contact is important for generation of effective lesions. Continued flow counters the effect of cooling, thus reducing the chance to achieve a full-thickness lesion. Because of this, complete vein occlusion is required for the creation of circumferential PV lesions and electrical PVI using the cryoballoon ablation catheter.[e276,e278,e279] The clinical results of catheter ablation of AF will be discussed in Section 8.

5.4. Ultrasound and laser ablation systems

Although point-by-point RF energy and cryoballoon ablation are the two standard ablation systems used for catheter ablation of AF today, balloon-based ultrasound ablation,[e280–e282] RF ablation,[e283] and laser based ablation systems[e284,e285] also have been developed for AF ablation. A novel RF point-by-point ablation catheter that relies on visually guided ablation through a virtual saline electrode is also in development.[e286] The first of these balloon ablation systems to be approved for clinical use in Europe was the focused ultrasound ablation system.[e280–e282] Although this balloon-based ablation system was demonstrated to be effective, it was removed from the market because of a high incidence of atrial esophageal fistulas, some of which resulted in patient death. Early data from Japan have demonstrated the safety and effectiveness of a hot balloon ablation system that relies on RF energy to heat a saline-filled balloon positioned in the PVs.[e283] A final balloon-based laser ablation system involves a compliant balloon ablation catheter through which arcs of laser energy are delivered under visual guidance. Initial results of small clinical trials have demonstrated the safety and effectiveness of this ablation system, which is now approved for use in Europe and is entering a pivotal randomized clinical trial in the United States.[e284,e285]

5.5. Multielectrode circumferential ablation catheters

A number of circumferential multielectrode ablation catheters have been developed to facilitate AF ablation and have undergone clinical evaluation. The principal purpose of these multielectrode circular ablation catheter systems is to provide ablation and mapping on a single platform.[e287–e293] One of these ablation systems relies on phased RF energy for ablation[e287,e291–e293] and the other uses standard RF energy delivered through a novel mesh electrode.[e288–e290] One of the potential limitations of such catheters is that operators are easily drawn to a more ostial location rather than the wider area circumferential antral ablation that can be achieved with a point-by-point ablation tip catheter under 3D guidance. The clinical results achieved with these multielectrode circular ablation catheters have been roughly equivalent in safety and efficacy to those achieved by point-by-point tip ablation catheters.[e287–e293] However, several recent studies have reported a higher incidence of silent microemboli following ablation with a multielectrode ablation catheter[e294,e295] (see Section 9.5.2 Silent Microemboli.) The precise mechanisms for development of these silent microemboli are not fully understood and remain an area of active investigation. Very recently the results of the TTOP Trial have been released.[e296] This trial enrolled 210 patients with persistent or longstanding persistent AF with the Medtronic Cardiac Ablation System, which incorporates several multielectrode ablation catheters, to either ablation

or antiarrhythmic drug therapy. At 6 months of follow-up, 55.8% of patients who underwent one or more ablation procedures had a >90% reduction in AF burden on a 48-hour Holter monitor as compared with 26.4% of patients treated with drug therapy. The rate of major complications was 12.3% including a 2.3% incidence of stroke.

5.6. Electroanatomic mapping systems

AF is a disease frequently progressing from paroxysmal to persistent AF. The mechanisms underlying the process of arrhythmia perpetuation are complex. Major contributions to the understanding of the initiating and perpetuating factors derive from mapping studies in both patients and animal models of AF. It is well known that mapping and ablation of AF require accurate navigation in the LA. This can be obtained using standard fluoroscopy or more commonly with electroanatomic mapping systems that combine anatomic and electrical information by a catheter point-by-point mapping, allowing an accurate anatomic reconstruction of a 3D shell of the targeted cardiac chamber.

There are two different electroanatomic mapping systems that are widely used in clinical practice. The current generation of the CARTO mapping system (CARTO-3) relies on both a magnet-based localization for visualization of the ablation catheter and an impedance-based system that allows for both tip and catheter curve visualization as well as simultaneous visualization of multiple electrodes.[e110,e291,e297] The second electroanatomic mapping system is an electrical impedance mapping system (NavX, St. Jude Medical Inc., Minneapolis, MN, USA) using voltage and impedance for localization.[e298] The use of these 3D mapping systems has been demonstrated to reduce fluoroscopy duration.[e298,e299] To further improve anatomic accuracy of the maps, integration of 3D images by computed tomography (CT) or magnetic resonance imaging (MRI) and of images acquired with intracardiac ultrasound during the procedure (before transseptal puncture) has become available.[e300–e302] Image integration is performed by defining landmark points on the CT or MRI reconstruction of the LA followed by merging the CT or MRI image with the anatomic map that has been constructed using the mapping catheter. Another approach involves use of 3D rotational angiography images, which can be merged with live two-dimensional fluoroscopy.[e303] However, it should be stressed that CT or MRI images are not real-time images, and that the accuracy of image integration is dependent on the accuracy of the image fusion. Another limitation of electroanatomic mapping systems is that they are only capable of sequential and not simultaneous multielectrode mapping. Because of this limitation, they are not capable of activation mapping of atrial fibrillation and other unstable cardiac arrhythmias.

Several studies performed to define the clinical benefit of image integration as compared to ablation guided only with a standard electroanatomic mapping system have generated mixed results. Whereas some studies have reported that use of these mapping systems with or without image integration improves the safety and efficacy of AF ablation,[e304–e306] other studies have reported contradictory findings.[e307,e308] Among Task Force members 90% employ electroanatomic mapping systems routinely when performing AF ablation (excluding cases where a balloon-based ablation system is used).

5.7. Robotic and magnetic catheter navigation

Catheter-based ablation of AF places significant demands on the skill and experience of the electrophysiologist. The objective of developing new technologies is to improve the efficacy and safety of procedures while containing or reducing costs. The concept of remote catheter navigation is appealing for the operator because these systems may reduce radiation exposure and the risk to the physician of developing orthopedic problems related to prolonged use of protective lead aprons during protracted cases. They also may facilitate analysis of intracardiac EGMs and 3D images because the catheter navigation and analysis can be performed from a work station where the operator is seated. The two technologies developed to meet these objectives include the magnetic navigation system designed by Stereotaxis, Inc.,[e309–e311] and a robotic controlled catheter system manufactured by Hansen Medical.[e312,e313] Both technologies have been used to ablate AF. No randomized multicenter studies have compared these technologies to ablation with a manual catheter to demonstrate whether either system shortens procedure time, reduces cost, improves outcomes of ablation, or improves the safety profile of these and other complex ablation procedures.

5.8. Intracardiac echocardiography

Intracardiac echocardiography, which allows for real-time imaging of cardiac anatomy, is used in many EP laboratories throughout the world to facilitate AF ablation procedures.[e91,e314–e317] Advocates of the use of ICE find it to be of value as it can (1) help identify anatomic structures relevant to ablation, including the PVs and esophagus, (2) facilitate transseptal access, (3) guide accurate placement of the multielectrode circular ablation catheter and/or balloon-based ablation system, (4) allow titration of delivered energy, (5) allow for recognition of thrombus formation on sheaths and catheters,[e318] and (6) allow early recognition of cardiac perforation and/or the development of a pericardial effusion. ICE does not replace TEE for screening for the presence of an LA thrombus. Fifty percent of Task Force members routinely use ICE to facilitate the transseptal procedure and/or to guide catheter ablation.

5.9. Pulmonary vein venography

PV venography is performed by many centers at the time of catheter ablation procedures.[e319,e320] The purpose of PV venography is to help guide catheter manipulation, determine the size and location of the PV ostia, and also assess PV stenosis, particularly among patients undergoing repeat ablation procedures. Among Task Force members, 50%

routinely use PV venography during their AF ablation procedures. There are three techniques that have been described for PV venography. The first technique involves selective delivery of contrast media into each of the PV ostia. This can be accomplished by positioning the transseptal sheath in the region of the right and left PV trunks and injecting contrast medium, or by selectively engaging each of the four PV ostia using a deflectable catheter or a multipurpose angiography catheter.[e320] A limitation of the selective PV venography approach is that noncatheterized PVs can be missed if a pre-acquired CT or MRI scan is not available to make sure that all PVs are identified. The second technique is performed by injection of contrast medium into the left and right pulmonary arteries or the pulmonary trunk. The location of the PVs can then be assessed during the venous phase of pulmonary arteriography. The third technique involves the injection of contrast media in the body of the LA or at the roof of the right or left superior PV ostium immediately after delivery of a bolus of adenosine to induce AV block. The contrast media will fill the LA body, PV antrum, and the proximal part of PV during the phase of ventricular asystole.

5.10. CT and/or MRI scans and rotational angiography to define the anatomy of the atrium, PVs, and antrum

The left atrial anatomy is complex. A detailed understanding of this anatomy is essential for a safe and effective AF ablation procedure. Left atrial imaging may facilitate AF ablation by (1) providing a detailed anatomic description of the PVs and LA preprocedurally, and (2) assisting in the detection of postprocedural complications.

There is significant inter- and intra-patient variability in the number, size, and bifurcation of the PVs.[e321–e327] Understanding these variations can be useful for the application of ablation lesions around or outside the PV ostia. One common variant is the existence of supernumerary right PVs. These have been shown to be present in 18% to 29% of the patients.[e321–e326] Knowledge of the presence of a right middle or right top PV may help avoid placing ablation lesions over their ostia, which may result in PV occlusion. Another common variant is the presence of a common PV trunk. This is more frequently encountered on the left-sided PVs (>30%).[e328,e329] The branching pattern of the PVs may also have procedural implications. A significantly longer distance between the PV ostium and first branch was demonstrated for the left-versus right PVs.[e324] A pre-procedural knowledge of the bifurcation pattern may also be important during cryoballoon PVI, where wiring of different branches may be needed to ensure optimal occlusion.[e330]

Pre-procedural CT and MR imaging can also be used for image integration. This technology helps facilitate AF ablation by providing detailed information about the anatomy.[e300,e301] When using these systems, it is critical to confirm accurate registration.

Intraprocedural acquisition of LA volumes using rotational angiography has recently been introduced.[e303,e331–e337] After contrast medium injection in the right heart chambers, the fluoroscopy c-arm is rapidly rotated around the patient, and images are acquired throughout the rotation to generate 3D volumetric anatomic rendering of the LA-PVs. Such images can be superimposed on the fluoroscopic projections of the heart or integrated into an electroanatomic mapping system. Recent studies have demonstrated that this modality can provide intra-procedural imaging with anatomic accuracy comparable to that of CT.[e333–e335,e337] This innovative technique might overcome the limitation of acquiring the images in a different time with respect to the ablation procedure, but the consistent iodinated contrast agent load and radiation dose are important limiting factors.[e338] Less than one-third of Task Force members employ rotational angiography as part of some or all of their AF ablation procedures.

5.11. Assessment of left atrial volume

Left atrial volume can be assessed by a variety of techniques. Perhaps the most widely employed approach is measurement of the end-systolic LAD in the parasternal long axis view according to the American Society of Echocardiography guidelines.[e339] Although this parameter is widely used clinically to determine eligibility for AF ablation with LAD cutoffs of 5 or 5.5 cm, recent reports have demonstrated that this parameter correlates poorly with true left atrial volume, as assessed by CT imaging.[e340,e341] Alternative methods to assess left atrial volume include 3D echo,[e342] CT imaging, MR imaging,[e343] left atrial angiography,[e344] 3D electroanatomic mapping,[e344] and TEE.[e341] Various approaches to calculating left atrial volume can be used with each of these approaches. Recent studies have demonstrated, for example, that calculation of left atrial volume based on three orthogonal left atrial dimensions obtained from CT, MR, or 3D echo imaging underestimates true left atrial volume as determined by the gold standard multiple-slice technique by 10–20%.[e342,e343,e345] In contrast, invasive techniques for determining LA volume such as angiography and point-by-point electroanatomic mapping result in an overestimation of LA size and left atrial volume.[e344] Recently, perhaps not surprisingly, a series of studies have demonstrated that LA volume is one of the strongest predictors of outcome following AF ablation.[e341,e346–e349]

5.12. MR imaging of atrial fibrosis and ablation lesions

Magnetic resonance imaging has been used to visualize myocardial inflammation and fibrous tissue by using delayed clearance of gadolinium from myocardial areas with high content of fibrous tissue, high volume of extracellular matrix, and high inflammatory activity. All of these result in enhanced extravasation of gadolinium and slower removal from cardiac tissue, which is then detectable as "delayed enhancement," ie, detectable deposition of gadolinium after the usual time needed to remove it from the tissue. This technique is well validated to visualize myocardial scars in

the left ventricular myocardium.[e350,351] Delayed enhancement can also visualize lesions induced by radiofrequency catheter ablation in atrial tissue.[e98,e352,e353] More recent studies from a single-center have demonstrated that the extent of LA fibrosis prior to ablation can predict the outcomes of catheter ablation of AF.[e98,e354] Further work is needed, however, to determine the reproducibility of MRI measurements of fibrosis by different centers and also to validate the predictive accuracy of MRI detected fibrosis in predicting outcomes of AF ablation. Based on this initial work, efforts are now underway to allow catheter ablation of AF to be performed under MRI guidance.[e355,e356] Despite the promise of using these MRI techniques to improve the outcomes of AF ablation, it is important to recognize that technical aspects of magnetic resonance-based imaging of atrial fibrosis and ablation lesions make it difficult to adapt these techniques for clinical use today.

5.13. Approaches to mapping atrial fibrillation including CFAEs, dominant frequency, nests, and rotors

Over the past decade, several mapping studies in human AF have made the following important observations: (1) atrial EGMs during sustained AF have three distinct patterns: single potential, double potential and CFAE[e82,e243,e244]; (2) the distribution of these atrial EGMs during AF has a proclivity to localize in specific areas of the atria[e82,e243,e357]; (3) CFAE areas are believed to reflect the AF substrate and to be important target sites for AF ablation by some investigators[e82,e92,e243,e244,e358]; (4) and high dominant frequency (DF) as assessed using fast Fourier transformation (FFT) is thought to represent drivers of AF.[e16,e48] Mapping of areas that harbor stable CFAE and/or high DF could identify sites that perpetuate AF and in turn be considered targets for AF ablation.

CFAEs are defined as low voltage ($\leq$0.15 mV) multiple potential signals and have one or both of the following characteristics: (1) atrial EGMs that have fractionated EGMs composed of two deflections or more, and/or have a perturbation of the baseline with continuous deflection of a prolonged activation complex; (2) atrial EGMs with a very short cycle length ($\leq$120 ms), with or without multiple potential; however, when compared to the rest of the atria, this site has the shortest cycle length. The distribution of CFAEs in the right and left atria is vastly different from one area to the others. In spite of regional differences in the distribution, CFAEs are surprisingly stationary, exhibiting relative spatial and temporal stability.[e357,e358] Thus, one can perform point-to-point mapping of these CFAE areas and incorporate into an electroanatomic map. Each of the currently available electroanatomic mapping systems has available software that allows for user defined, automated detection of CFAEs. Mapping is always performed during AF.[e358] Detailed mapping of the LA, CS, and occasionally the right atrium is performed. The primary target sites for AF substrate ablation are the CFAE areas that are stable that exhibit either very short cycle length ($<$100 ms) or continuous activity. The primary endpoints during RF ablation targeting CFAE sites are either complete elimination of the areas with CFAE, conversion of AF to sinus rhythm (SR), and/or non-inducibility of AF. For patients with paroxysmal AF, the endpoint of the ablation procedure using this approach is non-inducibility of AF. For patients with persistent AF, the endpoint of ablation with this approach is AF termination. When the areas with CFAEs are completely eliminated, but the arrhythmias continue as organized atrial flutter or AT, the atrial tachyarrhythmias are mapped and ablated.

It is noteworthy to recognize the recent observation that occurrences of CFAE may involve the complex interplay of the intrinsic cardiac nervous system on atrial tissues.[e76,e78–e80,e359] Hence, mapping CFAE areas may provide a surrogate for identification of the GPs. Please see section 2.7 of this document for more details. It is also important to recognize that CFAEs may be generated by "fibrillatory conduction" or far field signals and thus are not always critical for AF maintenance.

The purpose of DF mapping is to identify sites of maximal DF during AF.[e48,e360] There is evidence that ablation at such maximal DF sites results in slowing and termination in a significant proportion of paroxysmal AF patients, suggesting their role in AF maintenance.

Recently, a system for real-time spectral mapping using FFT in sinus rhythm was created to identify sites in which the unfiltered, bipolar atrial EGMs contain unusually high frequencies, namely fibrillar myocardium, or the so-called AF Nest.[e361–e363] Most investigators use customized amplifiers and software for real-time spectral mapping. The system applies FFT to the unfiltered bipolar atrial EGMs from the distal pair of electrodes on the ablation catheter. The full spectrum of each EGM is then continuously displayed in 3D. Ablation of the aforementioned AF nest sites in conjunction with PVI may improve outcomes of AF ablation in patients with paroxysmal AF.[e361,e362,e364] All of the above techniques are based on, and suited to, sequential single catheter techniques with all their inherent limitations.

5.14. Strategies for mapping and ablation of linear ablation lines including left atrial flutter

The development of a left AT or left atrial flutter (referred to as LAFL throughout this document) following AF ablation is common, occurring in between 1% and 50% of patients. LAFL is rarely observed in the context of paroxysmal AF ablation when the procedure is limited to PVI.[e212,e223,e225,e365–e368] The incidence of LAFL is relatively uncommon ($<$1%) when the cryoballoon is used for treatment of patients with paroxysmal AF.[e369] The likelihood of developing an LAFL increases markedly in patients with longstanding persistent AF, markedly dilated atria, and where linear ablation strategies are employed.[e223,e225,e231,e366–e368] There is debate as to whether the development of an LAFL following AF ablation should be considered a "proarrhythmic" complication of the procedure or whether it should be considered as partial success as evidenced

by significant modification of the atrial electrophysiologic substrate as compared with prior to ablation. Because the outcomes of catheter ablation of LAFL are superior to those associated with catheter ablation of AF alone, some consider the development of a LAFL evidence of partial success, while others do not.[e370] It is important to recognize that many patients with LAFL are highly symptomatic and/or have a very difficult to control ventricular response, making the performance of another ablation procedure mandatory in many patients.

5.14.1. Diagnostic mapping strategies

Evaluation of the 12-lead ECG is of some value in the diagnosis of an LAFL. The presence of a positive or biphasic but dominantly positive deflection in V_1 accompanied by deflections in other leads inconsistent with typical counterclockwise atrial flutter should suggest the presence of an LAFL.[e371–e375] It is also important to note that the demonstration of P waves on the 12-lead ECG separated by long isoelectric intervals should not lead to exclusion of a reentrant AT but rather may indicate microreentry involving slowly conducting isthmus often near one of the prior AF ablation lesions. Although the analysis of the surface ECG has been used to predict centrifugal vs macro-reentrant arrhythmias and identify perimitral circuits, the use of the 12-lead ECG for localization of the LAFL may be limited by extensive LA ablation, disease and dilatation.

The most widely used strategy for mapping these flutters relies on 3D electro-anatomic mapping systems using signals obtained either by a point-by-point roving catheter or a multipolar catheter. In addition to standard activation mapping strategies, color entrainment maps can be constructed using the return cycle length values obtained during flutter entrainment from various sites.[e376] A rapid deductive approach that involves a sequence of activation and entrainment mapping has also been described.[e377] Conventional mapping is also an effective strategy to establish the diagnosis of LAFL.

5.14.2. Catheter ablation of left atrial flutter

The macro-reentrant circuits that are dependent on the roof line or mitral isthmus line are easy to diagnose but may be difficult to ablate (see below). Drawing a roof line connecting both superior PVs is usually easier than the mitral isthmus line. Roof linear ablation is recommended at the roof of the LA rather than on the posterior left atrial wall because the latter is associated with an increased risk of atrial esophageal fistula. After restoration of sinus rhythm, demonstration of an ascending activation front in the posterior LA during pacing from the LA atrial roof or LAA ascertains complete linear roof block.[e222,e373] The ablation of localized centrifugal arrhythmias can be accomplished with focal RF energy delivery. Nonreentrant focal arrhythmias often originate at lesion edges.

5.15. Strategies, tools, and endpoints for creation of linear ablation lesions including mitral isthmus block

Linear lesion is considered a double-edged sword because an incompletely blocked line can be as much associated with man-made AT as a completely blocked line can provide freedom from it.[e225] Linear lesions typically are created between two anatomic or electrical barriers. Completeness of the linear ablation lesion should be demonstrated with pacing and/or mapping maneuvers.

In the context of AF ablation, mitral isthmus linear lesion was first proposed in 2004.[e223] The ablation of mitral isthmus is the most challenging linear lesion in AF ablation. This may be due to anatomic difficulties, increased tissue thickness, and heat sink effect of the CS. Two distinct strategies have been reported. The original description of the most commonly used approach consists of delivering the ablation lesion below the base of the left atrial appendage, corresponding to a 3–4 o'clock position in the LAO view. Ablation in this location is challenging, possibly because of the heat sink effect of the blood flowing in the epicardially located CS. As a consequence, ablation from inside the CS is frequently needed to achieve a transmural lesion. However, lesion at this location will produce no local delay in sinus rhythm as it lies in the region where the anterior and inferior activation wavefronts collide. Mitral isthmus linear ablation recently has been proposed in an anterior or more superior location than usual. Although there is no randomized comparison with conventional site of ablation, achieving complete mitral isthmus block seems to be facilitated by anterosuperior location of the linear lesion. However, its major drawback is that it can significantly modify the activation pattern in sinus rhythm, especially that of the left atrial appendage. The latter is activated with a substantial delay, sometimes simultaneously with or after the QRS. This could impact left atrial function significantly more than the inferior approach.

The most commonly used approach consists of using a fixed curved left atrial sheath to facilitate ablation by dragging the catheter from the mitral annulus to the ostium of the left inferior PV. However, the achievement of a complete isthmus block remains difficult. The occlusion of the segment of CS with a balloon to prevent a heat sink has been shown to facilitate creation of a mitral isthmus block but is currently not widely employed in clinical practice.[e117,e378] The roof line connecting both superior PVs is usually easier than the mitral isthmus line. The anatomy of the LA roof varies highly from being flat, concave, and even convex. Ablation is undertaken with the support of a sheath.

During ongoing AF, assessment of complete linear block is not possible. It is therefore recommended to assess linear block after the restoration of sinus rhythm. The endpoint of linear lesion is complete, bidirectional block across the linear lesion. The assessment of complete block is based on the concept of differential pacing that was initially demonstrated for cavotricuspid isthmus ablation. Briefly, pacing

Table 4 Anticoagulation strategies: Pre, during, and post ablation

Pre Ablation
- Anticoagulation guidelines that pertain to cardioversion of AF be adhered to in patients who present for an AF ablation in atrial fibrillation at the time of the procedure. In other words, if the patient has been in AF for 48 hours or longer or for an unknown duration, we require three weeks of systemic anticoagulation at a therapeutic level prior to the procedure, and if this is not the case, we advise that a TEE be performed to screen for thrombus. Furthermore, each of these patients will be anticoagulated systemically for two months post ablation.
- Prior to undergoing an AF ablation procedure a TEE should be performed in all patients with atrial fibrillation more than 48 hours in duration or of an unknown duration if adequate systemic anticoagulation has not been maintained for at least 3 weeks prior to the ablation procedure.
- Performance of a TEE in patients who are in sinus rhythm at the time of ablation or patients with AF who are in AF but have been in AF for 48 hours or less prior to AF ablation may be considered but is not mandatory.
- The presence of a left atrial thrombus is a contraindication to catheter ablation of AF.
- Performance of catheter ablation of AF on a patient who is therapeutically anticoagulated with warfarin should be considered.

During Ablation
- Heparin should be administered prior to or immediately following transseptal puncture during AF ablation procedures and adjusted to achieve and maintain an ACT of 300 to 400 seconds.
- Performance of AF ablation in a patient systemically anticoagulated with warfarin does not alter the need for intravenous heparin to maintain a therapeutic ACT during the procedure.
- Administration of protamine following ablation to reverse heparin should be considered.

Post Ablation
- In patients who are not therapeutically anticoagulated with warfarin at the time of AF ablation, low molecular weight heparin or intravenous heparin should be used as a bridge to resumption of systemic anticoagulation with warfarin following AF ablation.
- Initiation of a direct thrombin or Factor Xa inhibitor after ablation may be considered as an alternative post procedure anticoagulation strategy.
- Because of the increased risk of post procedure bleeding on full dose low molecular weight heparin (1 mg/kg bid) a reduction of the dose to 0.5 mg/kg should be considered.
- Systemic anticoagulation with warfarin or a direct thrombin or Factor Xa inhibitor is recommended for at least two months following an AF ablation procedure.
- Decisions regarding the continuation of systemic anticoagulation agents more than two months following ablation should be based on the patient's risk factors for stroke and not on the presence or type of AF.
- Discontinuation of systemic anticoagulation therapy post ablation is not recommended in patients who are at high risk of stroke as estimated by currently recommended schemes ($CHADS_2$ or CHA_2DS_2VASc)[e3].
- Patients in whom discontinuation of systemic anticoagulation is being considered should consider undergoing continuous ECG monitoring to screen for asymptomatic AF/AFL/AT.

from a site close to the line of block generates an activation wavefront that is blocked in the direction toward the line. The wavefront, then, necessarily travels in the direction away from the line and courses all around the LA to eventually reach the other side of the line. The following criteria establish the diagnosis of complete, bidirectional block across mitral isthmus linear lesion: (1) pacing from the site immediately posterior to the ablation line (usually distal bipole CS 1-2 of the catheter lying inside the CS) should be associated with a longer delay to the left atrial appendage as compared with pacing from a more proximal site (usually bipole CS 3-4); and (2) pacing from the base of the left atrial appendage, a site anterior to the line of block should result in a proximal to distal activation of the catheter lying in the CS with its distal bipole being the latest activated site as long as it is located below the ablation line. These criteria are robust and the only limitation is the presence of a very slowly conducting gap in the mitral isthmus line such that the activation through the gap would take longer than the activation around the mitral annulus. It is worth noting that it is easier to distinguish residual slow conduction from complete conduction block across a mitral ablation line as compared with a roof line, probably for anatomic reasons. In addition to these criteria, mapping the ablation line during pacing from a site adjacent to the line shows widely separated double potentials with no bridging activity. Any absolute value of perimitral conduction delay should not be considered a reliable indicator of block. Complete block has been observed with a delay as short as 100 ms. On the other hand, more than 200 ms of conduction delay may not be indicative of block.

The assessment of complete block across the roof can be undertaken during sinus rhythm or during pacing from the anterior LA. The concept is that during both rhythms, the posterior LA is activated downward from the anterior roof in the absence of block, while in the presence of complete block, the activation wave must proceed downward (after having arrived from right atrium over the Bachmann's bundle in sinus rhythm or from the pacing site) on the anterior wall and then upward on the posterior wall. Therefore, during both rhythms, the demonstration of block relies on an ascending activation front of the posterior LA. This is easily demonstrated by recording the local activation time high on the posterior wall, below the ablation line, and lower in the mid posterior LA. The former should be activated later in the presence of block. The comment on the absolute value of delay necessary to call it a blocked mitral line holds true for the roof line, too. Electroanatomic systems can, of course, be used to easily demonstrate the activation front

detour due to complete line of block during pacing after ablation.

6. Other technical aspects

6.1. Anticoagulation strategies to prevent thromboembolism during and following AF ablation

AF patients are at increased risk of thromboembolism (TE) during, immediately following, and for several weeks to months after their ablation.[e379,e380] This prothrombotic period results in a higher but transient TE risk in AF patients who were identified as low-risk before ablation. Careful attention to anticoagulation of patients before, during, and after ablation for AF is critical to avoid the occurrence of a TE event. Consensus recommendations for anticoagulation prior to, during, and following ablation are summarized in Table 4. The ablation procedure leaves patients with substantial areas of damaged LA endothelium that may become a nidus for thrombus formation. Transseptal sheath placement and insertion of electrode catheters can precipitate thrombus formation on the catheter or on or within the sheath during the procedure.[e318,e381–e384] The atrial tissue may be stunned for several weeks or even months post-procedure, leading to impairment of normal contraction.[e385] Anticoagulation, in turn, contributes to some of the most common complications of the procedure, including hemopericardium, pericardial tamponade, and vascular complications.[e386–e388] Therefore, attention must be paid to achieving the optimal safe level of anticoagulation throughout the process.

6.2. Screening transesophageal echocardiography

The risk of a thromboembolic event at the time of an AF ablation procedure varies depending upon a number of factors including: (1) the type of AF, (2) the presence, absence, and duration of AF as the presenting rhythm, and (3) the patient's stroke risk profile including left atrial size and $CHADS_2$ or CHA_2DS_2VASc score. The recommendations of this Consensus Writing Group are summarized in Table 4. Among these recommendations, several are of particular importance. First, we recommend that the anticoagulation guidelines that pertain to cardioversion of AF be adhered to in patients who present in AF for an AF ablation procedure. In other words, if the patient has been in AF for 48 hours or longer or for an unknown duration, we require three weeks of systemic anticoagulation at a therapeutic level prior to the procedure. If this is not the case, we advise that a TEE be performed to screen for thrombus. Furthermore, following the recommendations for cardioversion, we advise that patients are anticoagulated systemically for two months post ablation (Table 4).

Several studies have evaluated the incidence of LA thrombus on TEE among patients undergoing AF ablation who have been therapeutically anticoagulated.[e389–e391] The results of these three studies have been remarkably consistent, demonstrating that 1.6% to 2.1% of patients will demonstrate a thrombus or "sludge" in the left atrial appendage. The probability of identifying a thrombus was directly related to the $CHADS_2$ score in each of these studies. Other variables that were identified as risk factors were left atrial size and persistent AF. Among patients with a $CHADS_2$ score of zero a thrombus was identified in $\leq$0.3% of patients and in >5% of patients with a $CHADS_2$ score of two or greater.

There is wide variation among the Task Force Members concerning use of TEE prior to AF ablation. Approximately 50% of Task Force Members perform a TEE in all patients undergoing AF ablation regardless of presenting rhythm and $CHADS_2$ or CHA_2DS_2VASc score. Another 20% of the writing group only performs a TEE if a patient presents in AF of unknown duration or more than 48 hours' duration and has not been systemically anticoagulated for at least four weeks. The remaining one-third of Task Force Members employs clinical judgment and decides on a case-by-case basis whether to perform a TEE. For example, if a patient presents in sinus rhythm, has a normal LA size, and a $CHADS_2$ or CHA_2DS_2VASc score of zero, many members of the Task Force would not obtain a TEE regardless of preprocedure anticoagulation. But if a patient has had AF for >48 hours, a TEE would be obtained. Conversely, a TEE would be obtained in a patient with longstanding persistent AF with a $CHADS_2$ score greater than two and a large LA even if the patient has been therapeutically anticoagulated for four weeks or longer. Although there is no consensus among the Task Force as to whether a TEE should be performed in the subset of patients who have received four weeks of systemic anticoagulation, many in the group perform TEEs in all patients undergoing AF ablation.

6.3. Systemic anticoagulation prior to AF ablation

Many patients who are undergoing AF ablation have an elevated $CHADS_2$ or CHA_2DS_2VASc score or are in persistent AF prior to ablation and are therefore systemically anticoagulated with warfarin or with a direct thrombin or Factor Xa inhibitor.[e389,e392–e396]

There are two strategies that have been used for patients who have been anticoagulated with warfarin. Historically, patients would have their warfarin discontinued, and they would be "bridged" with intravenous or low molecular weight heparin prior to and following the ablation procedure. Although widely adopted throughout the world, it was recognized that this approach resulted in a high incidence of bleeding complications, especially at the site of vascular access.[e386–e388,e397] This has resulted in a new trend toward performing AF ablation procedures in patients who are continuously therapeutically anticoagulated with warfarin.[e388,e394,e398–e403] In the event of persistent bleeding or cardiac tamponade protamine is administered to reverse heparin. Fresh frozen plasma, prothrombin complex concentrates (PCC: Factors II, VII, IX, and X), or recombinant activated factor VII (rFVIIa) can be administered for reversal of warfarin.[e404] This strategy has proved

to be safe and effective and is now adopted by approximately 50% of Task Force members.

Another emerging anticoagulation strategy involves the use of a thrombin inhibitor (dabigatran) or Factor Xa inhibitor (rivaroxaban, apixaban) for systemic anticoagulation of patients with AF. The predictable pharmacological profile of these new agents allows us to use these drugs without the need for routine coagulation monitoring. Clinical experience with these new anticoagulation agents in association with an AF ablation procedure at the present time is limited.[e405]

6.4. Intracardiac ultrasound and CT to screen for left atrial thrombus

Intracardiac echocardiography and CT scanning are commonly employed prior to or during AF ablation procedures. Several studies have investigated whether these modalities can be used to screen for left atrial thrombi, with the hope of obviating the need for a screening TEE in high risk patients. Unfortunately, these studies have reported conflicting data. Whereas some studies have demonstrated that each of these modalities has reduced sensitivity in the detection of left atrial thrombi as compared with standard TEE,[e406,e407] other studies have reported that CT scanning can identify left atrial appendage thrombi with good sensitivity but moderate specificity.[e408] Consistent with these findings, the members of this Task Force do not recommend that ICE or CT imaging be used to screen for LA thrombi in patients who are at high risk of stroke, and TEE is warranted. Some members of the Task Force advocate that ICE, while not a substitute for TEE in high risk patients, may be of value in lower risk patients for distinguishing spontaneous echo contrast versus true thrombus.

6.5. Intra-procedural anticoagulation

Optimal anticoagulation using heparin with close attention to maintain therapeutic dosing during the procedure is important. One recommendation of the Task Force (Table 4) is that heparin should be administered prior to or immediately following transseptal puncture during AF ablation procedures and adjusted to achieve and maintain a target ACT (activated clotting time) of 300 to 400 seconds. This recommendation reflects the well-established observation that thrombi can form on the transseptal sheath and/or electrode catheter almost immediately after crossing the septum and that early heparinization substantially decreases this risk.[e318,e381–e384,e409–e411] More than 50% of the Task Force Members give heparin prior to the transseptal puncture. A heparin loading dose should be administered initially followed by a standard heparin infusion. Although no scientific data exist to guide the frequency with which ACT levels be monitored, the consensus of the writing group was that an ACT level should be checked at 10- to 15-minute intervals until therapeutic anticoagulation is achieved and then at 15- to 30-minute intervals for the duration of the procedure. The heparin dose should be adjusted to maintain an ACT of at least 300–350 seconds throughout the procedure. Approximately one-third of the Task Force uses a target ACT of 350 seconds, especially in patients with spontaneous echo contrast or significant atrial enlargement.[e402,e407,e411] It is also recommended that heparinized saline be infused continuously through each transseptal sheath to further reduce the risk of thrombi.[e383] The risk of systemic embolization of thrombus formed on a sheath may be reduced by withdrawing the sheath to the right atrium once a catheter is positioned in the LA. Heparin infusion can be discontinued once all catheters are removed from the LA, and the sheaths removed from the groin when the ACT is less than 200–250 seconds. Alternatively, the heparin effect can be reversed with protamine.[e412] This approach is used by approximately 50% of Task Force members. Controlled data to support either of these recommendations are lacking, and other practices may be as valid as the specific suggestions outlined above.

6.6. Post-procedural anticoagulation

The atria are often stunned after RF ablation as following direct current (DC) cardioversion. Optimal anticoagulation post-ablation can help prevent thrombus formation. After removal of all sheaths, warfarin should be reinitiated within four to six hours, and low-molecular weight heparin (LMWH) (enoxaparin 0.5–1.0 mg/kg twice daily) or intravenous heparin should be used as a bridge to resumption of INR 2.0–3.0. Alternatively, a direct thrombin or Factor Xa inhibitor can be administered following ablation.[e392,e393,e395,e396] If warfarin was not interrupted before ablation, use of LMWH can be avoided; continue warfarin maintaining INR 2.0–3.0. Another consensus recommendation from this Task Force (Table 4) is that systemic anticoagulation with warfarin or with a direct thrombin or Factor Xa inhibitor is recommended for all patients for at least two months following an AF ablation procedure. Although a single-center reported data suggesting that selected low-risk patients with $CHADS_2$ scores of zero or one can safely be discharged following left atrial ablation procedure on aspirin alone, this approach has not been adopted into widespread clinical practice.[e413] Other Consensus Recommendations of this Task Force that pertain to post-procedure anticoagulation strategies are: (1) decisions regarding the use of systemic anticoagulation more than two months following ablation should be based on the patient's risk factors for stroke and not on the presence or type of AF, (2) discontinuation of systemic anticoagulation therapy post ablation is not recommended in patients who are at high risk of stroke as estimated by currently recommended schemes ($CHADS_2$ or CHA_2DS_2VASc), and (3) patients who are at increased risk for stroke in whom discontinuation of systemic anticoagulation is being considered should undergo some type of continuous ECG monitoring to screen for asymptomatic AF/AFL, and AT. In considering these Consensus Recommendations, it is worth commenting that some patients who are at increased risk of stroke are highly motivated to stop systemic anticoagulation and are willing to accept an increased risk of stroke. It is for these patients that we recommend that some type of continuous monitor-

ing be performed to screen for silent AF at regular intervals as long as they remain off systemic anticoagulation. This complex and controversial topic is discussed in more detail in Section 7.10.

Less information is available concerning the optimal approaches to anticoagulation following surgical ablation of AF. Many variables need to be considered including whether the patient underwent ligation of the left atrial appendage as well as the patient's stroke risk profile. The surgical members of this Task Force recommend that anticoagulation should be continued after surgical ablation of AF for several months due to the relatively high incidence of early atrial tachyarrhythmias, which occur following surgical AF ablation procedures. Anticoagulation is often discontinued on a case by case basis after documentation of the absence of symptomatic or asymptomatic atrial arrhythmias on follow-up ECG monitoring. A postoperative echocardiogram is commonly obtained to rule out atrial stasis or thrombus prior to discontinuation of anticoagulation.

6.7. Anesthesia/sedation during ablation

Patients undergoing catheter ablation of AF are required to lie motionless on the procedure table for several hours. Repeated stimuli from ablation are sometimes painful. For these reasons, most patients are treated with conscious sedation or general anesthesia. The choice of approach is determined by the institutional preference and also by assessment of the patient's suitability for conscious sedation. General anesthesia is generally employed for patients at risk of airway obstruction, those with a history of sleep apnea, and also those at increased risk of pulmonary edema. General anesthesia may also be employed electively in healthy patients in order to improve patient tolerance of the procedure. Anesthesia or analgesia needs to be administered by well-trained and experienced individuals with monitoring of heart rate, non-invasive or arterial line blood pressure, and oxygen saturation.[e414] Guidelines for assessing levels of anesthesia and training requirements for administration of intravenous sedation during procedures have been developed by the American Society of Anesthesiologists and may be found on their website.[e415] Deep sedation has evolved as a third sedation alternative for catheter ablation of AF. This strategy can achieve a painless deep sedation without the need for intubation and general anesthesia. In a prospective study in 650 consecutive patients, the goal of keeping the patient in deep sedation while maintaining spontaneous ventilation and cardiovascular hemodynamic stability was accomplished.[e416] In that study, the sedation was administered by a trained nurse under the supervision of the electrophysiologist. More recently, general anesthesia with jet ventilation has been used at a number of centers that feel that it allows less respiratory motion and higher catheter stability.[e417,e418] Among Task Force Members, approximately 50% routinely employ general anesthesia for all their AF ablation procedures. It is important to recognize that the approach to sedation and anesthesia will differ in different hospital settings and countries.

6.8. Esophageal monitoring

A rare but potentially devastating complication of AF ablation is injury to the esophagus with the possible outcome of atrial esophageal fistula or esophageal perforation leading to mediastinal infection, stroke, and/or death.[e419,e420] Another complication that is thought to be related to thermal injury to the peri-esophageal vagal plexus is gastroparesis.[e421] More information concerning the incidence, presentation, and management of these complications is presented in Section 9.

Because of the severe consequences of an atrial esophageal fistula, it is important to attempt to avoid this complication. At the present time, a number of different approaches are being employed to prevent this complication. These approaches include: (1) modifying energy delivery, (2) visualizing the esophagus and using "abstinence," (3) esophageal thermal monitoring, and (4) active protection of the esophagus. The first of these, modifying energy delivery, is the most common practice. When using open irrigated RF energy in the posterior LA, it is common to decrease power delivery to less than 25 Watts. However, even this lower level of power may damage the esophagus if either the duration of ablation is prolonged or the catheter–tissue contact force is significant, such as when a deflectable sheath is being employed. Another strategy that has been employed is to move the ablation catheter every 10 to 20 seconds on the posterior wall; however, the effect of these strategies on long-term durability of electrical PVI is not fully defined. Some operators employ light conscious sedation and use pain as an assay for potential esophageal injury; however, there are conflicting data on the specificity of this approach. There also are a number of reports of using an alternative energy source such as cryoenergy when close to the esophagus in an effort to minimize injury. While there have not been any reports of an atrial esophageal fistula or peri-esophageal vagal plexus injury with cryoablation, one study reported the presence of esophageal ulceration in a subset of patients.[e422] There are also data that other heat-based energy sources such as ultrasound energy can damage the esophagus.[e282] The second strategy is to visualize the esophagus and use "abstinence" by either designing the ablation lesions to avoid the esophagus, using lower power, and moving more quickly when over the esophagus, or employing cryoenergy when lesions over the esophagus are required. The location of the esophagus can be "visualized" using a variety of approaches, including multidetector computerized tomography,[e423] topographic tagging of the esophageal position with an electroanatomic mapping system,[e424,e425] barium paste,[e426,e427] and ICE.[e428,e429] A third strategy involves use of luminal esophageal temperature monitoring to identify potentially dangerous heating of the esophagus.[e430–e432] Importantly, since the esophagus is broad, the lateral position of the temperature probe or mapping electrode may not align with the ablation electrode, and the operator may have a false impression of safety. Although there is general agreement among those operators

who employ temperature probes that an increase in esophageal temperature should trigger interruption of RF energy delivery, there is no consensus as to what degree of temperature elevation should trigger RF termination. A final strategy is to protect the esophagus with active cooling or displacement.[e433–e435]

Although each of these four approaches is variously adopted by different ablation centers, each remains largely unproven due to the rarity of an atrial esophageal fistula as a complication. Among the Task Force Members, 75% decrease RF power when ablating on the posterior wall of the atrium, two-thirds employ an esophageal temperature probe, one-fourth use ICE to monitor the location of the esophagus, 10% use barium paste, and 10% use 3D image integration and import the esophagus location into the electroanatomic map.

7. Follow-up considerations

7.1. ECG monitoring pre and post procedure

Arrhythmia monitoring is an important component of the initial evaluation of patients who are to undergo catheter ablation procedures for AF. Prior to undergoing a catheter ablation procedure, it is important to confirm that a patient's symptoms result from AF and to determine whether a patient has paroxysmal or persistent AF. This is of importance as the ablation technique, procedure outcome, anticoagulation strategies employed, and the need for TEE prior to the procedure may be impacted by the accurate characterization of the AF type and burden. An assessment of the adequacy of heart rate control is particularly important in patients with depressed left ventricular function who may demonstrate evidence suggesting a reversible tachycardia induced cardiomyopathy.[e436] Pre-procedure arrhythmia monitoring is also useful to determine if a patient has evidence of regular supraventricular tachycardia that degenerates to AF as a triggering mechanism or has a pattern of repetitive "focal firing."[e239] This "focal firing" pattern is characterized by the presence of frequent atrial premature beats (>1,000/24 hours) with frequent rapid salvos of nonsustained AT. Focal atrial fibrillation is characterized by localized triggers arising from the PVs.[e6] Either of these triggering patterns of AF initiation identifies a patient in whom a more limited ablation, targeted at only the triggering arrhythmia focus or PV(s), may be appropriate.[e239,e437]

ECG monitoring also plays an important role in the follow-up after an ablation procedure. Early recurrences of AF are common during the first one to three months following a catheter ablation procedure.[e438,e439] For this reason, arrhythmia monitoring to assess the efficacy of catheter ablation is typically delayed for at least three months following catheter ablation unless it is required to evaluate arrhythmia symptoms during the early post ablation period. Advocates of ECG monitoring during the three-month blanking period argue that documentation of AF recurrence allows them to identify patients at higher risk of needing a second ablation procedure or ongoing antiarrhythmic drug (AAD) therapy as early recurrence has been shown to be a strong predictor of late recurrence.[e440]

The two main reasons to perform arrhythmia monitoring following catheter ablation are clinical care and as part of a clinical research trial. From a purely clinical perspective, arrhythmia monitoring is useful to determine if a patient's complaints of "palpitations" result from recurrent AF. Several studies have demonstrated that complaints of "palpitations" often result from atrial or ventricular premature beats and are not an accurate predictor of recurrent AF.[e441,e442] Arrhythmia monitoring also has been shown to be of value in the asymptomatic patient. Multiple studies have demonstrated that asymptomatic AF commonly occurs in patients following catheter ablation.[e212,e441–e448] Detection of these asymptomatic episodes of AF may impact the characterization of the procedure as "successful." Arrhythmia monitoring is also an essential component of clinical trials aimed at assessing the outcomes of catheter ablation procedures. There is general agreement that arrhythmia monitoring should be incorporated in all clinical trials designed to assess the efficacy of AF catheter ablation tools and techniques. The suggested monitoring strategies and minimum standards to be used as part of clinical trials are discussed in section 9: Clinical Trial Considerations. These strategies and standards may be useful in tracking outcome of clinical care when assessing an institution's performance standards related to success and complications of AF ablation procedures. However, it is recognized that clinical endpoints for defining success may include such important secondary endpoints as elimination of symptomatic AF and control of AF with previously ineffective antiarrhythmic drugs after the AF ablation procedure.

7.2. Available methods for arrhythmia monitoring

Arrhythmia monitoring can be performed with the use of non-continuous or continuous ECG monitoring tools. Choice of either method depends on individual need and consequence of arrhythmia detection. Basically, more intensive monitoring is associated with a greater likelihood of detecting both symptomatic and asymptomatic AF.[e212,e441–e448] Identification of patients with AF and assessment of AF burden with intermittent monitoring has been shown to depend on a patient's actual AF burden and improves with an increasing frequency or duration of intermittent monitoring.[e449] Conversely, the more complex and longer the method of monitoring that is used, the lower the patient compliance.

Available non-continuous detection tools include scheduled or symptom-initiated standard ECGs, Holter (24 hours to 7 days) and transtelephonic recordings, patient and automatically activated devices, and external loop recorders. Scheduled 7-day Holter ECG recordings or daily plus symptom activated event recordings are estimated to document approximately 70% of AF recurrences, with an estimated negative predictive value for absence of AF between 25% and 40%.[e449,e450]

Continuous ECG monitoring is permanent monitoring for a long period (one, two, or more years). Continuous ECG monitoring can be facilitated with the use of implantable devices. Implantable pacemakers or defibrillators with

atrial leads allow the burden of AF to be assessed by tracking the number and duration of mode switch episodes, particularly when arrhythmia duration of ≥5 minutes is used as the cut-off value.[e451,e452] More recently a long-term subcutaneous implantable loop monitor has become available to facilitate continuous AF monitoring based on R-R interval analysis over a time period of two years.[e453,e454] These types of continuous ECG monitoring devices can be used to evaluate the results of AF ablation.[e448] Although implantable subcutaneous monitors hold promise for determination of AF burden long term, important limitations include less than 100% specificity due to myopotentials, and atrial and ventricular premature beats, as well as limited memory resulting in electrograms not being retrievable to verify the correct rhythm diagnosis.

7.3. Follow-up and monitoring guidelines for routine clinical care

There is consensus among the Task Force that all patients who undergo catheter ablation of AF, regardless of whether or not they are enrolled in a clinical trial, should be seen in follow-up at a minimum of three months following the ablation procedure, and then every six months for at least two years (Table 5). It is recommended that scheduled follow-ups are performed in collaboration with the treating AF ablation facility to ensure high experience and timely recognition of potential complications and outcome results.

ECGs should be obtained at all follow-up visits. More intense monitoring should be mainly driven by the clinical impact of AF detection with strict monitoring being necessary (eg, in patients with thromboembolic risk factors for determining the adequate anticoagulation approach). Frequent ECG recording using a manually activated event recorder and counseling patients to take their pulse to monitor for irregularity may serve as initial screening tools for asymptomatic AF episodes. A one to seven day Holter monitor is an effective way to identify frequent asymptomatic recurrences of AF.[e111,e325,e392,e455] A four-week autotrigger event monitor, mobile cardiac outpatient telemetry system, or implantable subcutaneous monitor may identify less frequent AF.[e442,e448,e449] Recommendations for follow-up of patients enrolled in clinical trials are discussed in section 12 of the document and summarized in Table 5.

7.4. Early recurrence of atrial fibrillation

Recurrence of AF is common early following catheter ablation and is observed regardless of the catheter technique and technology used.[e438,e439,e456–e458] Compared with the immediate pre-ablation period, the frequency of recurrent AF during the first days post-ablation is variable; however, it should be noted that about 15% of patients may complain of more frequent episodes than pre-ablation.[e457]

Although early recurrence of AF carries an independent risk of treatment failure,[e438,e439,e456–e458] its occurrence should not prompt immediate re-ablation attempts, as up to 60% of patients experiencing this event within the first months post-ablation will not have any further arrhythmias during long-term follow-up.[e392,e438,e439,e456–e459] In the study using three months of continuous automatic ECG loop recordings, 85% of the patients who did not experience AF within the first two weeks after PVI were complete responders at 12 months.[e460] In contrast, time of recurrence within the first three months after ablation was not significantly associated with procedural success or failure.[e460] Similarly, lack of early AF recurrence during the initial six-week period after ablation was found to be the only independent predictor of six-month freedom from AF (84% without early recurrences versus 38% with early recurrences) in another study.[e461] Similar to early recurrences of AF, early recurrences of AT after AF ablation also were found to be associated with a higher rate of late recurrences compared with patients without early recurrences of AT (41% versus 12%).[e462] Two studies have investigated the outcomes of patients who develop persistent AF or atrial flutter following catheter ablation of AF.[e462,e463] These studies revealed a high rate of recurrence of AF or atrial flutter among these patients. Freedom from AF and atrial flutter was higher when cardioversion was performed within 30 days of a persistent atrial arrhythmia after AF ablation compared with later cardioversion.[e462] Administration of antiarrhythmic drugs in patients at discharge from hospital for the first months after ablation is frequently described.[e457,e462,e464] The short-term use of antiarrhythmic drugs after AF ablation has been shown to decrease early recurrences of atrial arrhythmias but with no effect on prediction or prevention of arrhythmia recurrence at six months.[e461]

Most AF recurrences after PVI are associated with reconnection of the PVs. However, additional mechanisms of post-ablation early transient AF may be active such as non-PV triggers. Among possible causes are: (1) a transient stimulatory effect of RF secondary to the inflammatory response developing after thermal injury and/or pericarditis[e465,e466]; (2) a transient imbalance of the autonomic nervous system ultimately acting as an arrhythmia trigger[e91,e467]; and (3) a delayed effect of RF ablation, as previously observed with other arrhythmic substrates,[e467–e470] likely attributable to growth or maturation of the ablation lesions in the days immediately after the procedure.

7.5. Atrial tachycardias after atrial fibrillation ablation

ATs of new onset make up to 50% of all arrhythmias observed following ablation of AF.[e225,e226,e365,e373–e375,e457,e471–e481] Although right atrial cavotricuspid isthmus (CTI) dependent flutters may also occur, especially in the absence of prior RA flutter ablation, most of these tachycardias originate in the LA. Patients with a regular AT of new onset may complain of worsening symptoms due to a faster mean ventricular rate (frequently 2:1 ventricular response) than during their pre-ablation AF. Rhythm control is usually difficult with antiarrhythmic drugs.

The mechanisms underlying post-ablation regular left ATs of new onset following AF ablation have been dis-

Table 5 Definitions for use when reporting outcomes of AF ablation and in clinical trials of catheter or surgical ablation of AF

Acute Procedural Success	Acute procedural success is defined as electrical isolation of all pulmonary veins. A minimal assessment of electrical isolation of the PVs should consist of an assessment of entrance block. If other methods are used to assess PV isolation, including exit block and/or the use of provocative agents such as adenosine or isoproterenol, they should be pre-specified. Furthermore, it is recommended that the wait time used to screen for early recurrence of PV conduction once initial electrical isolation is documented be specified in all prospective clinical trials.
One Year Success*	One year success is defined as freedom from AF/AFL/AT off antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure.
Clinical/Partial Success*	Clinical/partial success is defined as a 75% or greater reduction in the number of AF episodes, the duration of AF episodes, or the % time a patient is in AF as assessed with a device capable of measuring AF burden in the presence or absence of previously ineffective antiarrhythmic drug therapy.
Long Term Success*	Long term success is defined as freedom from AF/AFL/AT recurrences following the 3-month blanking period through a minimum of 36 months' of follow-up from the date of the ablation procedure in the absence of Class I and III AAD therapy. **When reporting outcomes of AF ablation, the development of atrial tachycardia or atrial flutter should be included in the broad definition of recurrence following AF ablation. All studies should report freedom from AF, atrial tachycardia, and atrial flutter. These endpoints can also be reported separately. All studies should also clearly specify the type and frequency of ECG monitoring as well as the degree of compliance with the prespecified monitoring protocol.*
Recurrent AF	Recurrent AF/AFL/AT is defined as AF/AFL/AT of at least 30 seconds' duration that is documented by an ECG or device recording system and occurs following catheter ablation. Recurrent AF/AFL/AT may occur within or following the post ablation blanking period. Recurrent AF/AFL/AT that occurs within the post ablation blanking period is not considered a failure of AF ablation.
Early Recurrence of AF	Early recurrence of AF is defined as a recurrence of atrial fibrillation within three months of ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence."
Recurrence of AF	Recurrence of AF post ablation is defined as a recurrence of atrial fibrillation more than 3 months following AF ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence."
Late recurrence of AF	Late recurrence of AF is defined as a recurrence of atrial fibrillation 12 months or more after AF ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence."
Blanking Period	A blanking period of three months should be employed after ablation when reporting efficacy outcomes. Thus, early recurrences of AF/AFL/AT within the first 3 months should not be classified as treatment failure. If a blanking period of less than 3 months is acceptable and if is chosen, it should be pre-specified and included in the methods section.
Detectable AF	Detectable AF is defined as AF of at least 30 seconds' duration when assessed with ECG monitoring. If other monitoring systems are used, including implantable pacemakers, implantable defibrillators, and subcutaneous ECG monitoring devices, the definition of detectable AF needs to be pre-specified in the clinical trial based on the sensitivity and specificity of AF detection with the particular device. We recommend that episodes of atrial flutter and atrial tachycardia be included within the broader definition of a detectable AF/AFL/AT episode.
Entrance Block	Entrance block is defined as the absence, or if present, the dissociation, of electrical activity within the PV antrum. Entrance block is most commonly evaluated using a circular multielectrode mapping catheter positioned at the PV antrum. Entrance block also can be assessed using detailed point-by-point mapping of the PV antrum guided by an electroanatomic mapping system. The particular method used to assess entrance block should be specified in all clinical trials. Entrance block of the left PVs should be assessed during distal coronary sinus or left atrial appendage pacing in order to distinguish far-field atrial potentials from PV potentials.
Enrolled Subject	An enrolled subject is defined as a subject who has signed written informed consent to participate in the trial in question.

Table 5 Continued

Exit Block	Exit block is defined as the inability to capture the atrium during pacing at multiple sites within the PV antrum. Local capture of musculature within the pulmonary veins and/or antrum must be documented to be present to make this assessment. Exit block is demonstrated by a dissociated spontaneous pulmonary vein rhythm.
Non-ablative Strategies	The optimal non-ablative therapy for patients with persistent and longstanding persistent AF who are randomized to the control arm of an AF ablation trial is a trial of a new Class 1 or 3 antiarrhythmic agent or a higher dose of a previously failed antiarrhythmic agent.
Non-Inducibility of Atrial Fibrillation	Non-inducibility of atrial fibrillation is defined as the inability to induce atrial fibrillation with a standardized pharmacologic or electrical stimulation protocol. The stimulation protocol should be pre-specified in the specific clinical trial. Common stimulation approaches include a high dose isoproterenol infusion protocol or atrial burst pacing.
Patient Populations for Inclusion in Clinical Trials	It is considered optimal for clinical trials to enroll patients with only one type of AF: paroxysmal, persistent, or longstanding persistent. If more than one type of AF patient is enrolled, the results of the trial should also be reported separately for each of the AF types. It is recognized that "early persistent" AF responds to AF ablation to a similar degree as patients with paroxysmal AF and that the response of patients with "late persistent AF" is more similar to those with longstanding persistent AF.
Cardioversion and Surgical Ablation Related Definitions	
Failed Electrical Cardioversion	Failed electrical cardioversion is defined as the inability to restore sinus rhythm for 30 seconds or longer following electrical cardioversion.
Successful Electrical Cardioversion	Successful electrical cardioversion is defined as the ability to restore sinus rhythm for at least 30 seconds following cardioversion.
Immediate AF Recurrence Post Cardioversion	Immediate AF recurrence post cardioversion is defined as a recurrence of AF within 24 hours following cardioversion. The most common time for an immediate recurrence is within 30–60 minutes post cardioversion.
Early AF Recurrence Post Cardioversion	Early AF recurrence post cardioversion is defined as a recurrence of AF within 30 days of a successful cardioversion.
Late AF Recurrence Post Cardioversion	Late AF recurrence post cardioversion is defined as recurrence of AF more than 30 days following a successful cardioversion.
Hybrid AF Surgical Ablation Procedure	Hybrid AF surgical ablation procedure is defined as a joint AF ablation procedure performed by electrophysiologists and cardiac surgeons either as part of a single "joint" procedure or performed as two pre-planned separate ablation procedures separated by no more than six months of time.
Surgical Maze Ablation Procedure	Surgical Maze ablation procedure is defined as a surgical ablation procedure for AF which includes at a minimum the following components: 1) line from SVC to IVC, 2) line from IVC to the tricuspid valve, 3) isolation of the PVs, 4) isolation of the posterior LA, 5) line from MV to the PVs, 6) management of the LA appendage.
Minimum AF Documentation, Endpoints, and Success Rates in Clinical Trials	
Minimum Documentation for Paroxysmal AF	The minimum AF documentation requirement for paroxysmal AF is: (1) physician's note indicating recurrent self-terminating AF; and (2) one electrocardiographically documented AF within 6 months of the ablation procedure.
Minimum Documentation for Persistent AF	The minimum AF documentation requirement for persistent AF is: (1) physician's note indicating continuous AF $\geq$7 days but no more than 1 year; and (2) two electrocardiograms (from any forms of rhythm monitoring) showing continuous AF, with electrocardiograms taken at least 7 days apart.
Minimum Documentation for Longstanding Persistent AF	The minimum AF documentation requirement for longstanding persistent AF is: physician's note indicating at least 1 year of continuous AF plus a 24-hour Holter within 90 days of the ablation procedure showing continuous AF. The performance of a successful cardioversion (sinus rhythm $>$30 seconds) within 12 months of an ablation procedure with documented early recurrence of AF within 30 days should not alter the classification of AF as longstanding persistent.

Table 5 Continued

Minimum Effectiveness Endpoint for Patients with Symptomatic and Asymptomatic AF	The minimum effectiveness endpoint is freedom from symptomatic and asymptomatic episodes of AF/AFL/AT recurrences at 12 months following ablation, off antiarrhythmic drug therapy including a prespecified blanking period.
Minimum Chronic Acceptable Success Rate: Paroxysmal AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for paroxysmal AF at 12-month follow-up is 50%.
Minimum Chronic Acceptable Success Rate: Persistent AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for persistent AF at 12-month follow-up is 40%.
Minimum Chronic Acceptable Success Rate: Longstanding Persistent AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for longstanding persistent AF at 12-month follow-up is 30%.
Minimum Follow-up Screening for Paroxysmal AF Recurrence	For paroxysmal AF, the minimum follow-up screening should include: (1) 12-lead ECG at each follow-up visit; (2) 24-hour Holter at the end of the follow-up period (eg, 12 months); and (3) event recording regularly and at the time of symptoms with an event monitor from the end of the 3-month blanking period to the end of follow-up (eg. 12 months).
Minimum Follow-up Screening for Persistent or Longstanding AF Recurrence	For persistent and longstanding persistent AF, the minimum follow-up screening should include: (1) 12-lead ECG at each follow-up visit; (2) 24-hour Holter every 6 months; and (3) symptom-driven event monitoring.

cussed earlier in this document. Detailed activation and entrainment mapping of the tachycardia during a second procedure result in effective ablation of AT in approximately 90% of patients.[e123,e365,e377,e472,e482,e483]

7.6. Antiarrhythmic and other drug therapy post ablation

Suppressive antiarrhythmic drugs are commonly employed during the first one to three months after ablation.[e457,e484] The mechanism of AF in this setting may be different from that of the patient's clinical arrhythmia and may resolve completely upon resolution of the transient factors promoting early AF recurrences. Accordingly, some operators choose to treat all patients with suppressive antiarrhythmic agents for the first one to three months following ablation.[e457,e462,e464] The impact of empirical antiarrhythmic drug therapy for six weeks after AF ablation on the occurrence of AF was investigated in a randomized study.[e461,e485] The drugs employed for this purpose vary, but most commonly are the drugs that have been used unsuccessfully prior to ablation and include flecainide, propafenone, sotalol, dofetilide, dronedarone, or amiodarone. The short-term use of antiarrhythmic drugs after AF ablation decreased early recurrences of atrial arrhythmias but had no effect on prediction or prevention of arrhythmia recurrence at 6 months.[e461]

Since an inflammatory process after AF ablation may be one specific cause leading to early recurrences, the efficacy of corticosteroids for preventing early post ablation atrial arrhythmias was investigated in a randomized study.[e132] In the corticosteroid group, intravenous hydrocortisone was given on the day of the procedure, and oral prednisolone was administered for three days after ablation. In that study, the prevalence of immediate AF recurrences ($\leq$3 days after PVI) was significantly lower in the corticosteroid group compared to the placebo group (7% versus 31%).[e132] Less than 10% of Task Force members routinely administer steroids during or following AF ablation. Approximately two-thirds of Task Force members routinely prescribe either proton pump inhibitors or H_2 blockers for one to four weeks following ablation. It is important to note, however, that this practice is based on the observation that esophageal ulcerations may be observed on endoscopy following AF ablation (see Section 9.4). There are no data available to demonstrate that this approach reduces the incidence of development of an atrial esophageal fistula.

Attention to control of HTN and addressing other AF risk factors such as sleep apnea and obesity remains an integral part of AF management after the ablation procedu-

re.[e6] The impact of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on long-term outcome of AF ablation was investigated in a prospective registry of consecutive patients undergoing catheter ablation of paroxysmal or persistent AF.[e486] In that study, however, modulation of the renin-angiotensin-aldosterone system did not appear to affect maintenance of sinus rhythm after catheter ablation of AF.[e486] Thus, the hypothesis that so-called medical upstream therapy may positively influence the reverse atrial remodeling after catheter ablation of AF remains unproven. Of note, the role of statins post AF ablation has not been established.

7.7. Repeat atrial fibrillation ablation procedures

Recurrences of AF (or AT) after index AF ablation procedures leads to repeat ablation in 20% to 40% of patients.[e251] Since early recurrences of AF and/or the development of AT are common during the first two to three months after AF ablation and may resolve spontaneously, there is a consensus that repeat ablation procedures should be deferred for at least three months following the initial procedure (Table 5). It is also recognized, however, that some patients will develop highly symptomatic atrial arrhythmias that cannot be controlled with antiarrhythmic therapy or slowed with rate controlling medications and are best managed with a reablation procedure within the first three months post AF ablation.

Most studies have reported that patients who fail an initial attempt at ablation and undergo a repeat ablation procedure demonstrate resumption of conduction to (and from) the previously isolated PVs rather than new arrhythmogenic foci from non-targeted PVs or outside of the PVs.[e125,e211,e487–e489] Because of this, the first step when performing a second AF ablation procedure is to check each PV for reconduction of electrical activity. If reconduction is found to be extensive, which is often the case, the primary goal should be reisolation of the PVs. If, on the other hand, there is little evidence of PV reconduction, greater attention should be paid to searching for non-PV foci as well as greater use of substrate modification techniques. High dose isoproterenol infusions have been shown to be helpful in the provocation of PV and non-PV triggers.[e211,e487,e488]

7.8. Autonomic alterations

Mild changes in autonomic modulation of the sinus node have been described following ostial PVI as well as circumferential PV ablation.[e91,e92,e467,e487,e490,491] These changes, including a slightly higher resting sinus rate, a decrease in heart rate variability, and decreases in deceleration capacity and acceleration capacity, often resolve within a month following ostial PVI, but may be present at one year following circumferential PVI.

The mild changes in autonomic regulation generally have not been associated with inappropriate sinus tachycardia or other symptoms.

7.9. Very late recurrence (more than one year) after atrial fibrillation ablation

Recently, a number of groups have reported the incidence of late AF recurrence occurring between one and five years of follow-up.[e72,e73,e126,e492–e497] After a single procedure, this late incidence has been reported between 11% and 29%. After repeat procedures, late recurrence has occurred in between 7% and 24%. Variations in reported incidence of late recurrence may be related to the extent of ECG monitoring, and earlier recurrence may be missed in selected patients with no or minimal symptoms. The most consistent predictor of late recurrence is persistent AF.[e73,e126,e497] Other predictors have included age, left atrial size, diabetes, valvular heart disease, and non-ischemic dilated cardiomyopathy.[e73,e497] In patients undergoing repeat ablation procedures for late recurrence, the vast majority have demonstrated PV reconnection.[e72,e73,e497] However, non-PV foci and gaps in prior ablation lines may also play a role. These latter mechanisms may be responsible for a higher percentage of recurrences beyond the second procedure.[e73]

7.10. Anticoagulation considerations two or more months post ablation

Whether or not to continue oral anticoagulation two or more months post AF is an important, and as yet unanswered, question. It is the consensus of this Task Force Writing Group that systemic anticoagulation should be continued indefinitely in patients with a high risk for stroke as estimated by currently recommended schemes ($CHADS_2$ or CHA_2DS_2VASc),[e3] and especially in those who are 75 years of age or older or have had a prior stroke or TIA (Table 4). This recommendation is based on the following observations: (1) recurrences of AF are common both early and late following AF ablation, (2) asymptomatic AF is common following AF ablation, (3) AF ablation destroys a portion of the atria and the impact of this on stroke risk is uncertain, (4) there have been no large randomized prospective trials that have assessed the safety of stopping anticoagulation in this patient population, and (5) the use of direct thrombin inhibitors or Factor Xa inhibitors such as dabigatran, rivaroxaban, and apixaban is more convenient than warfarin.[e389,e392,e393,e395,e396,e498] Also relevant to this issue is a recent sub-analysis of data from the subgroup of 40 patients (1.6%) in the TRENDS study who experienced a stroke or systemic emboli.[e499] Among these 40 patients, all of whom had a dual chamber pacemaker to allow for AF detection, 29 (73%) had a zero AF burden within 30 days prior to the stroke or embolic event. These data have important implications for the post AF ablation population as they remind us that the mechanisms of stroke are not limited to cardioembolism due to AF. The subset of Task Force Members who support the discontinuation of systemic anticoagulation make the argument that: (1) continuing anticoagulation exposes patients to the risks for hemorrhage and the unfavorable effects of anticoagulation on long-term quality of life,[e500] and (2) there are several published studies that have reported a low risk of stroke in patients who

discontinue systemic anticoagulation several months or more following AF ablation.[e114–e117] These studies are presented in more detail below. It is important to recognize that the above discussion has focused on patients at high risk of stroke (ie, $CHADS_2$ score ≥ 2). There is far greater flexibility as to how anticoagulation is managed in patients at a low or moderate risk of stroke as current guidelines do not mandate systemic anticoagulation. A final comment worth mentioning is that patient preference plays a large role in this decision. It is our belief that patients should be made aware of the available data and Consensus Recommendation and then should be encouraged to consider the risks and benefits of continuing versus stopping systemic anticoagulation. Some patients who are at increased risk of stroke are highly motivated to stop systemic anticoagulation and are willing to accept an increased risk of stroke. For these patients we recommend that some type of continuous monitoring be performed to screen for silent AF at regular intervals as long as they remain off systemic anticoagulation. In the remainder of this section, we will briefly review the available data.

There are no randomized studies addressing this issue, but five observational reports have been published.[e114–e117,e501] The first study to examine this question analyzed late thromboembolic events in 755 patients who were followed for 25 ± 8 months post AF ablation. Late thromboembolic events were noted in two of 755 patients (0.3%), and interestingly, both of these patients were anticoagulated. This report included 180 patients who had greater than or equal to one risk factor for stroke, remained in sinus rhythm, and in whom anticoagulant therapy was stopped a median of 5 months post ablation. Although no thromboembolic events occurred in this subset of patients, their precise duration of follow-up after discontinuation of anticoagulation is not included in the report. Another single-center report described outcomes in 635 patients with one or more risk factors for stroke during a mean follow-up of 836 ± 605 days after an AF procedure.[e115] Anticoagulation was discontinued in 434 of 517 patients who remained in sinus rhythm, and aspirin and/or clopidogrel was prescribed. There were three ischemic strokes and two TIAs in the anticoagulation discontinuation group. The estimated five-year stroke rate in this group was 3%. A recent observational study from five large AF ablation centers included data from 3,344 patients who underwent AF ablation.[e117] Oral anticoagulant therapy was typically discontinued regardless of the $CHADS_2$ score if patients did not manifest one of the following: (1) any recurrence of atrial tachyarrhythmias, (2) severe PV stenosis, or (3) severe left atrial mechanical dysfunction. After discontinuation of anticoagulation, patients were treated with aspirin. If AF recurred, anticoagulation was restarted in those with a $CHADS_2$ score of one or more. There were 347 who had a $CHADS_2$ score of greater than two. Among these 347 patients, no thromboembolic events occurred. Another recent report examined the anticoagulation status and thromboembolic risk of 508 patients $\geq$65 years of age with 508 younger patients following AF ablation.[e114] A periprocedure CVA occurred in 0.8% and 1% of patients $\geq$65 and $<$65 years of age, respectively. Among patients $>$65 years of age, anticoagulation was stopped in 56% of those with a $CHADS_2$ score ≥ 1. Among the entire study population 180 patients had a $CHADS_2$ score of two or greater. The precise proportion of this patient population in whom anticoagulation was stopped, as well as the number of CVAs in this group, is not provided in the manuscript. During a mean follow-up of 3 ± 2 years, a late CVA occurred in 3% of patients $\geq$65 years of age and 1% of patients $<$65 years of age. Among patients $>$65 years of age, age $>$75 years was the only independent risk factor for CVA (O.R. 4.9) regardless of rhythm, anticoagulation status, or the $CHADS_2$ score. The authors conclude that these data suggest that the risk of CVAs in older patients results from mechanisms other than recurrent AF or anticoagulation status. The most recent report examined predictors of thromboembolic events in 565 patients following AF ablation.[e501] The only independent predictors of thromboembolic events were recurrence of AF despite multiple ablations and the $CHADS_2$ or CHA_2DS_2-VASc score. The event rate rose with increasing $CHADS_2$ and CHA_2DS_2-VASc scores. The overall ability of the two scores to differentiate between patients who did and did not have an adverse event was not significantly different. However, the CHA_2DS_2-VASc score was able to further subdivide patients categorized as low risk by the $CHADS_2$ score.[e501]

8. Outcomes and efficacy of catheter ablation of atrial fibrillation

8.1. Overview

The efficacy of any type of ablation procedure can be determined from a variety of sources including: (1) single-center randomized or nonrandomized clinical trials, (2) multicenter randomized or nonrandomized clinical trials, (3) meta-analyses of single and multicenter clinical trials, and (4) physician surveys. Among these sources of outcome data, it is recognized that data derived from large prospective randomized clinical trials are the most reliable assessment of outcomes: the outcomes that can be anticipated when a procedure is performed in clinical practice. There have been at least eight prospective randomized clinical trials that have investigated the outcomes of AF ablation.[e111–e113,e246,e279,e502–e505] In most of these trials, AF ablation was randomized against pharmacologic therapy. In addition, there have been a large number of non-randomized single-center and multicenter clinical trials, a number of meta-analyses of the data derived in these trials, and two international surveys of the outcomes of AF ablation. In this section of the document, we will provide an up-to-date review and summary of this body of data. Particular attention will be focused on identifying those areas in the field of AF ablation where the safety and efficacy of the procedure has been well established as well as identifying those areas

where there is less information and a need for further investigation.

Rather than provide individual citations for each of the extremely large numbers of non-randomized studies that have been performed, we have elected to cite several meta-analyses that summarize these data and provide comprehensive reference lists. We will also summarize in greater detail the results of the eight randomized clinical trials that have been performed. And finally, we will review the results of the two International Physician Surveys that have been published.[e386,e506]

When considering the published literature on catheter ablation of AF, it is important to recognize that until the writing of the initial Consensus Report in 2007, there had been no standardization in the design of clinical trials of AF ablation.[e1] There are many important aspects of an AF ablation trial that can impact the results. Among the most important is the patient population. It is now well recognized that the outcomes of AF ablation differ considerably depending on whether patients have paroxysmal, persistent, or longstanding persistent AF. Similarly, variables such as age, concomitant cardiac disease, obesity, the presence of sleep apnea, and LA size impact outcome. Other important considerations are the duration of the blanking period, the frequency and intensity of arrhythmia monitoring, whether patients with atrial flutter or AT during follow-up are classified as successes or failures, the use of antiarrhythmic drugs, and the frequency and timing of repeat ablation procedures. Whereas some studies have defined success as freedom from symptomatic AF during follow-up, other studies have defined success as freedom from symptomatic and asymptomatic episodes of AF. A third definition of success employed by other studies is "AF control" defined as a greater than 90% reduction of AF burden. And a fourth definition of success is the proportion of patients free of AF in a given period of time or on an ECG or Holter monitor administered a certain period of time following the ablation procedure. Each of these definitions can be further modified based on whether patients who remain on antiarrhythmic drugs at follow-up are classified as having had a successful ablation procedure, a partially successful ablation procedure, or a failed ablation procedure. As noted previously in this document, the likelihood of detection of AF is directly dependent on the duration and intensity of arrhythmia monitoring during follow-up. One of the goals of the first Consensus Document was to address some of these issues by recommending a standard definition of success and minimal follow-up duration.[e1] A number of other recommendations were made in an attempt to standardize this field. As a whole these recommendations have largely taken hold, and an increasing number of studies of AF ablation have defined success according to these recommendations for reporting outcomes. In this revised document we have moved further in providing recommendations for following and monitoring in clinical trials (Table 5).

8.2. Published literature review: randomized clinical trials

As of the time of preparation of this document there have been at least eight prospective randomized clinical trials that compared and examined the outcomes of AF ablation with antiarrhythmic drug therapy or with rate control agents alone.[e111–e113,e246,e279,e502–e505] The efficacy of AF ablation in these trials was 86%, 87%, 74%, 76%, 66%, 89%, 79%, and 66%, respectively. Most of these trials reported 12-month follow-up. In each trial, catheter ablation was more effective than antiarrhythmic drug therapy or rate control agents, with a reported efficacy of 22%, 37%, 58%, 17%, 9%, 23%, 40%, and 16%, respectively. Among these eight studies, two have been performed under the auspices of the FDA as part of an IDE approval process.[e279,e505] The first randomized 167 patients with paroxysmal AF to ablation or pharmacologic therapy with an antiarrhythmic or rate control medication.[e505] At 12 months of follow-up, catheter ablation resulted in 66% efficacy as compared with 16% efficacy for antiarrhythmic drug therapy.[e505] This study also revealed that catheter ablation reduced symptoms and improved quality of life.[e507] The second study was a prospective randomized trial of cryoballoon ablation. Although not published in final form, the results of this study revealed findings consistent with catheter ablation of AF being superior to antiarrhythmic drug therapy.[e279] In considering the results of these clinical trials, it is important to recognize that the trials enrolled predominantly middle-aged white men with paroxysmal AF and few co-morbidities. Furthermore, these trials predominantly enrolled patients who had previously failed at least one antiarrhythmic medication.

8.3. Published literature review: nonrandomized clinical trials

During the past several years a large number of meta-analyses have been performed in the hope of better defining the efficacy of AF ablation. One of the most recent meta-analyses examined the results of the randomized clinical trials cited above.[e508] Overall, the success rate was 77.8% in the ablation arm as compared with 23.3% in the control group. Catheter ablation decreased the recurrence of AF by 71% (relative risk 0.29). Several other similar meta-analyses of randomized clinical trials confirmed these findings.[e503,e509–e511]

Other meta-analyses have examined the results of both randomized and non-randomized clinical trials. One of these meta-analyses examined the safety and efficacy of catheter ablation of AF and antiarrhythmic drug therapy.[e512] The results of 63 RF ablation studies were included in these analyses. The single procedure success rate of ablation off antiarrhythmic therapy was 57% (95% CI 50%–64%), the multiple procedure success rate off AAD was 71% (95% CI 65%–77%), and the multiple procedure success rate on antiarrhythmic, or with unknown antiarrhythmic, drug us-

age was 77% (95% CI 73%–81%). In comparison, the success rate for antiarrhythmic therapy was 52% (95% CI 47%–57%).

Three recent meta-analyses have been performed that have examined the outcomes of catheter ablation of persistent and longstanding persistent AF. One of these focused on the outcomes of catheter ablation of longstanding persistent AF.[e471] This analysis concluded that, with the exception of PVI alone (21% success) and CFAE ablation alone (37% success), all contemporary substrate ablation techniques (including antral isolation alone, atrial isolation with lines, and antral isolation with CFAEs) for persistent/longstanding persistent AF provide comparable clinical results (mean success 47%). Three other meta-analyses examined the value of ablation of CFAEs.[e513–e515] These analyses revealed that ablation of complex fractionated EGMs increased the single procedure success of ablation of nonparoxysmal AF but increased the fluoroscopy duration and also the duration of RF energy application. No incremental benefit was seen for CFAE ablation in patients with paroxysmal AF over and above PVI alone.

8.4. Published literature review: survey results

A worldwide survey on the methods, efficacy, and safety of catheter ablation of AF was published in 2005.[e386] This survey was based on a detailed questionnaire that was completed by more than 180 centers located throughout the world. At the time the study was completed in 2002, the median number of AF ablation procedures that had been performed at these centers was 38. The outcomes of nearly 9,000 AF ablation procedures were reported by these centers. More than one ablation procedure was performed in 27% of patients. The success rate, defined as freedom from symptomatic AF in the absence of antiarrhythmic therapy, was 52%. An additional 24% of patients were free of symptomatic AF in the presence of a previously ineffective antiarrhythmic drug. The incidence of major complications was 6%.

In a more recent worldwide survey monitoring the outcome and safety features of AF ablation performed between the years 2003 to 2006,[e506] 85 participating centers proved to perform more efficiently than in the previous years. During a follow-up of 10 $\pm$ 8 months, 192 procedures per center were reported with a 70% efficacy rate free of antiarrhythmic drugs, and an additional 10% efficacy rate in the presence of previously ineffective antiarrhythmic drugs. A second procedure was required in every third patient in order to obtain these figures. Ablation of paroxysmal AF was associated with a 35% and 66% larger probability of success as compared to ablation of persistent and longstanding persistent AF, respectively. These results were obtained with about 50% of all procedures performed using a Carto-guided technique and about 25% using a Lasso-guided mapping/ablation technique. Despite a larger prevalence of centers reporting catheter ablation of persistent and longstanding persistent AF, the overall complication rate was 4.5%. There were 25 procedure-related deaths (0.15%), 37 strokes (0.23%), 115 transient ischemic attacks (0.71%), and 213 episodes of tamponade (1.31%).

8.5. Outcomes of AF ablation in patient populations not well represented in clinical trials

It is notable that most AF ablation procedures have been performed in white male patients less than 70 years of age.[e516] It therefore remains uncertain what the safety and efficacy of AF ablation are for other populations of patients, especially patients with persistent and longstanding persistent AF, elderly patients, and patients with heart failure. In this section of the document, we will review some of these data.

8.5.1. Outcomes of catheter ablation of persistent and longstanding persistent AF

The quality and quantity of data concerning the outcomes of AF ablation in patients with non-paroxysmal AF, including both persistent and longstanding persistent AF (>12 months of continuous AF), is considerably less than for patients with paroxysmal AF, as described above. In fact, there have been no prospective multicenter randomized clinical trials of ablation versus antiarrhythmic drug therapy that have precisely defined the outcomes of AF ablation in this patient population. The notable absence of a consistent body of evidence reflects the heterogeneity of the patient population and ablation strategies that are encompassed under the umbrella "nonparoxysmal AF." It is now increasingly well recognized that the duration of continuous AF is an important predictor of the efficacy of AF ablation. Patients with continuous AF of 12 months or less duration are very different from patients who have been in continuous AF for years. Whereas a consensus has been reached on the approach to ablation of patients with paroxysmal AF, no consensus exists for patients with nonparoxysmal AF.[e1,e3,e4,e82,e115,e231,e245,e517] This currently is an area of debate at most AF meeting and conferences. Whereas many electrophysiologists (EPs) prefer to perform circumferential PV isolation as the initial procedure in all AF patients,[e517] there are other EPs who feel strongly about creating linear ablation lesions and also targeted ablation of areas of the atrium demonstrating a high degree of CFAEs. And, a final group of EPs advocate for a stepwise approach to AF ablation whereby the procedure is continued until AF terminates.[e231] A meta-analysis of studies mentioned above that have reported the outcomes of catheter ablation of persistent and longstanding persistent AF concluded that the single procedure success rates of each of these strategies is similar, provided that circumferential PV ablation is performed with an endpoint of electrical isolation of the PVs.[e471] Several other meta-analyses cited above revealed that the ablation of CFAEs resulted in increased single procedure efficacy for ablation on nonparoxysmal AF. It is clear that this is an area where more research is needed to better define the optimal ablation approach and also the anticipated success rate in particular patient populations. In this regard it is important to recognize that AF recurrence

rates depend on concomitant cardiovascular diseases as well as on type of AF, and therefore should be balanced against the patient profile for a particular trial.

8.5.2. Outcomes of AF ablation in elderly patients

One recent study compared the safety and efficacy of the catheter ablation in three groups of patients: patients under the age of 65, between the ages of 65 and 74, and over the age of 75 over a 27-month follow-up period.[e127] No differences in the complication rate were observed between the three groups. However, patients over the age of 75 were more likely to demonstrate a partial response to ablation and require AAD therapy. Another large case series reported a 73% success rate and a 1% complication rate among 174 patients over 75 years of age who underwent AF ablation.[e518] Although the results of these studies are encouraging, it is clear that more research is needed. The CABANA trial is expected to be very valuable in this regard.

8.5.3. Outcomes of AF ablation in patients with congestive heart failure and the impact of ablation on left ventricular function

A number of clinical trials have examined the role of catheter ablation of AF in patients with heart failure. The initial study to address this important topic was published in 2004.[e519] This study examined the role of catheter ablation in 58 patients with heart failure with an EF less than 45% and 58 controls. During a mean follow-up of 12 ± 7 months, 78% of patients with heart failure and 84% of controls remained in sinus rhythm. Of particular note is that the EF improved by 21 ± 13%. Improvements also were seen in exercise capacity and quality of life. Another study is the Pulmonary Vein Antrum Isolation versus AV Node Ablation with Bi-Ventricular Pacing for Treatment of AF in Patients with Congestive Heart Failure (PABA-CHF) study that compared the efficacy of AF ablation with AV node ablation and pacemaker implantation.[e520] The primary endpoint of this prospective, multi-center clinical trial was a composite of EF, distance on a 6-minute walk, and Minnesota Living with Heart Failure (MLWHF) questionnaire score after a six-month follow-up. This study demonstrated an overall superiority of PVI to atrioventricular (AV) node ablation given by a lower score on the PABA-CHF questionnaire (60 vs 82), longer walking distance (340 m vs 297 m), and higher EF (35% vs 28%). A third case-controlled series reported that the efficacy of AF ablation was similar in patients with and without LV systolic dysfunction and also reported an improvement in EF at 6-month follow-up.[e521] And a recent meta-analysis reported that the single procedure efficacy of AF ablation was lower in patients with systolic dysfunction, but with repeat procedures, a similar success rate could be achieved among patients with and without systolic dysfunction.[e522] Taken as a whole, the results of these studies suggest that catheter ablation of AF is reasonable in highly selected patients with heart failure. However more research with larger multicenter clinical trials is clearly needed.

8.6. Outcomes of cryoballoon ablation

Over the past five years a large numbers of studies have been published describing the technique and outcomes of catheter ablation of AF using the cryoballoon ablation system. These data include a large number of single-center experiences, several small multicenter experiences, one meta-analysis, and one prospective randomized clinical trial of cryoballoon ablation versus antiarrhythmic drug therapy. As with RF ablation, we have elected not to review each of these trials individually but to summarize the results of the meta-analysis and review in more detail the results of the prospective randomized clinical trial. Several other highly relevant articles will also be reviewed briefly.

A recently published meta-analysis has analyzed the data from 23 studies that have reported the outcomes of cryoballoon ablation.[e278] Among these studies, 20 reported the outcomes of patients with paroxysmal AF, one reported the outcomes of persistent AF, and two reported outcomes for ablation of both persistent and paroxysmal AF. Overall, 1,221 patients had cryoballoon ablation for paroxysmal AF and 87 for persistent AF. The average patient age was 57.5 ± 1.9 years, and 73.6% were men. The average LA dimension was 44.4 ± 4.8 mm. The average procedure time was 206 ± 72 minutes with an average fluoroscopy time of 46 ± 13 minutes. A 28-mm cryoballoon catheter was used in 80% of patients. Centers with extensive experience reported a progressive decrease in procedure time, fluoroscopy time, cryo applications, and need for focal ablation touch up. Acute procedural success was achieved in 92% of patients. One study reported that 2.8% of veins had reconduction within a 60-minute post ablation observation period. Five studies reported 12-month outcomes with 73% of patients free of recurrent AF. Three studies compared the efficacy of cryoballoon ablation and RF ablation in a nonrandomized fashion and reported no difference in efficacy.[e523–e525] The only prospective randomized clinical trial of cryoballoon ablation is the STOP-AF trial that enrolled 245 patients, with 163 randomized to cryoballoon treatment and 82 patients randomized to pharmacologic therapy.[e279] There was a 69.9% success rate in the elimination of AF in these cryo treated patients, which was significantly better than 7.3% seen in the drug-treated group. Nineteen percent of patients required a repeat procedure, and 12% of patients remained on a membrane-active antiarrhythmic drug therapy.

The meta-analysis also reported data from 22 studies that reported adverse events among 1,308 patients undergoing cryoballoon ablation. The most common complication was phrenic nerve paralysis with an incidence of 4.7%. Most patients recovered with 0.37% experiencing phrenic nerve paralysis 12 months post ablation. The incidence of other complications were less frequent, including an incidence of vascular complications, cardiac tamponade/effusion, thromboembolic complications, significant PV stenosis, and atrial esophageal fistula of 1.8%, 1.5%, 0.6%, 0.2%, and 0%, respectively. Although no cases of atrial esophageal fistula

were reported, three small studies have examined the esophagus following cryoballoon ablation with one reporting a 17% incidence of ulceration and two other studies reporting no esophageal ulceration.

8.7. Long-term efficacy of catheter ablation of atrial fibrillation

During the past five years, a large number of studies have been published that have examined the important issue of the long-term efficacy of AF ablation. Prior to this time, most clinical studies presented data from short-term follow-up, often less than 12 months in duration. The first of these studies was published five years ago and described the long-term outcomes of a series of 264 patients who were AF free and off antiarrhythmic drug therapy at the 12-month point following an initial ablation procedure.[e496] During a mean follow-up of 28 ± 12 months, AF recurred in 23 patients (8.7%). The actuarial recurrence rate of AF at five years was 25.5%. AF recurrence was more likely in patients with HTN and hyperlipidemia with a recurrence rate of 75% if both of these risk factors were present. Similar findings have been reported in each of the subsequent trials.[e72,e73,e119,e124,e126,e495] One recent study reported that 29% of patients who underwent AF ablation at their center were AF free at 5 years following a single ablation procedure.[e73] It is now recognized that when a patient is brought back to the EP lab with recurrent AF, recurrence of PV conduction in one or more veins is almost universally observed. This finding highlights the difficulty with which permanent PVI can be achieved with current ablation technologies. In considering the results of the large number of studies that have reported long term outcomes of AF ablation, it is important to recognize that in these studies follow-up was often incomplete and that standardized monitoring protocols and end-points were generally not employed.

8.8. Summary of the efficacy of catheter ablation of atrial fibrillation

The results of the studies and surveys reviewed above provide substantial evidence of the efficacy of catheter ablation for treatment of patients with AF. However, it is also important to recognize that most studies have enrolled patients with predominantly paroxysmal AF who are otherwise free of significant comorbidities. Although data are emerging to demonstrate the safety and effectiveness of AF ablation in other patient populations, especially the very elderly, those with longstanding persistent AF, and patients with reduced systolic function and heart failure, these remain areas in need of further investigation. We are hopeful that the recommendations made for clinical study design in this document will be utilized by future investigators designing clinical trials to further define the efficacy and safety of catheter ablation of AF in a variety of patient populations.

8.9. Impact of catheter ablation of atrial fibrillation on quality of life

As symptomatic improvement is a primary objective in the treatment of patients with AF, formal assessment of quality of life has played an increasingly important role in the evaluation of ablation outcomes.[e500,e526,e527] These measures may provide a more global reflection of symptom change, symptomatic arrhythmia burden, and the difference between actual and desired health and function than more focused endpoints of rhythm status at specific points in time. Generic tools such as the SF-36 health survey,[e528] applicable to a broad range of disease states and health conditions, and the Symptom Checklist,[e529] developed to assess symptom burden in patients with arrhythmias, have been most widely employed. Patients with AF, as reflected by standardized SF-36 scores, have substantially impaired QOL, below population norms, and comparable to patients with coronary artery disease and congestive heart failure.[e526,e527,e530] A number of single-center nonrandomized observational studies of AF ablation outcomes have demonstrated significant and sustained improvements in QOL reflected by SF-36 and Symptom Checklist scores following catheter ablation.[e500,e527] Taken alone, these findings need to be interpreted cautiously, as in the absence of a comparison group or treatment blinding, placebo effects cannot be entirely excluded. However, two recent studies demonstrated that over a 12-month period following treatment, changes in QOL scores were strongly related to the presence or absence of documented AF recurrence within the previous 30 days.[e507,e531] Of much greater importance, however, are the results of three randomized clinical trials that compared catheter ablation to antiarrhythmic drug therapy in patients with paroxysmal AF, and also evaluated QOL as an outcome measure.[e112,e113,e505] All three studies, comprising a total of 241 patients, demonstrated superiority of catheter ablation over antiarrhythmic drug treatment by rhythm control endpoints. In each study, catheter ablation was also associated with significant improvement in SF-36 scores relative to baseline, with restoration to levels at or above population norms. QOL scores were significantly higher than in patients treated with drug therapy, in which there was little change from baseline scores. Similar significant trends were observed for Symptom Checklist scores. In the two trials with multiple QOL assessments over the first year post randomization, differences in QOL scores between treatment groups was observed early (at three months) and remained consistent and sustained over the remainder of trial follow-up.[e113,e507] One randomized study examined QOL in 146 patients with persistent AF, randomized to catheter ablation or cardioversion alone.[e246] This study demonstrated that catheter ablation was more effective in maintaining sinus rhythm. Patients who were in sinus rhythm demonstrated a greater improvement in the symptom severity score than those patients with recurrent AF or flutter.

Concerns have been raised that generic QOL instruments are not sufficiently sensitive or focused to detect changes in disease specific symptoms, such as those associated with AF.[e500,e532] AF-specific QOL measures, including the AF Effect on Quality of Life (AFEQT) questionnaire[e533] and the Mayo AF Symptom Inventories,[e500] have been developed and are in the process of validation. A recent study reported that disease specific assessment of QOL is superior to generic questionnaires.[e534] Preliminary findings indicate that these tools also demonstrate substantial improvements in QOL with ablation, and may more accurately reflect ablation efficacy. Their use of QOL measures will be discussed further in section 12.

8.10. Impact of catheter ablation of atrial fibrillation on LA size and function

Extensive experimental and clinical research has demonstrated that AF results in electrical and structural remodeling of the atrium.[e25,e86,e535,e536] The results of these studies suggest that AF can be viewed in part as a rate-related atrial cardiomyopathy. To the extent that other types of rate-related cardiomyopathies lead to reversible chamber dilatation and dysfunction, it was anticipated that reverse remodeling also could occur in a subset of patients who underwent AF catheter ablation.

Several studies have examined LA size before and after catheter ablation.[e209,e537–e539] These studies have demonstrated a 10%–20% decrease in the dimensions of the LA after catheter ablation of AF regardless of whether echocardiography, MR imaging, or CT was used for LA imaging. Although the precise mechanism of this decrease in size is not known, it appears consistent with reverse remodeling. Another possible reason for a decrease in atrial size is scar formation from the ablation procedure. This explanation is unlikely because atrial size appears to decrease only when sinus rhythm has been successfully restored.[e538]

The impact of catheter ablation of AF on LA transport function was investigated in two studies with conflicting results.[e540,e541] However, because AF eliminates essentially all contractility of the LA, there is general agreement that restoration of sinus rhythm in patients with persistent AF improves atrial function. The issue of whether catheter ablation in patients with paroxysmal AF who are predominantly in sinus rhythm improves or impairs LA contractility is unsettled and requires further study. However, a recent study has reported a series of patients who developed LA diastolic dysfunction and pulmonary hypertension following AF ablation.[e542] This precise cause of the "stiff left atrial syndrome" and methods to prevent it will clearly be an area for further study going forward.

8.11. Predictors of success following AF ablation

A large number of studies have been performed that have examined clinical predictors of the efficacy of AF ablation.[e98,e346,e440,e543–e545] Factors that have been identified as predictors of a poorer outcome, at least in some trials, include: (1) non-paroxysmal AF and particularly longstanding persistent AF, (2) sleep apnea and obesity, (3) increased left atrial size, (4) increased age, (5) HTN, and (6) left atrial fibrosis as detected by cardiac MRI.[e98] A recent systematic review of predictors of AF recurrence after AF ablation analyzed data from 45 studies, 25 of which included a multivariable analysis of predictors of recurrence.[e543] Among the 17 studies that examined AF type as a predictor of recurrence, 11 studies reported no impact of AF type on recurrence, whereas six studies reported that the presence of nonparoxysmal AF was an independent predictor of a higher rate of recurrence [hazard ratio (HR) ranging from 1.8 to 22]. Seventeen studies evaluated EF as a predictor of recurrence. Very few patients in any of these studies had an EF less than 40%. Among these 17 studies, only five reported a significant association between lower EF and a higher rate of AF recurrence. Twenty studies examined left atrial diameter as a predictor of AF recurrence. Very few patients in any study had a left atrial dimension (LAD) >60 mm. Among these 20 studies, four reported a significant association between larger LAD and a higher rate of recurrence of AF. Among 21 studies that examined the presence of structural heart disease as a predictor, only one reported a significant association at 12 months of follow-up. Most studies examined gender, and no association between recurrence and gender was found. Only one of 22 studies reported an independent association between age and recurrence, and in this study, older age was associated with a lower recurrence rate.

8.12. Cost-effectiveness of AF ablation

Several studies have described the costs of catheter ablation of AF, but few data are available on cost-effectiveness. Radiofrequency catheter ablation of paroxysmal AF was demonstrated in one study to significantly reduce health care resource utilization, with a reduction in the annual cost of health care (not including procedural costs) from a mean of \$1,920 $\pm$ \$889 pre-ablation to \$87 $\pm$ %68 post-ablation.[e546] In that study, the procedural cost of ablation was approximately \$17,000 (2001 dollars), an amount considerably lower than the total charges for the procedure, which typically are greater than \$50,000 in the United States. Another study retrospectively compared the costs of radiofrequency catheter ablation and drug therapy in patients with paroxysmal AF.[e547] In that study, the initial cost of catheter ablation was approximately 4,700 Euros (2001 Euros), then approximately 450 Euros/year afterward. In comparison, the mean annual cost of pharmacological management before catheter ablation was approximately 1,600 Euros, suggesting that the total costs of radiofrequency catheter ablation would be lower than the cost of medical management after five years. However, the mean duration of follow-up was less than one year, and the cost of redo procedures for late recurrences of AF were not considered in the analysis.

Only one study formally analyzed the cost-effectiveness of catheter ablation compared to amiodarone therapy and a rate-control strategy.[e548] This study was performed using a

Markov decision analysis model. Among 65-year-old patients at moderate risk of stroke, the incremental cost-effectiveness ratio (ICER) of catheter ablation was $51,800 (2004 dollars) per quality-adjusted life-year (QALY). In 55-year-old patients at moderate risk of stroke, catheter ablation had an ICER of $28,700 per QALY compared to rate control. However, in patients with no risk factors for stroke, catheter ablation had an ICER of $98,900 per QALY. Further analysis indicated that in 65-year-old patients at moderate risk of stroke and with an 80% one-year success rate of catheter ablation, the relative risk of stroke after catheter ablation would need to decrease by ≥42% compared with anticoagulated patients in AF for the ICER of catheter ablation to be <$50,000. Of note is that $50,000 generally is considered to be the threshold value for cost-effectiveness of a therapy. However, the model assumed that successful ablation of AF eliminates the excess risk of stroke, which is yet to be proven in a prospective study.

The limited data available on cost-effectiveness suggest that catheter ablation of AF may be cost-effective in patients with one or more risk factors for stroke but not in patients who have no risk factors.

9. Complications of catheter ablation of atrial fibrillation

9.1. Overview

Catheter ablation of AF is one of the most complex interventional electrophysiologic procedures. It is therefore to be expected that the risk associated with AF ablation is higher than for ablation of most other cardiac arrhythmias. This section reviews the complications associated with AF ablation procedures. Particular attention is focused on the most frequently occurring complications and those likely to result in prolonged hospitalization, long-term disability or death. We recognize that some rare complications with significant sequelae can occur, and a few of these are reviewed. It must be remembered that the publications from which these data are derived originate from large volume centers where complications would be expected less frequently than in lower volume centers. The first worldwide survey of AF ablation reported that at least one major complication was seen in 6% of patients but with only four early deaths recorded in 8,745 patients.[e386] A follow-up survey, conducted in a similar way, produced further data on the safety and efficacy of AF ablation[e506] and identified the most common fatal complications.[e549] Although these data might be regarded as providing more representative complication rates, it must be recognized that the data were from voluntary surveys and likely underestimated the true complication rates. The Task Force strongly recommends that standardized reporting of complications be included in all published reports on the outcome of AF ablation. In this document we have provided definitions of the most important complications associated with AF ablation that we hope can be incorporated into the design of future clinical trials of AF ablation (Table 6).

9.2. Cardiac tamponade

Cardiac tamponade is the most common potentially life-threatening complication associated with AF ablation. It is also a well-recognized but infrequent complication of routine cardiac electrophysiology procedures. The markedly higher incidence of cardiac tamponade during AF ablation[e386,e550–e554] can be attributed to a number of important differences, including extensive intra-cardiac catheter manipulation and ablation, the common need for two or more transseptal punctures, and the need for systemic anticoagulation. The most common causes of cardiac perforation leading to cardiac tamponade during AF ablation are: (1) misdirected transseptal punctures either with punctures performed too posteriorly exiting the right atrium into the pericardium before entering the LA or punctures exiting the LA via the roof, LA appendage, or the lateral LA wall, (2) direct mechanical trauma, especially through the LA appendage, and (3) overheating during radiofrequency energy delivery, with or without the development of a "pop." Among the series of AF ablation reports reviewed for this document, cardiac tamponade was reported as a complication in two-thirds, with an incidence of up to 6%. Risk factors for tamponade in one study were identified as linear ablation lesions and higher ablation power.[e553] A "pop" was heard during eight of these 10 cases of tamponade. Another large series reported cardiac tamponade during 15 of 632 ablation procedures (2.4%).[e550] Two of these patients required surgical intervention. In contrast to the prior study, no "pop" was reported. The two Worldwide Surveys of AF Ablation reported a 1.2% and a 1.3% incidence of cardiac tamponade, respectively.[e386,e506] A meta-analysis of cryoballoon ablation procedures reported an overall incidence of cardiac tamponade of 1.5%.[e278] A more recent report from the Worldwide Survey group has called attention to delayed cardiac tamponade, defined as cardiac tamponade occurring one hour or more following an AF ablation procedure. This complication occurred following 45 of 27,921 procedures (0.2%).[e555] Most but not all patients presented with warning symptoms but 13% of patients presented with hypotension and shock.

Cardiac tamponade presents either as an abrupt dramatic fall in blood pressure or, more insidiously, as a gradual decrease in blood pressure. In the latter case, administration of fluid may return the blood pressure to normal before it subsequently declines. However, it is vital that operators and staff be vigilant to the development of cardiac tamponade as a delay in diagnosis may be fatal. All members of this Task Force continuously monitor the systemic arterial pressure during and following AF ablation procedures. Two-thirds of Task Force members use an arterial line for BP monitoring during the AF ablation procedure. The development of hypotension in any patient should be assumed to indicate tamponade until proven otherwise by immediate echocardiography. An early sign of cardiac tamponade is a reduction in the excursion of the cardiac silhouette on fluoroscopy with a simultaneous fall in systemic blood pres-

Table 6 Definitions of complications associated with AF ablation

Major Complication	A major complication is a complication that results in permanent injury or death, requires intervention for treatment, or prolongs or requires hospitalization for more than 48 hours. Because early recurrences of AF/AFL/AT are to be expected following AF ablation, recurrent AF/AFL/AT within 3 months that requires or prolongs a patient's hospitalization should not be considered to be a major complication of AF ablation.
Serious Adverse Device Effect	A serious adverse device effect is defined as a serious adverse event that is attributed to use of a particular device.
Atrio Esophageal Fistula	An atrio esophageal fistula is defined as a connection between the atrium and the lumen of the esophagus. Evidence supporting this diagnosis includes documentation of esophageal erosion combined with evidence of a fistulous connection to the atrium such as air emboli, an embolic event, or direct observation at the time of surgical repair. A CT scan or MRI scan are the most common methods of documentation of an atrial esophageal fistula.
Bleeding	Bleeding is defined as a major complication of AF ablation if it requires and/or is treated with transfusion or results in a 20% or greater fall in HCT.
Bleeding Following Cardiac Surgery	Excessive bleeding following a surgical AF ablation procedure is defined as bleeding requiring re-operation or $\geq$2 units of PRBC transfusion within any 24 hours of the first 7 days following the index procedure.
Cardiac Perforation	We recommend that cardiac perforation be defined together with cardiac tamponade. See Cardiac Tamponade/Perforation
Cardiac Tamponade	We recommend that cardiac tamponade be defined together with cardiac perforation. See Cardiac Tamponade/Perforation.
Cardiac Tamponade/ Perforation	Cardiac tamponade/perforation is defined as the development of a significant pericardial effusion during or within 30 days of undergoing an AF ablation procedure. A significant pericardial effusion is one that results in hemodynamic compromise, requires elective or urgent pericardiocentesis, or results in a 1-cm or more pericardial effusion as documented by echocardiography. Cardiac tamponade/perforation should also be classified as "early" or "late" depending on whether it is diagnosed during or following initial discharge from the hospital.
Deep Sternal Wound Infection/Mediastinitis following Cardiac Surgery	Deep sternal wound Infection/mediastinitis following cardiac surgery requires one of the following: (1) an organism isolated from culture of mediastinal tissue or fluid; (2) evidence of mediastinitis seen during operation; (3) one of the following conditions: chest pain, sternal instability, or fever ($>$38 °C), in combination with either purulent discharge from the mediastinum or an organism isolated from blood culture or culture of mediastinal drainage.
Esophageal Injury	Esophageal injury is defined as an erosion, ulceration, or perforation of the esophagus. The method of screening for esophageal injury should be specified. Esophageal injury can be a mild complication (erosion or ulceration) or a major complication (perforation).
Gastric Motility/Pyloric Spasm Disorders	Gastric motility/pyloric spasm disorder should be considered a major complication of AF ablation when it prolongs or requires hospitalization, requires intervention, or results in late disability, such as weight loss, early satiety, diarrhea, or GI disturbance.
Mediastinitis	Mediastinitis: is defined as inflammation of the mediastinum. Diagnosis requires one of the following: (1) an organism isolated from culture of mediastinal tissue or fluid; (2) evidence of mediastinitis seen during operation; (3) one of the following conditions: chest pain, sternal instability, or fever ($>$38 °C), in combination with either purulent discharge from the mediastinum or an organism isolated from blood culture or culture of mediastinal drainage.

Table 6 Continued

Myocardial Infarction in the Context of AF Ablation	The universal definition of myocardial infarction (Thygesen JACC 2007) cannot be applied in the context of catheter or surgical AF ablation procedures because it relies heavily on cardiac biomarkers (troponin and CPK), which are anticipated to increase in all patients who undergo AF ablation as a result of the ablation of myocardial tissue. Similarly, chest pain and other cardiac symptoms are difficult to interpret in the context of AF ablation both because of the required sedation and anesthesia and also because most patients experience chest pain following the procedure as a result of the associated pericarditis which occurs following catheter ablation. We therefore propose that an MI, in the context of catheter or surgical ablation, be defined as the presence of any one of the following criteria: 1) detection of ECG changes indicative of new ischemia (new ST-T changes or new LBBB), which persist for more than one hour; 2) development of new pathological Q waves on an ECG; 3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
Pericarditis	Pericarditis should be considered a major complication following ablation if it results in an effusion that leads to hemodynamic compromise or requires pericardiocentesis, prolongs hospitalization by more than 48 hours, requires hospitalization, or persists for more than 30 days following the ablation procedure.
Phrenic Nerve Paralysis	Phrenic nerve paralysis is defined as absent phrenic nerve function as assessed by a sniff test. A phrenic nerve paralysis is considered to be permanent when it is documented to be present 12 months or longer following ablation.
Pulmonary Vein Stenosis	Pulmonary vein stenosis is defined as a reduction of the diameter of a PV or PV branch. PV stenosis can be categorized as mild $<$50%, moderate 50%–70%, and severe $\geq$70% reduction in the diameter of the PV or PV branch. A severe PV stenosis should be considered a major complication of AF ablation.
Silent Cerebral Embolism	Silent cerebral embolism is defined as an occlusion of a blood vessel in the brain due to an embolus that does not result in any acute clinical symptoms. Silent cerebral embolism is generally detected using a diffusion-weighted MRI.
Stroke or TIA Post Ablation	We agree with the definition for stroke and TIA published by Leon et al in JACC as a standardized definition from the Valve Academic Research Consortium.[e734]
Unanticipated Adverse Device Effect	Unanticipated adverse device effect is defined as complication of an ablation procedure that has not been previously known to be associated with catheter or surgical ablation procedures.
Vagal Nerve Injury	Vagal nerve injury is defined as injury to the vagal nerve that results in esophageal dysmotility or gastroparesis. The vagal nerve injury is considered to be a major complication if it prolongs hospitalization, requires hospitalization, or results in ongoing symptoms for more than 30 days following an ablation procedure.
Vascular Access Complication	Vascular access complications include development of a hematoma, an AV fistula, or a pseudoaneurysm. A major vascular complication is defined as one that requires intervention such as surgical repair or transfusion, prolongs the hospital stay, or requires hospital admission.

*Stroke diagnostic criteria[e734].

- Rapid onset of a focal or global neurological deficit with at least one of the following: change in level of consciousness, hemiplegia, hemiparesis, numbness or sensory loss affecting one side of the body, dysphasia or aphasia, hemianopia, amaurosis fugax, or other neurological signs or symptoms consistent with stroke.
- Duration of a focal or global neurological deficit $\geq$24 hours; OR $<$24 hours if therapeutic intervention(s) were performed (eg, thrombolytic therapy or intracranial angioplasty); OR available neuroimaging documents a new hemorrhage or infarct; OR the neurological deficit results in death.
- No other readily identifiable nonstroke cause for the clinical presentation (eg, brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences)^
- Confirmation of the diagnosis by at least one of the following: neurology or neurosurgical specialist; neuroimaging procedure (MR or CT scan or cerebral angiography); Lumbar puncture (ie, spinal fluid analysis diagnostic of intracranial hemorrhage)
- Stroke definitions
  - Transient ischemic attack: new focal neurological deficit with rapid symptom resolution (usually 1 to 2 hours), always within 24 hours; neuroimaging without tissue injury
  - Stroke: (diagnosis as above, preferably with positive neuroimaging study);
    Minor—Modified Rankin score $<$2 at 30 and 90 days†
    Major—Modified Rankin score $\geq$2 at 30 and 90 days

^Patients with non-focal global encephalopathy will not be reported as a stroke without unequivocal evidence based upon neuroimaging studies.
†Modified Rankin score assessments should be made by qualified individuals according to a certification process. If there is discordance between the 30- and 90-day modified Rankin scores, a final determination of major versus minor stroke will be adjudicated by the neurology members of the clinical events committee.

sure. ICE has been reported to allow earlier detection of a pericardial effusion,[e550] and 90% of the members of this writing group have an echo machine immediately available to the EP laboratory. However, only 50% of the group routinely undertake an echo either immediately at the end of the ablation procedure and/or prior to discharge to examine for a pericardial effusion. It is important to recognize that small asymptomatic pericardial effusions are commonly observed following AF ablation procedures. Monitoring filling pressures in the left and right atria may be helpful in order to evaluate progression of the effusion and/or effective drainage of the pericardial collection.

The majority of episodes of cardiac tamponade can be managed successfully by immediate percutaneous drainage and reversal of anticoagulation with protamine. This is best achieved by sub-xiphoid Seldinger puncture of the pericardial sac and placement of an intra-pericardial catheter. The pericardial tap can be performed either with fluoroscopic guidance based on anatomic landmarks or with echo guidance.[e556] After initial aspiration, the blood pressure promptly returns to normal. Once the pericardial space has been drained, the patient needs to be monitored for ongoing bleeding with the drainage catheter in place. Rarely, if there has been a tear, percutaneous drainage may be inadequate and surgical drainage and repair is needed.[e550] It is for this reason that AF ablation procedures should only be performed in hospitals equipped or prepared to manage these types of emergencies with access to emergency surgical support when required. Three cases have been reported of emergent drainage of a pericardial effusion through a sheath, either inadvertently or purposely placed into the pericardial space using an endocardial approach,[e552,e554,e57] although this would not be considered to be a standard approach. Early recognition and rapid appropriate treatment of cardiac tamponade are mandatory to prevent irreversible deterioration of cerebral and cardiac perfusion. In a dedicated Worldwide Survey, cardiac tamponade was reported to be the most frequent cause of peri-procedural death,[e549] with 25% of all fatalities occurring in association with this complication. A recent report described the outcomes of 40 patients at three centers who experienced cardiac tamponade either with a therapeutic INR due to warfarin (N = 17) or with an INR <2.0 (N = 23).[e558] All patients were successfully treated, and none required surgery. Heparin was reversed with protamine in approximately 90% of patients in both groups. Warfarin was reversed by fresh frozen plasma or factor V11a in 35% of patients with a therapeutic INR and in 17% of patients with an INR <2.0. They concluded that cardiac tamponade is not more difficult or severe in patients with a therapeutic INR at the time of AF ablation.[e558]

9.3. Pulmonary vein stenosis

PV stenosis is a well-recognized complication of AF ablation that results from thermal injury to the PVs, including the media, intima, adventitia, and PV musculature. Since first reported in 1998, numerous studies have sought to determine the incidence, cause, diagnostic strategy, and treatment approach for PV stenosis.[e206,e257,e262,e274,e559–e562] Although the precise pathophysiological mechanisms are still uncertain, a progressive vascular reaction leading to replacement of necrotic myocardium by collagen has been reported after extensive radiofrequency energy application to canine PVs.[e562] The published incidence of PV stenosis varies widely from 0% to 38%.[e206,e257,e262,e274,e324,e559,e560,e562] This variation results from differences in the ablation technique, definition of PV stenosis, intensity of screening for this complication, and the date at which the study was performed. It was initially thought that cryoablation was free from this complication. However, recent publications have indicated that PV stenosis can rarely complicate cryoablation,[e279,e563] implying that any thermal injury to the PVs can result in stenosis. Thus, as with RF ablation, it is important to perform cryoablation outside the ostia of the PVs. This is one of the reasons most operators now initially employ the 28-mm balloon. When PV ablation for treating AF began in the late 1990s, investigators were unaware that PV stenosis was a potential complication. In contrast, today, operators understand that PV stenosis can be prevented by avoiding RF energy delivery within a PV. This increased awareness and improvements in imaging modalities have enabled better identification of the true PV ostium and resulted in a dramatic reduction in the incidence of PV stenosis. It is notable that less than one-fourth of the members of this consensus Task Force routinely screen for asymptomatic PV stenosis during follow-up, with most only investigating for PV stenosis in patients with suggestive symptoms, acknowledging that even severe PV stenosis can be asymptomatic. It is unknown whether early diagnosis and treatment of asymptomatic PV stenosis provides any long-term advantage to the patient. For quality control purposes, centers beginning to perform AF ablation procedures, or those transitioning to a new AF ablation technique or approach, should consider obtaining follow-up CT or MR scans within three to six months of the procedures to screen for PV stenosis in a series of patients.

CT or MR imaging of the PVs prior to, and several months following, catheter ablation are the most precise methods for detecting PV stenosis.[e257,e262,e321] Studies show that both of these imaging modalities are equally accurate in determining PV size and detecting PV stenosis. A ventilation perfusion scan may be useful to screen for severe PV stenosis when a CT or MR scan cannot be obtained. According to the percentage reduction of the luminal diameter, the severity of PV stenosis is generally defined as mild (<50%), moderate (50%–70%), or severe (>70%). In this Consensus Statement we recommend that a significant PV stenosis be defined as a >70% reduction in luminal diameter (Table 6). Symptoms are more likely with severe stenoses, but even severe PV stenosis or complete PV occlusion may be asymptomatic. Symptoms of PV stenosis include chest pain, dyspnea, cough, hemoptysis, re-

current lung infections and symptoms of pulmonary HTN.[e257,e324] Patients undergoing AF ablation should be warned of these possible symptoms to avoid inappropriate subsequent presentation to respiratory or other specialist physicians. Symptomatic amelioration has been observed after PV occlusion without treatment, indicating collateral formation or recruitment. Late progression of PV stenosis is reported, but the precise incidence is poorly defined.[e564,e565]

Among the series of AF ablations reviewed for this document, PV stenosis was reported in <10% of series. Although these may reflect the infrequency of PV stenosis, few performed routine follow-up CT or MR imaging to screen for asymptomatic PV stenosis. Saad et al[e262] recently reported severe PV stenoses following 21 of 608 AF ablation procedures (3.4%) where the development of symptoms correlated with severe PV stenosis involving more than one PV. The Worldwide Survey of AF Ablation reported a 0.32% incidence of acute PV stenosis and a 1.3% incidence of persistent PV stenosis. Percutaneous or surgical intervention for treatment of PV stenosis was required in 53 cases (0.6%).[e386]

The preferred therapy for severe symptomatic PV stenosis is PV angioplasty.[e262,e566,e567] Whether there is additional benefit from elective PV stenting is uncertain, but this may be required if balloon angioplasty alone is inadequate acutely or is followed by restenosis. However, restenosis can develop despite stent placement. The role of surgery is not defined but may be considered for clinically important PV occlusion where angioplasty and stenting have failed.

9.4. Injury to the esophagus and peri-esophageal vagal nerves

9.4.1. Anatomic considerations

The esophagus descends in the mediastinum posterior to the LA and to the right of the descending aorta; however, as it descends more inferiorly, it tends to run anterior and slightly to the left of the aorta before it passes through the diaphragm into the abdomen.[e258,e568,e569] The relationship of the esophagus to the posterior wall and PVs is variable. It tends to be located furthest from the right superior PV, but it can be close to any of the others depending on its course and may be within a few millimeters at the point of closest proximity. Moreover, there is some evidence that the esophagus may shift from the time that a CT or MR image is performed until the patient reaches the electrophysiology laboratory, or its position may change while the ablation is performed. Because it is invariably in close apposition to the posterior wall of the LA and one or more PVs, the esophagus and peri-esophageal nerves are at risk of injury when ablation is performed in these areas.

Branches of the vagus nerve control peristalsis, the pyloric sphincter, and motility in the gastric antrum. Two branches descend on the anterior surface of the esophagus to form the anterior esophageal plexus, which enters the abdomen through the esophageal diaphragmatic opening. The anterior plexus passes external to the pericardium but within 2.5–6.5 mm of the posterior atrial wall or the junctions of the PVs and the posterior LA.[e570] The vagus nerve mediates gastric antral contraction followed by pyloric relaxation in the late phase of gastric emptying.[e571]

9.4.2. Esophageal injury

Esophageal ulceration, perforation, or development of a left atrial-esophageal fistula have been reported after catheter or surgical ablation of AF using unipolar radiofrequency current[e386,e420,e506,e549,e572–e579] and after catheter ablation using high-intensity focused ultrasound (HIFU).[e282,e572] These are both energy sources that ablate through tissue heating. From our knowledge of cryoablation lesion characteristics, as well as our cumulative experience and the results of the recent meta-analysis of cryoballoon ablation, there have been no atrial esophageal fistulas in this patient population. However, as noted previously in this document, ulcerations of the esophagus have been observed in 17% of patients in one study. Although the precise mechanism of esophageal injury is not precisely understood, potential mechanisms of injury include direct thermal injury, acid reflux, infection from the lumen, and ischemic injury through thermal occlusion of end-arterioles. Left atrial-esophageal fistula is associated with a very high morbidity that includes air embolism and sepsis and a mortality rate that is greater than 80%. Although left atrial-esophageal fistulae are rare (occurring after less than 0.1%–0.25% of AF ablation procedures),[e386,e420,e506,e549] injury to the esophagus is common following AF ablation. In several clinical studies, endoscopy performed 1–3 days after AF ablation using RF energy, HIFU, laser balloon or cryothermia identified an asymptomatic esophageal ulcer (directly behind the LA) in 4%–60% (generally 15%–20%) of patients.[e282,e428,e432,e580–e588] The asymptomatic esophageal ulcers were usually healed on repeat endoscopy at 2–3 weeks following treatment with a proton pump inhibitor and a cytoprotective agent such as sucralfate.[e583,e586] One recent study performed endoscopy in 267 patients who underwent AF ablation using RF energy. The power on the posterior wall was limited to 25 W. Among these patients, 6 (2.2%) had either erythema (N = 2) or a necrotic ulcer (N = 4) on endoscopy. Multivariate analysis revealed that the distance between the LA and esophagus was the only independent predictor, although an LA isthmus line and CS ablation showed a trend. Each patient was treated with a proton pump inhibitor in combination with an H_2-blocker (pantoprazole or esomeprazole), and sucralfate and all recovered without development of an atrial esophageal fistula.[e589]

Survivors of left atrial-esophageal fistulae are often left with disability from cerebrovascular events. Early diagnosis is important because there have been a number of patients with esophageal perforation who have achieved full recovery by urgent surgical intervention or placement of an esophageal stent.[e590]

The clinical manifestations of an atrial-esophageal fistula usually present 2–4 weeks after the ablation procedure. The most common symptoms are fever, chills, and recurrent neurological events (septic emboli), but patients may pres-

ent in septic shock or death. The best diagnostic modalities are CT or MR imaging of the esophagus.[e282,e574] Although a barium swallow may detect a fistula, its sensitivity is low. If an atrial-esophageal fistula is suspected, endoscopy should be avoided or undertaken with caution, since insufflation of the esophagus with air may result in a large air embolus producing stroke or death. The early recognition of an atrial-esophageal fistula may be missed due to the low awareness of this rare complication. It is important for patients to be educated as to warning signs and to contact the AF Ablation program should any worrisome symptoms develop. Approximately two-thirds of Task Force members routinely prescribe either proton pump inhibitors or H_2 blockers for one to four weeks following ablation. It is important to note, however, that this practice is based on the observation that esophageal ulcerations may be observed on endoscopy following AF ablation. There are no data available to demonstrate that this approach reduces the incidence of development of an atrial esophageal fistula.

9.4.3. Peri-Esophageal vagal nerve injury

Injury to the vagal anterior esophageal plexus can occur when radiofrequency energy is applied to the posterior wall of the LA and may cause acute pyloric spasm and gastric hypomotility. Common symptoms include nausea, vomiting, bloating and abdominal pain developing within a few hours to a few weeks after the ablation procedure.[e591–e594] Some patients also experience sinus tachycardia.[e591] The incidence of gastric problems may be as high as 1%.[e593] Although some patients recover within two weeks, the course can be very protracted.

The initial evaluation may include endoscopy or a barium swallow study to look for residual food after an overnight fast. Computed tomography shows marked gastric dilation. Solid food labeled with Technetium-99 demonstrates delayed gastric emptying.[e591] Real time magnetic resonance imaging has been used to assess gastric motility and pyloric spasm.[e594] The integrity of the vagal innervation to the gastrointestinal system can be assessed by the pancreatic polypeptide response to sham feeding. Patients with this complication exhibit an abnormal kinetic and peak response. The normal response is a biphasic increase in pancreatic polypeptide. Injury to the vagus nerve impairs the first phase of the response.[e595]

Because pyloric spasm was the prominent component of this syndrome, pyloric dilatation was performed, mechanically in one patient and by local injection of botulinum toxin in the other, with transient improvement. Management of this complication depends on the severity of symptoms and whether gastric immotility or pylorospasm predominates. Small low-fat and low-fiber meals may alleviate symptoms. Metoclopramide can be used to promote gastric motility for one to three months, but long-term treatment is associated with a risk of movement disorders. Botulinum injections or surgery may be required to alleviate pyloric spasm.[e430,e596] In severe cases surgery or gastric pacing may be required.[e430,e593]

While there is no established method to prevent injury to the vagal nerves, the risk may be reduced by using the same techniques used to avoid an atrial esophageal fistula.

9.5. Phrenic nerve injury

Phrenic nerve injury is an important complication of AF ablation.[e256,e276,e597–e602] It results from direct thermal injury, usually to the right phrenic nerve, which is located near the right superior PV and the SVC.[e256,e597,e598] Very rarely, ablation within the LA appendage can result in left phrenic nerve damage. The development of phrenic nerve injury has resulted from AF ablation using RF, cryoablation, ultrasound, and laser ablation.[e256,e276,e597–e602] The most common scenario in which phrenic nerve injury has been reported is cryoballoon ablation of the right sided PVs. It has been speculated that this may reflect a number of factors including the circumferential and broader thermal gradient created by balloon devices as well as the distorting effect of an inflated balloon on the anatomic distance between the RSPV endocardium and the right phrenic nerve. The second most common scenario is electrical isolation of the SVC with RF energy and point by point ablation. Ablation within a persistent left SVC can result in left phrenic nerve paralysis. It is exceedingly uncommon to develop phrenic nerve paralysis with circumferential wide area PV isolation using RF energy. Due to the close anatomic relationship of the right phrenic nerve to the right superior PV, the risk for phrenic nerve injury is higher with ablation lesions close to the PV ostium as compared to those within the LA. Thus, with cryoballoons, the smaller balloons, inevitably placed more distally within the PVs, carry a higher risk for phrenic nerve injury as compared to bigger balloons with more proximal energy application.[e603] In a 3-center study, phrenic nerve injury was seen in 26 of 346 patients (7.5%). Of the 26, 24 were caused by use of the smaller cryoballoon. All recovered during follow-up.[e369] A large meta-analysis of 22 studies of cryoballoon ablation in 1,308 patients reported that the most common complication was phrenic nerve paralysis with an incidence of 4.7%. Most patients recovered with 0.37% experiencing phrenic nerve paralysis 12 months post ablation. Although it is more commonly seen with cryotherapy to the right upper PV, phrenic nerve palsy can follow cryotherapy to the right lower PV so that the measures described below to prevent phrenic nerve injury should be applied when treating both right PVs. The reported incidence of phrenic nerve injury with RF energy is less than 1%.[e256,e597]

Phrenic nerve damage can be asymptomatic or can cause dyspnea, hiccups, atelectasis, pleural effusion, cough, and thoracic pain.[e256,e276,e597,e601] When suspected, the diagnosis can be confirmed by a sniff test performed during fluoroscopy showing unilateral diaphragmatic paralysis. Strategies to prevent phrenic nerve damage include high output pacing to establish whether the phrenic nerve can be captured from the proposed ablation site before ablation, phrenic nerve mapping by pacing along the SVC to identify the location of the

phrenic nerve, ensuring proximal/antral ablation when ablating around the right upper PV, manual monitoring of diaphragmatic excursion caused by pacing the phrenic nerve from the SVC during ablation, and fluoroscopic monitoring of diaphragmatic motion from voluntary breathing during ablation. SVC pacing of the right phrenic nerve during ablation while palpitating the abdomen is currently considered to be the optimal approach for preventing phrenic nerve injury. This technique is now considered a standard part of cryoballoon ablation of the right PVs, and can also be considered during SVC isolation using RF energy. Energy delivery should be interrupted immediately at the first sign of phrenic nerve injury. A technique to monitor the myopotential of the right hemidiaphragm using a standard EP lab system during cryoablation of the right-sided pulmonary veins has recently been described.[e604] The fall in amplitude of the myopotential can be measured objectively and is more sensitive than abdominal palpation, predicting the later fall in diaphragmatic excursion. Additional experience with this new approach will be needed to better define its clinical role as a technique to avoid phrenic nerve injury during cryoablation procedures. Phrenic nerve function usually returns to normal within minutes.[e256,e597] In most reports of longer lasting phrenic nerve palsy, phrenic nerve function recovered between one day and more than 12 months. There is no active treatment known to aid phrenic nerve healing.

9.6. Stroke, TIA, and silent microemboli

9.6.1. Stroke and TIA

Embolism of air or thrombus is one of the most significant complications of ablation of AF and both are potential causes of cerebral, coronary, or peripheral vascular compromise.

The incidence of thrombo-embolism associated with AF ablation is reported to be between 0% and 7%.[e45,e90,e116,e207,e379,e386,e437,e605,e606] More than two-thirds of the clinical trials reviewed for preparation of this document reported one or more cerebrovascular events. Thromboembolic events typically occur within 24 hours of the ablation procedure with the high risk period extending for the first two weeks following ablation.[e116]

A number of potential explanations for the development of thromboembolic complications have been proposed. These include the development of thrombi on or within stationary sheaths[e429] or ablation catheters positioned within the LA, char formation at the tip of the ablation catheter and at the site of ablation, disruption of a thrombus located in the atrium prior to the ablation procedure, and, possibly, electrical cardioversion during procedures. Incidence of these events may be reduced by a combination of detailed pre-procedural imaging, a strict anticoagulation protocol, and careful control of radiofrequency energy to minimize the risk of char formation. Maintaining a constant heparinized flush through all long sheaths with access to the LA is strongly advised.

Diagnosis of a symptomatic thrombo-embolic event is usually straightforward when ischemia or infarction results from arterial occlusion interrupting perfusion of dependent tissue. The manifestation depends upon where the occlusion occurs: intra-cranial, coronary arterial, abdominal, or other peripheral arterial beds. We have previously discussed the prevention of thromboembolism by intraprocedural and post procedural anticoagulation in section 6.1 Other Technical Aspects. Treatment of a thrombo-embolic event will vary according to the location of the embolus. Peripheral arterial embolization may be amenable to surgical thrombectomy, whereas cerebral embolization has traditionally been managed conservatively and the consequences accepted. However, there is growing interest in aggressive early management of such events, with either thrombolytic drugs or percutaneous interventional techniques. In one series that surveyed 26 embolic stroke events that occurred in a series of 3,060 patients, long-term neurologic outcomes were as follows: severe impairment (3 patients with 2 possibly related deaths), moderate impairment (10 patients), mild impairment (9 patients) and unknown (4 patients).[e606]

9.6.2. Silent microemboli

Silent cerebral embolism is defined as an occlusion of a blood vessel in the brain due to an embolus that does not result in any acute clinical symptoms and is therefore "silent." Emboli can result from a thrombus, air, gas, tissue, or fat. During an AF ablation procedure potential sources of these microemboli include thrombi, which may develop on intracardiac catheters, sheath materials, air introduction through a sheath during catheter insertion or exchanges, dislodgement of thrombi in the heart, or as a result of thrombi or gas that forms during the ablation process. Diffusion-weighted MRI (DW-MRI) is very sensitive to acute ischemic injury and can detect a cerebral lesion created by an embolus as early as 30 minutes post ablation.

Recently, several centers have reported that DW-MRI can detect new acute lesions created by emboli following 7%–38% of AF ablation procedure.[e294,e295,e607–e610] In 674 AF ablation patients reported in the literature in whom a DW-MRI was obtained prior to and 24–48 hours following ablation, the overall incidence of acute lesions was 17%. The incidence appears to vary according to the system used for ablation and has been reported to be highest with the use of non-irrigated circumferential multielectrode ablation catheters.[e610,e611] No neurologic symptoms were observed in all except two patients. One recent study examined the important question concerning whether these lesions persist on repeat DW-MRI and T2 FLAIR scanning. In this study, 14 patients who had 50 new silent cerebral emboli detected post AF ablation had a repeat MRI a median of three months later. It was notable that 47 of the 50 lesions (94%) resolved. The three lesions in three patients that resulted in a residual deficit at repeat scanning were large (>10 mm) defects initially and one of these patients had neurologic symptoms. When considering the significance of the silent cerebral embolism that has been observed following AF

ablation, it is important to note that cerebral embolism also has been observed after most types of cardiac invasive procedures, including coronary angiography, carotid artery stenting, and cardiac valve replacement.[e612,e613] Importantly, as of now, a direct link between silent cerebral embolism and a decline in neuro-cognitive function has not been proven.[e613,e614]

Despite this observation, the EP and AF ablation community has taken this issue very seriously and studies are underway to answer the many questions that have arisen. Even in the absence of a proven negative impact on neurological function in patients with acute DW-MRI lesions, a reduction in the incidence of silent cerebral embolism is desirable. Factors that are now being closely examined in ongoing studies include (1) evaluating the chronic incidence of these lesions and their impact on neuro-cognitive function, (2) determining whether the incidence of silent thromboemboli can be reduced by performing AF ablation in patients on warfarin with an INR >2.0 and/or by anticoagulating with heparin prior to the transseptal and maintaining the ACT >350 throughout the procedure, and (3) increased attention on continuous flushing of sheaths and a heightened vigilance for air embolism.

9.7. Air embolism

The most common cause of air embolism is introduction of air into the transseptal sheath. While this may be introduced through the infusion line, it can also occur with suction when catheters are removed. Air embolism has been reported with coronary angiography, percutaneous interventions requiring access to the LA, and during ablation procedures.[e382,e411,e615–e617] Air embolism to the cerebral vasculature can be associated with altered mental status, seizure, and focal neurological signs. The central nervous system dysfunction is attributable to both mechanical obstruction of the arterioles and thrombotic-inflammatory responses of air injured epithelium.[e615,e617] While immediate diagnosis and treatment is based on clinical suspicion, prompt MRI or CT scans obtained before the intravascular air is absorbed may show multiple serpiginous hypodensities representing air in the cerebral vasculature, with or without acute infarction.[e382,e411] Most importantly, atrio-esophageal fistula should be ruled out if air embolism is documented after the ablation. A common presentation of air embolism during AF ablation is acute inferior ischemia and/or heart block. This reflects the preferential downstream migration of air emboli into the right coronary artery. The preferential manifestation of air emboli into the RCA territory may reflect the superior position of the RCA ostium in the supine patient. Support care usually results in complete resolution of symptoms and signs within minutes. However, pacing and cardiopulmonary resuscitation may be needed if the hypotension and atrioventricular block persist.[e3] It is imperative that all infusion lines be monitored closely for bubbles. Whenever catheters are removed, they should be withdrawn slowly to minimize suction effects, and the fluid column within the sheath should be aspirated simultaneously. Particular care is advised when inserting and removing balloon catheters through large sheaths.[e618] Treatment should be initiated immediately in the laboratory if cerebral air embolism is suspected. The most important initial step is to maximize cerebral perfusion by the administration of fluids and supplemental oxygen, which increases the rate of nitrogen absorption from air bubbles. For large air emboli, it may be beneficial to briefly suspend the patient in a head-down position.[e616,e617] Treatment with hyperbaric oxygen may reverse the condition and minimize endothelial thrombo-inflammatory injury if it is started within a few hours.[e615] Heparin appears to limit injury in animal models of cerebral arterial air embolism.[e619]

9.8. Vascular complications

Vascular complications are the most common complications of AF ablation and include groin hematoma, retroperitoneal bleed, femoral arterial pseudoaneurysm, or femoral arteriovenous fistula. Most hematomas can be managed conservatively or with ultrasound guided compression if required. More significant vascular complications can lead to substantial morbidity and prolonged hospital stay and can necessitate blood transfusion and percutaneous or open surgical repair.[e620] Rarely, vascular complications with large tense hematomas can lead to femoral neurological sequelae and a requirement for rehabilitation.

The published incidence of vascular complications varies from 0% to 13%. One literature review on AF ablation described a 13% incidence of hematoma and a 1% incidence of an arteriovenous fistula at the puncture site.[e621] A worldwide survey of 8,745 AF ablation procedures found an incidence of femoral pseudoaneurysm and arteriovenous fistulae of 0.53% and 0.43%, respectively.[e386]

The incidence of these complications likely reflects the number and size of venous sheaths deployed and the insertion of an arterial pressure line in the setting of intense anticoagulation prior to and following the ablation procedures. In most EP laboratories, patients are fully anticoagulated during and following the ablation procedure with interruption of anticoagulation for less than four to six hours to allow sheath removal.

More recently a growing trend of performing AF ablation on uninterrupted anticoagulation with warfarin has emerged with favorable safety results.[e379,e387,e400,e402,e403,e622–e624] This approach may avoid the large or rapid swings in the level of anticoagulation that can occur with heparinization.

The approach used to gain femoral venous access may impact on the risk of vascular complication. When an inferior approach to femoral vein access is adopted, unnamed but well recognized small medial branches of the femoral artery, which can run across and superficial to the femoral vein, can be penetrated by the Seldinger needle before entry to the femoral vein. When a superior approach is used, there is a potential for a retroperitoneal bleeding complication

where substantial blood loss can occur before becoming clinically evident.

9.9. Acute coronary artery occlusion

Damage to the coronary arteries usually does not occur during left atrial catheter ablation. Acute coronary artery occlusion of the left circumflex coronary artery has been reported in a single case report following RF energy delivery to create a "mitral isthmus" linear lesion.[e625] The diagnosis is made from the 12-lead ECG, which changes according to the distribution of the circumflex artery and its dominance. Depending on the level of sedation, the patient may complain of chest pain. When treatment is required, standard percutaneous therapy for acute coronary occlusion should be initiated.

9.10. Radiation exposure during catheter ablation of atrial fibrillation

Catheter ablation of AF is often a complex and long procedure requiring long fluoroscopy exposure time and often preceded and followed by CT scans. An important, less easily recognized, and rarely considered, potential complication of AF ablation is the delayed effect of the radiation received by the patients, including acute and sub-acute skin injury,[e1–e3] malignancy, and genetic abnormalities.[e626–e635] Prolonged fluoroscopy is required for the various components of the procedure, such as double transseptal catheterization, PV angiography, and extensive RF applications. One study reported mean fluoroscopy durations for AF procedures of greater than 60 minutes in both left anterior oblique (LAO) and right anterior oblique (RAO) projections. The mean peak skin doses were 1.0 ± 0.5 grays (Gy) in RAO and 1.5 ± 0.4 Gy in LAO projection. This translates into a lifetime risk of excess fatal malignancies (normalized to 60 minutes of fluoroscopy) of 0.07% for female and 0.1% for male patients. The relatively low radiation exposure to the patients in this study despite the prolonged fluoroscopy durations was attributable to the state-of-the-art very low frame rate pulsed fluoroscopy, the avoidance of magnification, and the optimal adjustments of fluoroscopy exposure rates. The resulting lifetime risk of malignancy was thus within the range previously reported for ablation of junctional reentry tachycardias. However, this study demonstrated that catheter ablation of AF required significantly greater fluoroscopy duration and radiation exposure than simpler catheter ablation procedures. Thus, and especially because AF ablation procedures often need to be repeated, electrophysiologists should make every attempt to minimize radiation exposure and should recognize that obesity is a major determinant of radiation exposure.[e636]

Increasing availability and familiarity of electrophysiologists with 3D mapping systems[e308,e455,e637–e641] may significantly reduce fluoroscopy time and the need for biplane fluoroscopy. This can only be achieved, however, by an awareness of the importance of reducing fluoroscopy time, and therefore radiation exposure, by the operator. Although it is hypothesized that use of remote navigation systems will reduce radiation exposure to patients and operators, this remains unproven. Another option to minimize radiation exposure to the operator and also to alleviate the orthopedic implications of conventional lead aprons is the use of a radioprotection cabin or a suspended lead apron (Zero Gravity).[e642]

9.11. Pericarditis

Pericarditis following catheter ablation of AF is a rarely reported but almost certainly an under-diagnosed consequence of AF ablation. When transmural lesions are generated during catheter ablation of AF, some epicardial inflammation, and therefore some pericarditis, is inevitable. However, more extensive pericarditis may complicate AF ablation procedures acutely and with some delay. These presentations include Dressler's syndrome,[e643] pericarditis leading to cardiac tamponade,[e644] and constrictive pericarditis.[e645] All of these three cases presented between 18 days and three months after their RF ablation procedures. The standard international practice for a short hospital stay after AF ablation procedures may well contribute to an underappreciation of early post ablation pericarditis.

One recent study with a protocol that required their patients to remain in hospital for one week after the ablation found a relationship between post-procedural pericarditis and the timing and long-term behavior of recurrent AF. Immediate recurrence of AF ($\leq$3 days of the ablation) was associated with increased inflammatory markers with pericarditis seen in 33% of these patients.[e646] However, fewer of this group had recurrent AF at six months after the ablation compared with those patients in whom the AF recurred later than three days after the procedure. This suggests an inflammatory mechanism for the immediate recurrence rather than atrial to pulmonary venous reconnection.

9.12. Mitral valve trauma and circular catheter entrapment

Entrapment of a circular multielectrode mapping catheter by the mitral valve apparatus is an uncommon but well established complication of AF ablation.[e647–e652] It results from inadvertent positioning of the circular electrode catheter near to the mitral valve or into the left ventricle, often during attempts to position the circular mapping catheter into the left inferior PV. This complication is usually suspected when attempts to reposition the catheter into another PV are met with resistance. When suspected, it is important to confirm the diagnosis with echocardiography. Although successful freeing of the catheter has been reported with gentle catheter manipulation and advancing the sheath into the ventricle in two patients,[e648] there have also been a number of cases reported in which the mitral valve apparatus and/or papillary muscles are torn during attempts to free the catheter.[e649,e652] There also have been several cases reported in which the distal tip of the circular catheter broke

off during attempts at catheter removal and had to be subsequently removed either with a snare or with an open surgical procedure.[e650,e651] We recommend that if gentle attempts to free the catheter fail, elective surgical removal of the catheter should be performed. It is important for all EPs who perform this procedure to be aware of this rare but potentially serious complication. Every effort should be made to be certain that the circular catheter is kept as far as possible from the mitral valve, with particular care taken when approaching the left inferior PV.

9.13. Mortality risk of AF ablation

Although AF ablation is generally considered to be safe, devastating complications may occasionally occur, some of them ultimately leading to death. In a recent survey, death was reported in 32 of 32,569 (0.1%) patients undergoing 45,115 AF ablation procedures worldwide.[e549] The most frequent cause of death was cardiac tamponade, accounting for 25% of the deaths, of which 3% occurred later than 30 days after the procedures. Stroke was responsible in 16%, of which 6% occurred later than 30 days. Atrio-esophageal fistula also accounted for 16% of the deaths, with massive pneumonia responsible for 6%. Less common causes of death observed in the peri-procedural phase included myocardial infarction, irreversible torsades de pointes, septicemia, sudden respiratory arrest, extra-pericardial PV perforation, occlusion of both lateral PVs, hemothorax, and anaphylaxis, which were each responsible for 3% of early deaths. Twenty-two percent of all deaths occurred more than 30 days after the procedure. Among identified causes of late death were asphyxia from tracheal compression secondary to subclavian hematoma, intra-cranial bleeding, acute respiratory distress syndrome, and esophageal perforation from intra-operative TEE probe, with each cause contributing 3% of all late deaths. Awareness about the risk of death and the possible causes may help physicians set more appropriate and efficient standards for procedural safety and need to be considered in the patient decision-making process.

10. Training requirements and competencies

10.1. Overview

The strategies, specific methods, and technology pertaining to ablation of AF are evolving. Accordingly, the guidelines for training to perform this procedure must be flexible in recognition of different approaches and technologies that will change with advances in the field. Training for ablation of AF should encompass six fundamental principles: 1) appropriate selection of patients, 2) knowledge of the anatomy of the atria and adjacent structures, 3) conceptual knowledge of strategies to ablate AF, 4) technical competence, 5) recognition, prevention, and management of complications, and 6) appropriate follow-up and long-term management.

The training required in each of these areas differs from other ablation procedures because in comparison, ablation of AF is technically more difficult, is associated with greater risks, and requires more careful follow-up.

10.2. Appropriate selection of patients

Trainees should recognize clinical attributes that may increase the difficulty of a transseptal puncture, increase the risk of the procedure, and affect long-term outcomes. These factors are discussed in sections 8 and 9 of this document. The trainee should also develop the judgment to decide whether conscious sedation or general anesthesia would be most appropriate for the case under consideration. It is also important to assess the severity of symptoms related to AF and the potential benefit of an ablation procedure. Trainees should be experienced in counseling patients about the potential risks and benefits of an ablation procedure and should be able to apply this knowledge for recommendations specific to the needs of individual patients. They should also take into consideration the prior use of antiarrhythmic drugs and pharmacologic alternatives to ablation of AF.

It is also important for electrophysiologists involved with catheter ablation to be knowledgeable about surgical ablation techniques for AF. In particular, electrophysiologists who perform AF ablation procedures must be aware of the indications, techniques, and outcomes of surgical approaches for ablation of AF. This applies both to the new minimally invasive surgical approaches, AF surgery combined with other cardiac surgical procedures, and the Cox-Maze-III procedure (see section 11: Surgical Ablation of AF).

10.3. Anatomy of the atria and adjacent structures

Detailed knowledge about the anatomy of the LA and its adjacent structures is crucial for performing the technical aspects of transseptal puncture and cannulation, LA mapping, and isolation of the PVs or modification of the substrate that sustains AF. The trainee must recognize the anatomic relationship of the atria, SVC and PVs to the pulmonary arteries, aorta, mitral annulus, phrenic nerves, sympathetic and parasympathetic innervation, esophagus, and other mediastinal structures. These anatomic relationships affect the ability to perform the procedure successfully and to avoid complications.

10.4. Conceptual knowledge of strategies to ablate atrial fibrillation

Trainees should understand the pathophysiology of AF and its implications for strategies to ablate AF. This includes the role of the PVs, the SVC the musculature of the LA, and the potential impact of autonomic stimulation. They should understand the rationale for isolation of the PVs and elimination of foci that trigger AF and the basis for broad circumferential ablation of tissue or elimination of fractionated potentials that appear to alter the substrate that sustains AF.

10.5. Technical competence

The technical skills needed for ablation of AF are substantial. These include transseptal needle puncture and cannulation of the LA, precise manipulation of the catheter for mapping and ablation, identification of the pulmonary ostia, adjustment of the energy used for ablation, and the appropriate use of fluoroscopy, radiographic contrast for imaging, 3D mapping systems or intra-cardiac echocardiography. There are substantial differences among laboratories in the use of radiographic contrast imaging, electroanatomic mapping or intra-cardiac echocardiography, and the number and types of catheters used to identify electrical endpoints and to perform ablation. The degree of expertise gained in the use of a specific technology will depend on where training is completed. Nonetheless, trainees should be expected to understand the potential advantages and limitations of these systems and should have the ability to interpret basic images and electrical recordings obtained from these different methodologies. They should be well versed in the principles of radiation safety for patients and the medical personnel who perform ablation procedures.

Training programs should emphasize the interpretation of intra-cardiac EGMs for recognition of PV potentials and determination of when electrical isolation of a PV has been achieved, the role of CS pacing in the differentiation of far field EGMs from PV potentials, identification of fractionated low-amplitude LA potentials, and techniques required to map and ablate right and/or LA tachycardias or atrial flutter. Concepts related to entrainment are especially important. Trainees need to be skilled in identifying the presence, mechanism, origin, and ablation of other supraventricular tachycardias that may act as triggering mechanisms for AF such as AV nodal reentrant tachycardia and AV reentrant tachycardia.

Most laboratories use RF energy to ablate AF; however, many laboratories use cryothermal balloons. Trainees should be familiar with the advantages and limitations of each energy source and associated delivery systems. The use of remote navigation technologies is also evolving. As these or other technical advances become integrated into common usage, their utility and limitations should be incorporated into the body of knowledge that is required for trainees.

The American College of Cardiology/American Heart Association 2008 update of the clinical competence statement on invasive electrophysiology studies, catheter ablation and cardioversion proposed a minimum of 30–50 AF ablation procedures for those who undergo fellowships in clinical cardiac electrophysiology.[e653] This recommendation is in accordance with the Canadian Guidelines, which also recommend that trainees perform 15–20 complex flutter ablations.[e654] These numbers underestimate the experience required for a high degree of proficiency. Exact numerical values are difficult to specify because technical skills develop at different rates. Nonetheless, comparisons of high and low volume centers suggest that outcomes are better at centers that have performed more than 100 procedures.[e386] Trainees who intend to perform ablation of AF independently might consider additional training after the standard fellowship is completed if they performed less than 50 AF ablation procedures during training.

Electrophysiologists who have already completed fellowship training and are proficient in performing ablation procedures may wish to develop the skills required to perform ablation of AF. The technical proficiencies required for these procedures exceed those employed for most standard ablation procedures. Moreover, the risks of ablation procedures for AF are greater than other common procedures performed in the electrophysiology laboratory. Accordingly, electrophysiologists who have already completed a fellowship and choose to undergo training for ablation of AF should observe colleagues with a high degree of expertise, and a period of supervision is advisable. In the absence of definitive data, numerical requirements are arbitrary, but as a guideline, it seems appropriate for experienced electrophysiologists to be supervised when they begin to perform these procedures. The exact number may depend on prior experience with transseptal punctures and cannulation of the LA. Electrophysiologists should perform several ablation procedures for AF per month if they intend to remain active in this area. All electrophysiologists should track the outcomes of their procedures and verify that appropriate follow-up has been arranged. It would be inappropriate for cardiologists who are not trained in electrophysiology to consider performing ablation procedures for AF. The selection of patients and interpretation of atrial flutter and other ATs that are often seen in patients with AF require training that is unique to electrophysiology fellowships.

10.6. Recognition, prevention, and management of complications

As previously discussed, ablation of AF is associated with substantial risks that must be recognized. Training programs must emphasize techniques that reduce these risks. This includes careful manipulation of catheters, appropriate use of anticoagulation, modification of energy delivered on the posterior wall of the LA, and the risk of applying energy within the PVs or LA appendage. Fellows should be trained to suspect cardiac tamponade or internal bleeding as a common cause of hypotension. Training should also include management of these complications. It is preferable for fellows to undergo training in pericardiocentesis. If trainees do not gain proficiency in pericardiocentesis, they must recognize the need for immediate access to a physician who has mastered these skills. They should understand the risks of conscious sedation, which include hypoventilation, aspiration, and respiratory arrest. They should also recognize the delayed time course associated with the development of atrial-esophageal fistulas or PV stenosis, as well as the appropriate steps needed to diagnose and manage these problems.

10.7. Appropriate follow-up and long-term management

Management of patients after hospital discharge can be complex and requires commitment from the following physician. Individuals undergoing training in AF ablation should participate in a longitudinal clinic in which these patients are followed. Experience must be gained in diagnosis and management of post-procedure complications, including esophageal injury, PV stenosis, and late hematoma, pseudoaneurysm or AV fistula. Since the prevalence of some of these complications is very low, it is possible that the trainee will not have firsthand experience with patients. Therefore, supplementation of clinical experience with didactic presentations on diagnosis and management of post-ablation complications is required. Prophylaxis against and management of post-procedure atrial arrhythmias, including timing of repeat ablation and use of concomitant antiarrhythmic drugs, must be taught to trainees. Finally, the training experience must address the risk–benefit decision-making regarding the use of intermediate and long-term anticoagulation therapy.

11. Surgical ablation of atrial fibrillation

11.1. Development of the Cox-Maze procedure

Following experimental investigation, the Maze procedure was introduced for the surgical treatment of AF in 1987 by Dr. James Cox.[e24,e655,e656] This procedure was designed to interrupt all macro-reentrant circuits that might potentially develop in the atria, thereby precluding the ability of the atrium to flutter or fibrillate. Fortuitously, the operation also isolated all of the PVs and the posterior LA. In contrast to previous procedures, such as the corridor and the left atrial transection procedures,[e657,e658] the Cox-Maze procedure successfully restored both atrioventricular synchrony and sinus rhythm and decreased the incidence of late stroke.[e659] This effect was attributed to both AF control and amputation of the LA appendage. The operation involved creating multiple strategically placed incisions across both the right and left atria. The surgical incisions were placed so that the sinus node could "direct" the propagation of the sinus impulse throughout both atria. It also allowed most of the atrial myocardium to be activated, resulting in preservation of atrial transport function in most patients.[e660] The final iteration of this procedure, the Cox-Maze III, became the standard for the surgical treatment of AF.[e661–e664] Long-term outcomes of 198 patients who underwent the Cox-Maze III procedure for treatment of paroxysmal (N = 113) or persistent/longstanding persistent AF (N = 85) have been reported. The mean follow-up was 5.4 ± 2.9 years. Among the 112 patients who underwent surgery only for AF treatment, 96% were in sinus rhythm with or without antiarrhythmic drug therapy and 80% were in sinus rhythm and free of antiarrhythmic drug therapy at last follow-up. Among the 86 patients who underwent AF surgery in conjunction with other cardiac surgery, 97.5% were in sinus rhythm with or without antiarrhythmic drug therapy and 73% were in sinus rhythm and free of antiarrhythmic drug therapy. The incidence of major complications among the 112 patients who only underwent AF surgery was 10.7%. Among these were two perioperative deaths and two perioperative strokes or TIAs. Nine patients (8%) required pacemaker placement. The incidence of major complications among the 86 patients who only underwent AF surgery at the time of other cardiac surgical procedures was 13.9%. Among these were one perioperative death and one perioperative stroke. Twenty patients (23%) required pacemaker placement. In considering the results of these early reports of cardiac surgery for treatment of AF, it is now recognized that these patients did not undergo rigorous follow-up by present standards. Most of the rhythms were documented only by means of a mailed questionnaire or telephone interview. Very few of the patients had any monitoring more than an ECG to document their rhythm.[e665] It is clear to all that the pioneering work of Dr James Cox was invaluable in paving the way for the current less invasive Cox-Maze IV operation, other surgical approaches for AF ablation, as well as the field of endocardial catheter ablation of AF.

11.2. New surgical ablation technology

Despite its efficacy, the Cox-Maze procedure did not gain widespread application. Few cardiac surgeons were willing to add the operation to coronary revascularization or valve procedures due to its complexity, technical difficulty, and risks. In an attempt to simplify the operation and make it more accessible to the average surgeon, groups around the world replaced the incisions of the traditional cut-and-sew Cox-Maze procedure with linear lines of ablation. These ablation lines are created using a variety of energy sources including RF energy, cryoablation, and high-intensity focused ultrasound.[e666,e667]

The various technologies can be organized into two major groups: those that use a unipolar energy source and those that use a bipolar clamp. The unipolar energy sources (cryosurgery, unipolar RF energy, HIFU) radiate either heat or cold from a single source. The unipolar devices do not reliably provide the surgeon with an indication of when the ablation results in a transmural lesion. Since most of these ablation systems were released clinically without dose–response studies, their use has led to occasional collateral cardiac and extracardiac damage.[e575,e668,e669] Moreover, unipolar energy sources have had difficulty creating transmural lesions when used from the epicardial surface on the beating heart.[e670–e675] This is because the circulating intracavitary blood pool makes transmural lesions difficult to achieve.[e676] HIFU results in a focused delivery of energy, avoiding collateral damage seen with other unipolar devices. However, these energy sources have a fixed depth of penetration, which may make their use in pathologically thickened atria problematic.

Bipolar RF ablation has been able to overcome some of these shortcomings.[e677–e679] Since energy is delivered between two closely approximated electrodes embedded in the jaw of a clamp device, the energy is focused and results in discrete lesions. The energy is confined to within the jaws of the clamp, reducing the possibility of collateral cardiac or extra-cardiac damage. By measuring the tissue conductance between the two electrodes, algorithms have been developed that help predict lesion transmurality in the experimental laboratory.[e677,e680,e681] The weakness of these devices is that they can only ablate tissue that can be clamped within the jaws of the device. This has limited the potential lesion sets, particularly in the beating heart. Moreover, in the clinical situation, multiple ablations have often been required to achieve entrance and exit block. These devices have been incapable of fully ablating the right and LA isthmus and have required adjunctive unipolar ablation to perform a complete Cox-Maze III lesion set.[e682]

Nevertheless, the development of these new ablation technologies has benefited the surgical treatment of AF by making a technically difficult and time-consuming operation easier for all cardiac surgeons to perform. At present, more than 50% of the patients undergoing open-heart surgery who have AF are offered concomitant AF surgery.[e683] Replicating the full Cox-Maze lesion set with linear lines of ablation has been shown to be both feasible and clinically effective. A number of groups have reported excellent results with ablation-assisted Cox-Maze procedures.[e665,e682,e684–e686]

The largest of these experiences included 282 patients who underwent the Cox-Maze IV procedure over a seven-year period with either paroxysmal (N = 118), persistent (N = 28), or longstanding persistent AF (N = 135).[e665] One hundred and twenty-four patients (44%) underwent surgery only for AF treatment, and 158 patients (56%) had other cardiac surgery performed, which included mitral valve surgery in approximately 50%. Among the entire patient cohort, 89% of patients were in sinus rhythm with or without antiarrhythmic drug therapy, and 78% were in sinus rhythm and free of antiarrhythmic drug therapy at 12-month follow-up. In contrast to early studies of surgical AF ablation, more intensive monitoring was performed with Holter monitors every three months in 70% of patients. The incidence of major complications was 11%, including an operative mortality of 2% and a 1.7% incidence of stroke. Pacemakers were implanted in 9% postoperatively. A propensity analysis, matching patients who underwent an ablation-assisted Cox-Maze with those having had a traditional cut-and-sew Cox-Maze III, showed no differences in freedom from AF at 3, 6, and 12 months.[e687]

Currently the limitations of the energy delivery devices and the attempt to deploy them through minimal access incisions or ports place constraints on the location and number of ablation lesions that can be performed. The impact of these alternative lesion patterns and the less invasive surgical approaches on results requires further observational prospective analysis and randomized trials.

We recommend that the term "Maze" procedure is appropriately used only to refer to the biatrial lesion set of the Cox-Maze operation. It requires ablation of the RA and LA isthmuses. Less extensive lesion sets should not be referred to as a "Maze" procedure, but rather as a surgical AF ablation procedure. In general, surgical ablation procedures for AF can be grouped into three different groups: (1) a full Cox-Maze procedure, (2) PVI alone, and (3) PVI combined with left atrial lesion sets.

11.3. Surgical atrial fibrillation ablation concomitant to other heart operations

In patients undergoing cardiac surgery, the issue that prior AF might place the patient at risk for early and late mortality has not been fully resolved. Patients who have AF before cardiac surgery have been shown to be at an increased risk, and are generally older, have worse ventricular function, and other comorbidities.[e688–e691] Recent studies have tried to assess whether AF is an independent risk factor for death. Late survival was reduced as determined from propensity-matched studies and multivariable analysis in patients undergoing coronary artery bypass grafting.[e690,e691] Similar large-scale propensity matched analyses have not been performed in other patient cohorts, but several studies have reported that patients with AF who are undergoing aortic valve replacement (AVR) and mitral surgery are older, have more cardiac and noncardiac comorbidities, and also have an increased long-term morbidity and mortality.[e688,e689] Therefore, AF may not be just a marker for high-risk patients, but it may be an independent risk factor for increased long term morbidity and mortality. We recognize that until large randomized prospective clinical trials are performed, this remains an unproven hypothesis. Assuming AF does increase late morbidity and mortality, AF surgery may improve survival or reduce late adverse cardiac events.

There have been six prospective randomized clinical trials of surgical AF ablation performed in conjunction with other cardiac surgical procedures.[e692–e697] These trials randomized 70, 30, 97, 43, 69, and 43, patients, respectively, either to a concomitant AF surgical procedure or to cardiac surgery alone without an AF ablation procedure. Importantly, a variety of left atrial lesion sets and ablation tools were used in these trials including RF, microwave, and cryoablation. The largest of these trials was reported in 2005.[e694] In this study 97 patients referred for mitral surgery with six months or more of continuous AF were randomized to receive mitral surgery and left atrial RF ablation (RFA) or mitral valve surgery alone. At 12-month follow-up, sinus rhythm was present in 44% of RFA patients and 4.5% of controls ($P < .001$). Restoration of sinus rhythm in the RFA group was accompanied by greater improvement in mean shuttle-walk distance compared with controls ($P = .003$).

Patients randomized to receive RFA had similar rates of post-operative complications and deaths as control patients. Each of the other five randomized trials also showed higher rates of sinus rhythm in the patients undergoing AF surgery in the absence or presence of antiarrhythmic medications versus controls (79%, 82%, 80%, 73%, and 57% versus 27%, 21% 33%, 43%, and 4%, respectively).[e692,e693,e695–e697] This wide range of efficacy is likely due to the differing effectiveness of the energy sources, the differing lesion sets, the small number of patients in each series, and surgeon experience. A biatrial Cox-Maze procedure was used in only three of the studies. None of these studies was statistically powered to determine a difference in survival between the two groups.

More recent retrospective studies have documented success using a variety of different technologies, most commonly bipolar RF ablation, for the treatment of AF with concomitant mitral or other cardiac operations.[e682,e698–e706] In these series, success rates have varied between 65% and 95% at six months.[e706] There has been great variation in the results between different centers. This can be attributed to many factors, including surgeon experience, differing lesion sets, and the use of different ablation technologies. The precise lesion set has had the biggest impact on late results. Generally, more extensive lesion sets have had better long-term freedom from AF. There has been one randomized study in which 105 patients undergoing AF or valve surgery were randomly assigned to three groups: PVI alone or two more extensive LA lesion sets, both of which included a linear ablation line to the mitral valve (LA isthmus).[e707] Mean follow-up was 41 ± 17 months. The percent of patients who were in normal sinus rhythm at last follow-up was 76% in the two more extensive LA lesion sets, but only 29% in those patients who had PVI only. The poor efficacy of PVI alone in patients with longstanding AF and mitral valve disease has been supported by a number of other retrospective studies.[e708–e710] In the largest of these studies, 101 patients underwent PVI with a spherical cryoprobe. At last follow-up, normal sinus rhythm was seen in only 53% of patients.[e709] Normal sinus rhythm without antiarrhythmic drugs was present in 25 patients. One of the largest reports to date reported on the outcomes of 575 patients who underwent surgical treatment of AF at a single institution between 1991 and 2004.[e703] Among these 35 patients, 6% had AF as their only indication for surgery. In contrast, 75% required mitral valve surgery. Procedures included PVI alone (N = 68, 12%), PVI with left atrial connecting lesions (N = 265, 46%), and Cox-Maze (N = 242, 42%). There were 12 in-hospital deaths (2%), a 1.9% incidence of stroke or TIA, and a 5% need for reoperation for bleeding. Fifty patients (8.7%) required pacemaker implantation. At one year, 18% of patients remained on antiarrhythmic drug therapy and 76% were free of AF by ECG. Patient-related risk factors for increased prevalence of AF at follow-up included older age, larger LA, and longer duration of preoperative AF. The Cox-Maze procedure and lesion sets resembling it created with alternative energy sources had a similar low prevalence of late post-operative AF. A large meta-analysis of retrospective studies has also demonstrated significantly better late results with biatrial lesion sets when compared to LA lesion sets alone.[e711] A recent study reported the outcomes of a prospective multicenter clinical trial of the Synergy Ablation System, which employs bipolar RF energy.[e712] Fifty-five patients underwent concomitant AF surgical ablation using a Cox-Maze IV procedure at the time of other cardiac surgery. At six months of follow-up, 74% of patients were AF free off antiarrhythmic drug therapy. The incidence of a major pre-specified complication was 9%.

The primary advantage of adding a full Cox-Maze procedure to concomitant surgery, aside from the resumption of sinus rhythm, is a reduction in the risk of stroke.[e659] For patients with a classic Maze operation, the risk of stroke at 10 years has been less than 1% in large published series.[e659,e661,e662,e664] Whether this is related to resumption of sinus rhythm and atrial systole or due to closure or removal of the LA appendage or continued use of warfarin in a small subset of patients is not certain. It is important to recognize that all patients received warfarin for several months following their surgical AF ablation procedure, and thereafter anticoagulation is typically managed by referring cardiologists. The stroke reduction from adding a Cox-Maze procedure also applies to patients who undergo mitral valve surgery, including replacement with a mechanical valve, which requires continued anticoagulation with warfarin.[e713] The success of stroke reduction using the newer techniques has not yet been investigated.

A recent report from the STS data base examined the question as to whether concurrent surgical AF correction procedures were associated with an increased risk of morbidity or mortality among AF patient undergoing mitral valve surgery.[e683] A retrospective review of outcomes for 67,389 patients with AF having cardiac surgery between January 2004 and December 2006 was conducted. Multivariable logistic regression was performed to assess whether concomitant AF correction procedures increased risk in the mitral valve surgery cohort. Overall, 38% (25,718 of 67,389) of patients with AF undergoing cardiac surgery had an AF correction procedure, increasing from 28.1% in 2004 to 40.2% in 2006. Surgical AF correction was performed in 52% (6,415 of 12,235) of mitral valve surgery patients, 28% (2,965 of 10,590) of those having aortic valve surgery, and 24% (5,438 of 22,388) of those having isolated coronary artery bypass grafting. After adjusting for differences in preoperative characteristics, mitral valve surgery patients with a surgical AF correction procedure did not have a significantly higher risk of mortality (adjusted odds ratio, 1.00; 95% CI, 0.83 to 1.20) or major morbidity. The risk for new permanent pacemaker implantation was higher (adjusted odds ratio, 1.26; 95% CI, 1.07 to 1.49) in the AF correction with mitral valve surgery group.

11.4. Stand-alone operations for atrial fibrillation

There has been over two decades of experience with operations performed solely for treatment of AF when additional cardiac surgical procedures are not performed (stand-alone operations). Although the term "lone AF" has been commonly employed in the surgical literature to refer to stand-alone procedures for AF, this has resulted in some confusion as cardiologists and electrophysiologists use the term "lone AF" to refer to a highly selected subgroup of AF patients who are young and do not have evidence of structural heart disease. The largest reported series of stand-alone operations for AF has been the 112 patients who underwent the Cox-Maze III procedure by Dr. James Cox and colleagues cited earlier.[e662] Among the 112 patients 96% were in sinus rhythm with or without antiarrhythmic drug therapy, and 80% were in sinus rhythm and free of antiarrhythmic drug therapy at last follow-up. There was one late stroke in this group, and 88% of patients were off chronic anticoagulation at last follow-up. The only risk factor for late recurrence was the preoperative duration of AF.[e662]

With the introduction of new ablation technology, including bipolar RF energy and new cryoablation systems, there has been renewed interest in less invasive procedures for stand-alone AF ablation. These new tools can be used in the open chest or through small incisions between the ribs. When used in the open chest and a full biatrial Cox-Maze lesion set is performed, the procedure has been termed the Cox-Maze IV procedure. Techniques for a Cox-Maze IV procedure through a small, right inframammary incision have been perfected. As noted in the earlier section on new surgical ablation technology, the outcomes achieved with the Cox-Maze IV procedure are similar to those achieved with the Cox-Maze procedure. Importantly, the cross clamp times are shorter with the Cox-Maze IV procedure.[e665]

The minimally invasive surgical approach using video-assisted PV ablation and exclusion of the left atrial appendage was first described in 2005.[e714] A bipolar RF clamp was used for PVI on the beating heart in 27 patients, among whom 18 had paroxysmal AF. Among the 23 patients followed for more than three months, 21 (91%) were free of AF and 65% were off all antiarrhythmic drugs. There were four major complications but no deaths and no pacemakers were implanted. A larger series of 50 patients predominantly with paroxysmal AF underwent a "box" isolation of all four PVs using epicardial microwave energy performed endoscopically on the beating heart.[e715] At last follow-up, 25% of patients were on amiodarone, 5% on propafenone, and 50% on warfarin; 79.5% of patients were in sinus rhythm. The freedom from symptomatic AF and re-intervention at last follow-up was 49%. There were no in-hospital deaths, one late death, and a 4% major complication rate, including diaphragmatic paralysis. An additional ablation strategy that has been reported is minimally invasive PVI and partial autonomic denervation.[e716] This study reported the outcomes of 74 patients who underwent video-assisted bilateral PVI with confirmation of block and partial autonomic denervation. In this study, success was defined as freedom from AF more than 15 seconds in duration with longer-term monitoring. At six months follow-up, 84% of patients with paroxysmal AF were AF free and 57% of patients with persistent or longstanding persistent AF were AF free. There was one death, one hemothorax, one case of transient renal insufficiency, and one patient with a transient brachial plexopathy. A second larger report from this group in 114 patients reported that 72%, 46.9%, and 32% of patients with paroxysmal, persistent, and longstanding persistent AF were free of AF and off antiarrhythmic medications at 195 days of follow-up.[e717] Another single-center study experience with minimally invasive PVI and autonomic ganglia ablation in 45 patients reported that 65% of patients were free of recurrence of any atrial arrhythmia greater than 30 seconds in duration at 12-month follow-up. There were no deaths, one phrenic nerve injury, and two pleural effusions.[e718] The results of these and other trials cited earlier in this section have made it clear that a more extensive lesion set than PVI alone is required for successful surgical treatment of persistent and longstanding persistent AF.

The largest challenge to replicating the Cox-Maze III lesion set on the full beating heart is making the connection to the mitral annulus. The other connecting lesions can be done through the transverse sinus. When connection lines to the mitral annulus are added, however, the success rates are shown to be comparable with the cut-and-sew Maze.[e719] In traditional techniques, the connection to the mitral valve is ablated across the left atrial isthmus. However, there are three inhibitors to doing this on the full beating heart. First, the traditional connection is to the posterior annulus, but visualization behind the full beating hearts' LA is very limited. Second, there is the risk of collateral damage to the circumflex coronary artery overlying the mitral valve. Third, the CS, which is used as the epicardial landmark for the mitral annulus, is unreliable, and may leave a gap.[e720] This leads to a significant risk of incomplete ablation or introducing atrial flutter, because of reentry or electrical bridging by tissue.[e223,e721,e722]

To address these problems, the Dallas Lesion Set was developed.[e723–e725] The set replicates the left atrial lesions of the Cox-Maze III. Early results have been published on 30 patients.[e726] The group included 10 patients with persistent AF, and 20 patients with longstanding persistent AF. Electrocardiographic long-term monitoring and the use of antiarrhythmic drug data were collected six months postoperative, and follow-up was 100%. Procedural-related complications did not occur during follow-up, nor were there any deaths. At six-month follow-up, 90% in persistent AF patients and 75% in longstanding persistent AF patients were in sinus rhythm. Antiarrhythmic drug therapy was continued in 22% of patients

with persistent AF and 53% of patients with longstanding persistent AF cases. Further unpublished results of a multicenter registry including 124 patients showed less optimal safety assessment, but outcomes remained satisfactory (unpublished data provided by J.R.E.). Operative mortality was 0.8%, and procedure-related major complications occurred in 10% (renal failure, pericarditis, pneumothorax, pleural effusion, reoperation for bleeding). After six months, sinus rhythm was achieved in 71%–94%, depending on previous catheter ablation and measurement by ECG or long-term monitoring. One-year success rate obtained by long-term monitoring demonstrated a success rate of 63% in a group that had previously undergone catheter ablation (N = 21).

In considering the results of stand-alone surgical AF ablation procedures, it is important to recognize that there have been no randomized studies performed comparing the stand-alone surgical treatment of AF with endocardial catheter ablation procedures. Further frontiers include investigating the outcomes of hybrid ablation strategies.[e727]

11.5. Surgical ablation of AF: summary and current indications

In summary, while surgery for AF has been performed for two decades, prospective multicenter clinical trials are needed to better define the relative safety and efficacy of various surgical tools and techniques. It is critical for future studies to better document the possible survival benefits of adjunctive AF surgery. At present, an ongoing randomized National Institutes of Health (NIH) multicenter trial is examining the efficacy of surgical ablation in patients with persistent AF and mitral valve disease. Moreover, surgeons need to adopt consistent definitions of procedural success and follow-up methodology, as defined in this and previous consensus documents, in order to compare the different surgical series and the surgical results to catheter ablation.[e1,e728] The type and frequency of follow-up have varied widely between series. The true success rates of these procedures are likely to be lower than have been reported if more extensive monitoring is performed in the future.[e450] Even considering these shortcomings, the Cox-Maze procedure has had good long-term results when used as a stand-alone procedure or when performed as a concomitant procedure in patients undergoing other indications for cardiac surgery. The advent of ablation technology has simplified the surgical treatment of AF and expanded the indications, particularly for concomitant AF procedures in patients undergoing other cardiac surgery. Minimally invasive and hybrid approaches could expand the indications for stand-alone surgery AF in the future.[e727]

Shown in Table 2 and described in Section 3 of this document are the indications for surgical ablation of AF developed by this Task Force group. Based on the results of clinical trials and clinical experience, we feel that it is appropriate to consider all patients with symptomatic AF undergoing other cardiac surgery for AF ablation. Importantly, this assumes that there is a reasonable chance for success, and the surgery is performed by an experienced surgeon. An LA procedure should consist of PVI, ideally with a connecting lesion to the mitral valve annulus. A biatrial procedure should be considered for those with persistent and longstanding persistent AF. When it can be safely performed, complete occlusion of the LA appendage should be considered.

The referral of patients for surgery with symptomatic, medically refractory AF in lieu of catheter ablation remains controversial. There have been no head-to-head comparisons of the outcomes of catheter and surgical ablation of AF. The decision-making in these instances needs to be based on each institution's experience with catheter and surgical ablation of AF, the relative outcomes and risks of each in the individual patient, and patient preference.

12. Clinical trial considerations

12.1. Overview

Despite the tremendous progress that has been made in the development of catheter and surgical ablation of AF, and also in defining the outcomes of these procedures, many questions remain unanswered. Nevertheless, the long-term impact of catheter or surgical AF ablation on major morbidity and mortality, particularly in the setting of underlying disease, is not currently available. Other unresolved questions include, but are not limited to, the following:

1. What is the long-term impact of catheter or surgical AF ablation on stroke risk, the development of heart failure, and major morbidity and mortality?
2. Has the concept of "slowing progression of AF" any clinical value in the context of AF ablation?
3. Is there a comparative effectiveness advantage to catheter based vs surgical interventions?
4. What are the comparative success rates of various ablative techniques in differing patient populations, particularly persistent and longstanding persistent AF?
5. What is the benefit of AF ablation in patients not well represented in clinical trials of AF ablation, including the elderly, women, those with heart failure, African Americans, and those with longstanding persistent AF?
6. Is there an age limit to successful ablative intervention?
7. Are there patients in whom oral anticoagulation can be safely discontinued following ablation, and what is the impact of direct thrombin inhibitors and factor Xa inhibitors on anticoagulation strategies prior to, during and following AF ablation?

8. Is there acceptable rationale for ablation applied as first line therapy for AF?
9. Is ablative intervention cost-effective or is drug therapy more economically efficient?
10. Beyond placebo effect, what is the relative quality of life benefit of ablation vs drug therapy?
11. What are the safety and efficacy outcomes of newer ablation technologies such as cryoballoon and laser balloon ablation?
12. Can useful, robust performance measures characterizing outcomes of ablation be developed?
13. What are the very long-term outcomes (>5 years) of catheter and surgical AF ablation?

12.2. Investigational studies: current and future

These unresolved issues provide the strong incentive for conducting additional clinical trials of specific design to answer critical questions in the ablative arena. These include randomized mortality studies, multicenter outcome trials, comparative effectiveness research, industry-sponsored device approval studies, and carefully constructed single and multicenter registry studies.

12.3. Mortality trials

While large, multicenter randomized clinical trials are expensive and require years for completion, they are mandatory for determining the impact of therapy on mortality and other long-term outcomes. The randomized trial design is most likely to provide an unbiased understanding of the outcomes of specific aspects of ablative intervention and provide information that can be extrapolated to the largest possible number of patients. These studies are appropriately held to a higher standard or burden of proof, and should require the comparison of ablative therapy against best available drug therapy, or other ablative interventions supported by extensive data from preexisting trials. The CABANA trial that is now underway is designed to enroll a sufficiently large number of patients, and continue for a long enough period of time to determine if there is a mortality benefit to catheter ablation of AF.[e118] In addition, the CABANA study will investigate other outcomes of AF ablation and drug therapy including cardiovascular death, occurrence of disabling stroke, serious bleeding and cardiac arrest. Rather than comparing any specific drug therapy against an individual ablative intervention, this trial will examine pharmacologic rate and rhythm control strategies and ablative intervention with the intention of eliminating AF. It is hoped that this study will collect mortality information and will expand our understanding of the role of drug and non-drug therapy in those with advancing age, underlying heart disease, and more established AF, which will be applicable to a broader range of patients commonly seen in real life clinical practice. Finally, this trial will gather information needed for assessing the impact of therapy on quality of life and health care resource utilization.

The EAST trial is likewise gearing up in Europe to examine composite serious endpoints, including mortality and other major morbidities. EAST tests whether early rhythm control therapy, applied on top of usual care, can improve hard outcomes in AF patients compared to usual care alone. In contrast to CABANA, EAST does not compare AF ablation to antiarrhythmic drug therapy, but rather tests whether a structured, early application of rhythm control therapy encompassing ablation, antiarrhythmic drugs, or both can prevent strokes, cardiovascular deaths, acute coronary syndromes, or decompensated heart failure compared to usual care. The rationale for "early rhythm control therapy" has been explained previously.[e729] CABANA and EAST will help to answer the open question whether AF ablation has benefit beyond quality of life.

12.4. Multicenter outcomes trials

The disadvantage of mortality studies is the accompanying cost and length of time required for completion. As such, the science of ablation will be more immediately fostered by a variety of additional smaller, more agile, multi-centered trials. These have the advantage of more quickly providing answers to specific questions as considered earlier. The Radiofrequency Ablation vs Antiarrhythmic drug for AF Treatment (RAAFT) trial, for example, is currently underway to further evaluate the safety and efficacy of RF catheter ablation as first line therapy versus drug therapy in patients with AF. Similar trials in patients with various types of AF or underlying disease, as conducted in consortium research groups, could provide outcomes data more applicable to a wider range of patients, without the limitations of single-center studies or requisite randomization against drug therapy.

Recently, the Institute of Medicine listed AF as one of the foremost U.S. health problems and underscored the need for the assessment of drug versus ablative treatment as one of the most important topics to be pursued in medicine. Furthermore, the National Heart, Lung and Blood Institute has recently sounded a clarion call for Comparative Effectiveness Research in a number of cardiovascular areas. Comparative studies in patients with AF were included as being critically important for the future of health care.

12.5. Industry-sponsored device approval studies

There currently are a number of prospective, randomized clinical trials underway to evaluate the safety and efficacy of AF ablation using investigational catheters and systems as part of FDA and other regulatory agency approval processes. Since most of these investigations are industry sponsored, these studies have almost universally limited enrollment to generally patients with paroxysmal AF. A number of different standard or novel ablation systems are being evaluated as part of these trials that should provide important insights into the safety and efficacy of catheter ablation. These studies are limited, however, by restrictive inclusion and exclusion criteria and the fact that these trials are often carried out in highly experienced centers. Despite these

limitations, industry-sponsored device trials provide very high quality clinical data on the safety and efficacy of ablation technologies, and in doing so have proved invaluable to the clinical community that works to provide optimal patient care.

To date, there have been two large industry-sponsored randomized clinical trials evaluating investigational catheters and systems that have been completed and published in manuscript form or presented at a national meeting.[e279,e505] In addition, there are a number of industry-sponsored trials studying various other investigational devices to gain regulatory approval. Given the concordance of the clinical trial data revealing the superiority of ablation over drugs for symptomatic paroxysmal AF recurrences, and given the difficulty in enrolling and conducting drug versus ablation studies, these newer studies have predominantly been designed to compare the novel device to an existing approved device. We believe that this is appropriate, although there should be careful consideration to the possibility of a downward "creep" in acceptable effectiveness (if each device is numerically inferior but statistically equivalent to the prior comparative device). In the future, we expect that devices designed to treat symptomatic paroxysmal AF patients may be evaluated in non-randomized trials using performance criteria as the endpoint. However, given the rapid evolution of the field of AF management, it should be understood that such performance criteria are not yet fully defined. They will need to take into account: (1) the burden of AF occurrences in the population being studied; (2) the highly variable presentation of clinical recurrences in post-ablation patients; (3) the fact that longer-term (1-5 years) follow-up studies have revealed that late recurrences are a significant problem; and (4) the number one demonstrated cause of both early and late AF recurrences is electrical reconnection of PVs. Particularly because of the latter, there should be consideration given to novel trial designs to directly investigate electrical endpoints that have been clearly demonstrated to be important in clinical outcome. For example, while acute electrical isolation of the PVs is not an adequate endpoint, a performance endpoint such as durable PVI could be considered; that is, patients who undergo an ablation procedure could all undergo a second procedure a few months later (approximately 3 months later) to assess the durability of PVI.

Finally, while most industry sponsored trials have enrolled patients with paroxysmal AF without significant underlying disease, there is at least one industry-sponsored trial in progress examining the role of ablation therapy in the treatment of non-paroxysmal AF patients. Use of clinical trial designs that are not randomized against drug therapy should streamline such future studies.

12.6. Ablation registry studies

National registries to collect ablation data should also be encouraged. Critically, registries provide information concerning "real world" practice patterns and outcomes, which are likely to differ from those in the Randomized Clinical Trials, which were performed on highly selected patients in the most experienced ablation centers. Registries would also facilitate the collection of a sufficiently large patient experience to provide information on the efficacy and safety of AF ablation in the setting of less common underlying conditions, such as hypertrophic obstructive cardiomyopathy or valvular heart disease. An extended understanding of the occurrence of rare complications such as Pulmonary Vein stenosis and atrial esophageal fistula formation are also more likely to be forthcoming from registries.

Registries, however, have limitations, including the fact that the data are typically of lower quality than those generated in Randomized Clinical Trials. Data quality reviews and registry audits are resource-intensive but ensure higher data validity. One of the most achievable goals of registries is to focus on the short-term in hospital complication rate. This data in turn can be used to develop quality performance measures for AF ablation procedures. In this regard, the collection of complete safety data at each center and by each operator should foster appropriate physician introspection and lead to a better understanding of practice patterns and physician and center performance. In contrast, it is more difficult to examine the longitudinal efficacy of AF ablation in a registry format because of the ongoing and long-term follow-up and arrhythmia monitoring that is required. Considerations of the need for informed patient consent for registries that are designed to provide longitudinal assessments of efficacy are also important.

The First and Second Worldwide Survey of AF Ablation, for example, have provided important perspectives on AF ablation outcomes outside of the largest academic centers.[e386,e506] However, these surveys are not ongoing. Other regional registries are under way in different parts of the world, allowing larger data sets of patients and/or involvement of more centers. These registries will further add to our understanding of the impact and outcome of AF ablation in "real-world" settings. During the past several years, efforts have been underway in the United States to investigate the feasibility of developing an AF registry, referred to as SAFARI.[e730,e731] A data collection form and data definitions has been developed in collaboration with the FDA. Efforts are now underway to begin a pilot trial of the SAFARI Registry. The future promise of an atrial fibrillation ablation registry is exemplified by the National Cardiovascular Data Registry (NCDR) database which has now been linked both to Medicare and Medicaid longitudinal administrative data for both the CathPCI registry and the national ICD registry. This linkage will produce long-term outcome data, creating opportunities to play a pivotal role in Post Market Surveillance.

Registries have their greatest benefit if there is equal transparency to their origination, audit processes, and financial support. The potential value of the desired launch of the SAFARI registry in terms of assessing short-term safety and efficacy outcomes and long-term efficacy for the clinical community and patients alike is vast. Efforts are underway to address the barriers to registry development to assure the clin-

ical community accurate assessments of the safety and long term efficacy of atrial fibrillation ablation in the community.

12.7. Standards for reporting outcomes in clinical trials

Arriving at a clear understanding of the safety and efficacy of AF ablation is also impeded by the highly variable definitions and endpoints used in reports from single-centers. There are substantial differences in ablation strategies and lesion sets, endpoints of acute and long-term success, post-ablation blanking periods, intensity, duration and nature of follow-up, frequency and nature of redo procedures and cross-over treatments, as well as variability in accounting for asymptomatic AF and incomplete accounting for complications. As part of the creation of this Consensus Document we have developed a series of Consensus Definitions of various types of AF (Table 1) and also definitions of complications (Table 6), which we encourage those involved in the investigation of AF ablation to adopt. In addition we have provided recommendations concerning the duration of a blanking period, definitions of success, recommendations for minimal monitoring, the timing of repeat procedures and also the definition of a major complication and a device-related complication (Tables 6). The Task Force has reached a Consensus that freedom from AF/flutter/tachycardia off antiarrhythmic therapy is the primary endpoint of AF ablation. For research purposes, time to recurrence of AF/flutter/tachycardia following ablation is an acceptable end point after AF ablation, but may under represent true benefit. However, it also recognized that freedom from AF/flutter/tachycardia at various points following ablation may be a better marker of true benefit and should be considered as a secondary endpoint of ablation. We recommend that single procedure outcomes be reported in all trials of AF ablation. It is our hope that broad adoption of these definitions and recommendations for the design of clinical trials will be useful in the design of future clinical trials. It is only with a standard language that the field of AF ablation can move forward at a rapid pace.

Although it is recognized that the endpoints of a particular study have to be related to the design and purpose of the study, consistent monitoring techniques should be employed. It is critical that an indication of percentage compliance with monitoring requirements be included in every published study of AF ablation. The duration of recommended monitoring may vary depending on the type of AF that was ablated. Recommendations concerning minimal follow-up screening in clinical trials are shown in Table 5. The Task Force acknowledges that monitoring tools are a work in progress and may not be uniformly available or practical for all patients. The suggested monitoring techniques represent a target standard for evaluating procedural efficacy.

The Task Force believes that having all categories of outcomes reported allows the readers to determine the relevant outcome for themselves and may provide important insights into the role of AF ablation in AF management. However, the gold standard for reporting the efficacy of new techniques and technology should remain freedom from AF/flutter/tachycardia of greater than 30 seconds in duration off all antiarrhythmic drugs. It is recognized that based on the particular monitoring system employed in a particular study that a somewhat longer duration of AF may be required to achieve adequate sensitivity and specificity of AF detection. If a duration of AF greater than 30 seconds is employed, a specific rationale for doing so should be provided.

Although Kaplan-Meier analyses are commonly used to report outcomes of AF ablation, particularly in randomized clinical trials, this methodology may underestimate the true effectiveness of AF ablation. This underestimation results from the fact that isolated recurrences of AF following catheter ablation beyond the blanking period are commonly observed. The members of this writing group accept the notion that patients with these types of sporadic recurrences may go on to achieve excellent long-term AF control and clinical benefit from the procedure. Because this pattern of benefit will be missed by a Kaplan-Meier analysis, it is recommended that other alternative and/or secondary endpoints be reported in clinical trials. We would therefore propose that clinical trials also report AF/flutter/tachycardia at various points following ablation.[e116] Another endpoint that should be considered in clinical trials is an assessment of "AF burden" at various points in time during follow-up. It is essential that the method used for monitoring in the treatment and control arms be reported as part of this type of analysis.

It is anticipated that well designed clinical trials will continue to provide a solid evidence base upon which to formulate practice guidelines in the future. The above reporting standards will lead to sufficient comparability to facilitate that goal.

13. Conclusion

Catheter and surgical ablation of AF are commonly performed procedures throughout the world. This document provides an up-to-date review of the indications, techniques, and outcomes of catheter and surgical ablation of AF. Areas for which a consensus can be reached concerning AF ablation are identified and a series of Consensus Definitions have been developed for use in future clinical trials of AF ablation. These include Class I, IIa, IIb, and III recommendations for the appropriate indications of catheter and surgical AF ablation. It is our hope that this document can improve patient care by providing a foundation for those involved with ablation of AF. It is recognized that this field continues to evolve rapidly and that this document will need to be updated. Successful AF ablation programs optimally should consist of a cooperative team of electrophysiologists and surgeons to ensure appropriate indications, procedure selection, and follow-up.

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Author relationships with industry and other entities

Writing group	Employment	Consultant/advisory board	Speakers' bureau/honoraria	Research grant	Fellowship support	Board Mbs/stock options/partner	Others
Josep Brugada	Hospital Clinic, University of Barcelona, SPAIN	St. Jude Medical (b) Biotronik (b) Sanofi-Aventis (b) Sorin (b)	None	St. Jude Medical (b) Biotronik (b) Sorin (b) Boston Scientific (b) Medtronic (b)	None	None	None
Hugh Calkins	John Hopkins Hospital, Maryland, USA	Medtronic (c) Biosense Webster (b) Sanofi-Aventis (b) Toray Medical (b) Atricure (c)	None	Medtronic (d) Boston Scientific (d) St. Jude Medical (d)	Biosense Webster (d)	iRhythm	None
A. John Camm	St. George's University of London, London, UNITED KINGDOM	Sanofi-Aventis (e) Merck (c) Boehringer-Ingelheim (c) Bayer (b) Daiichi Sankyo (b) BMS (b) Servier (c) Novartis (c) Johnson & Johnson (c) Medtronic (b) Boston Scientific (b)	None	Sanofi-Aventis (e) Daiichi Sankyo (f) BMS (e) Pfizer (e) Servier (e) Johnson & Johnson (e)	None	None	None
Riccardo Cappato	Arrhythmia and EP Center, IRCCS Policlinico San Donato, Milan, ITALY	Boston Scientific (c) Biosense Webster (c) Sorin Group (c) Bard (c) St. Jude Medical (c)	Boston Scientific (c) Biosense Webster (c) Sorin Group (c) St. Jude Medical (c)	Boston Scientific (c) Biosense Webster (c) Sorin Group (c) Bard (c) St. Jude Medical (c)	Boston Scientific (c) Biosense Webster (c) Sorin Group (c) St. Jude Medical (c)	None	None
Shih-Ann Chen	Taipei Veterans General Hospital, TAIWAN	St. Jude Medical (b) Medtronic (b) Sanofi-Aventis (b) Boehringer-Ingelheim (b)	None	St. Jude Medical (e)	None	None	None
Harry J.G. Crijns	University Hospital Maastricht, THE NETHERLANDS	Merck (b) Sanofi-Aventis (b) Boehringer-Ingelheim (b)	Merck (b) Sanofi-Aventis (b) Boehringer Ingelheim (b)	Merck (f) Sanofi-Aventis (e) Boehringer Ingelheim (f) Boston Scientific (f)	H	None	None
D. Wyn Davies	Imperial College Healthcare NHS Trust, UNITED KIMGDOM	Medtronic (b)	None	None	None	None	None
Ralph Damiano	Washington University School of Medicine, Missouri, USA	Atricure (d) Medtronic (b)	None	Atricure (c) Medtronic (e)	Edwards Lifesciences (d)	None	None
John DiMarco	University of Virginia Health System, Virginia, USA	Medtronic (c) Novartis (d) Sequel (b) Boston Scientific (b) St. Jude (c)	None	None	None	None	None

Continued

Writing Group	Employment	Consultant/Advisory Board	Speakers' Bureau/Honoraria	Research Grant	Fellowship Support	Board Mbs/Stock Options/Partner	Others
James Edgerton	The Heart Hospital, Baylor, Plano, Texas, USA and Cardiopulmonary Research, Science, and Technology Institute, Texas, USA	Atricure (e) Medtronic (b)	Atricure (d) Medtronic (b)	Atricure (c)	None	None	None
Kenneth Ellenbogen	Virginia Commonwealth University, Virginia, USA	Medtronic (b) Boston Scientific (b) Cardionet (b) Biotronik (b) St. Jude Medical (b)	Medtronic (b) Boston Scientific (b)	Medtronic (d) Boston Scientific (d) St. Jude Medical (b) Biosense Webster (d)	Medtronic (d) Boston Scientific (d) Biosense Webster (d)	None	None
Michael Ezekowitz	Jefferson Medical College, Pennsylvania, USA	Medtronic (b) Eisai (b) Merck (b) Johnson and Johnson (b) Gilead (b) Janssen Scientific Affairs (b) Astra Zeneca (b) Boehringer Ingelheim (d) ARYx Therapeutics (c) Pfizer (c) Sanofi (c) Bristol Myers Squibb (c) Portola (c) Diachii Sanko (c)	Boehringer Ingelheim (d)	None	None	None	None
David Haines	William Beaumont Hospital, Michigan, USA	None	None	St. Jude Medical (b) Medtronic (b) Toray Medical (b)	None	nContact Surgical, Inc. (b)	None
Michel Haissaguerre	Université De Bordeaux, Hôpital Cardiologique, FRANCE	Biosense Webster (b) CardioInsight Technologies (b)	None	None	None	None	None
Gerhard Hindricks	University of Leipzig, Leipzig, GERMANY	Biosense Webster (b) Biotronik (b) St. Jude Medical (b) Siemens (b)	None	Biosense Webster (c) Biotronik (d) St. Jude Medical (f)	None	None	None
Yoshito Iesaka	Tsuchiura Kyodo Hospital, JAPAN	None	None	None	None	None	None
Warren M. Jackman	University of Oklahoma Health Science Center, Oklahoma, USA	Biosense Webster (c) Endosense (c) CyberHeart (b) CardioFocus (b)	Biosense Webster (c) St. Jude Medical (b) Boston Scientific (b) Biotronik (b)	None	None	ACT (c) VytronUS (c) Rhythmia Medical (c)	None
Pierre Jais	Université De Bordeaux, Hôpital Cardiologique, FRANCE	Biosense Webster (b) St. Jude Medical (b) Bard (b)	None	None	St. Jude Medical (c)	None	None
Jose Jalife	University of Michigan, Michigan, USA	Topera (c)	None	None	None	None	None

Continued

Writing Group	Employment	Consultant/Advisory Board	Speakers' Bureau/Honoraria	Research Grant	Fellowship Support	Board Mbs/Stock Options/Partner	Others
Jonathan Kalman	Royal Melbourne Hospital, Melbourne, AUSTRALIA	None	None	Medtronic (e)	St. Jude Medical (d) Medtronic (e)	None	None
David Keane	St. Vincent's University Hospital, Dublin, IRELAND	Sanofi-Aventis (b) Bard (b)	None	None	None	None	None
Young-Hoon Kim	Korea University Medical Center, Seoul, KOREA	St. Jude Medical (d) Bayer AG (b)	None	St. Jude Medical (d)	None	None	None
Paulus Kirchhof	University of Birmingham Centre for Cardiovascular Sciences, Birmingham, UNITED KINGDOM	3M Medica (b) MEDA Pharma (b) AstraZeneca (b) Bayer Healthcare (b) Boehringer Ingelheim (b) Daicchi-Sankyo (b) Medtronic (b) Merck (b) MSD (b) Otsuka Pharma (b) Pfizer/BMS (b) Sanofi-Aventis (b) Servier (b) Siemens (b) TAKEDA (b)	None	3M Medica/MEDA Pharma (d) Cardiovascular Therapeutics (d) Medtronic (d) OMRON (d) Sanofi-Aventis (d) St. Jude Medical (d) BMBF (d) Fondation Leducq (d) German Research Foundation (d) DFG (d) European Union (d)	None	None	None
George Klein	University Hospital, London, CANADA	Biotronik (c) St. Jude Medical (b) Bard (b) Medtronic (d) Boston Scientific (b)	None	None	None	None	None
Hans Kottkamp	Clinic Hirslanden Zurich, SWITZERLAND	Biosense Webster (b) St. Jude Medical (b)	None	None	None	None	None
Karl Heinz Kuck	Allgemeines Krankenhaus St. Georg, Hamburg, GERMANY	St. Jude Medical (b) Stereotaxis (b) Edwards Lifesciences (b)	None	Biosense Webster (b) CryoCath Technologies, Inc. (b) Stereotaxis (b) Medtronic (b) St. Jude Medical (b) Cordis Webster–Johnson & Johnson (b) Edwards Lifesciences (b)	None	None	None
Koichiro Kumagai	Fukuoka Sanno Hospital, JAPAN	None	None	None	None	None	None
Bruce Lindsay	Washington University School of Medicine, Missouri, USA	Medtronic (b) Boston Scientific (b) CardioInsight (b) Biosense Webster (b)	None	None	Medtronic (d) St. Jude Medical (d) Biosense Webster (d) Boston Scientific (d)	None	None

Continued

Writing Group	Employment	Consultant/Advisory Board	Speakers' Bureau/Honoraria	Research Grant	Fellowship Support	Board Mbs/Stock Options/Partner	Others
Moussa Mansour	Massachusetts General Hospital, Massachusetts, USA	Biosense Webster (b) St. Jude Medical (b) Medtronic (b)	None	Biosense Webster (d) St. Jude Medical (d) Rhythmia (d) MC10 (c) Voyage Medical (c)	None	None	None
Francis Marchlinski	Hospital of the University of Pennsylvania, Pennsylvania, USA	Biosense Webster (b) Biotronik (b) Boston Scientific (b) Cardiofocus (b) Medtronic (b) St. Jude Medical (b)	None	Biosense Webster (b) St. Jude Medical (b)	Biosense Webster (b) Biotronik (b) Medtronic (b) St. Jude Medical (b)	None	None
Patrick McCarthy	Northwestern Memorial Hospital, Illinois, USA	None	None	None	None	None	Atricure (b)
J. Lluis Mont	Hospital Clinic, University of Barcelona, SPAIN	St. Jude Medical (b) Boston Scientific (b) Sanofi-Aventis (b) Sorin Group (b) Biosense Webster (b) Medtronic (b) Menarini (b)	None	St. Jude Medical (d) Boston Scientific (d) Sanofi-Aventis (d) Biosense Webster (d) Medtronic (d)	St. Jude Medical (c) Boston Scientific (c)	None	None
Fred Morady	University of Michigan Health System, Ann Arbor, Michigan, USA	Medtronic (c)	St. Jude (b) Biotronik (b) Boston Scientific (b)	None	None	Medtronic (c)	None
Koonlawee Nademanee	Pacific Rim EP Research Institute Center, California, USA	Biosense Webster (a)	None	Biosense Webster (a)	None	None	Biosense Webster (a)
Hiroshi Nakagawa	University of Oklahoma Health Sciences Center, Oklahoma, USA	Biosense Webster (e) Stereotaxis (c) Rhythmia Medical (c) Endosense SA (c)	None	Biosense Webster (e) St. Jude Medical (d) Stereotaxis (d) Rhythmia Medical (d) Endosense SA (d)	None	None	None
Andrea Natale	St. David's Medical Center, Texas, USA	Boston Scientific (b) Biosense Webster (c) Life Watch (b) Medtronic (b) Biotronik (b)	None	None	None	None	None
Stanley Nattel	Montreal Heart Institute, Quebec, CANADA	Merck (b) Pierre Fabre (b) Xention (b)	Boehringer-Ingelheim (b) Pfizer (b) St. Jude (b)	AstraZeneca (f)	None	None	None
Douglas Packer	Mayo Foundation, Minnesota, USA	None	None	NIH (f) Medtronic (f) Thermedical (d) EpiEP (c) St. Jude Medical (f) Minnesota Partnership for Biotechnology and Medical Genomic/University of Minnesota (f) Biosense Webster (f)	None	None	Blackwell Publishing (royalty) (b) St. Jude Medical (royalty) (e)

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Writing Group	Employment	Consultant/Advisory Board	Speakers' Bureau/Honoraria	Research Grant	Fellowship Support	Board Mbs/Stock Options/Partner	Others
Carlo Pappone	Maria Cecilia Hospital, Cotignola, ITALY	St. Jude Medical (d)	None	Biotronik (e)	None	None	None
Erik Prystowsky	The Care Group, LLC, Indiana, USA	Medtronic (f) Stereotaxis (d) Bard (c) Boehringer-Ingelheim (c) Sanofi-Aventis (c)	None	None	Medtronic (d) Boston Scientific (d) St. Jude (d)	Topera (f) CardioNet (f) Stereotaxis (c)	None
Antonio Raviele	Umberto I Hospital, Venice, ITALY	Sanofi-Aventis (c) Boehringer-Ingelheim (b) St. Jude Medical (b) Biosense Webster (b)	None	None	None	None	None
Vivek Reddy	Mount Sinai School of Medicine, New York, USA	None	None	St. Jude Medical (b) Biosense Webster (b) Endosense (b) Medtronic (b) CardioFocus (b) Atritech (b) Phillips (b) Voyage Medical (b) SentreHeart (b)	None	St. Jude Medical (b) Biosense Webster (b) Endosense (b)	None
Jeremy Ruskin	Massachusetts General Hospital, Boston, Massachusetts, USA	Biosense Webster (b) Portola (b) Sanofi-Aventis (b) CardioInsight (b) GE Healthcare (b) Med-IQ	None	None	None	Pfizer (b) Portola (b)	None
Richard Shemin	David Geffen School of Medicine at UCLA, California, USA	None	None	None	None	None	None
Hsuan-Ming Tsao	National Yang Ming University Hospital, TAIWAN	None	None	None	None	None	None
David Wilber	Loyola University Medical Center, Illinois, USA	Medtronic (b) CardioInsight (b) Biotronik (b) Guidant (b) St. Jude (b) Biosense Webster (b) Sanofi-Aventis (b)	None	None	Biosense Webster (d) St. Jude (d) Medtronic (d)	None	None

(a) = $0.
(b) = <$10,000.
(c) = >$10,000 to <$25,000.
(d) = >$25,000 to <$50,000.
(e) = >$50,000 to <$100,000.
(f) = >$100,000.

Peer reviewer author relationships with industry and other entities

Writing group	Employment	Consultant/advisory board	Speakers' bureau/ honoraria	Research grant	Fellowship support	Board Mbs/ stock options/ partner	Others
Niv Ad	Inova Heart and Vascular Institute, Falls Church, VA, USA	Bitech (b) Medtronic (b) St. Jude Medical (b)	None	None	None	None	None
Jennifer Cummings	University Of Wisconsin Hospital and Clinic, Madison, WI, USA	St. Jude Medical (b) Boston Scientific (b) Medtronic (b) Sanofi-Aventis (b)	Sanofi-Aventis (b)	None	None	None	
A. Mark Gillinov	Cleveland Clinic, Cleveland, OH, USA	Edwards Lifesciences (d) Atricure (b) Onyx Lifesciences (b)	None	None	None	Pleuraflow (b)	None
Hein Heidbuchel	University Hospital Gasthuisberg, Leuven, BELGIUM	Boehringer-Ingelheim (b) Daiichi-Sankyo (b) Bayer (b) Pfizer (b) Sanofi-Aventis (b) Medtronic (b) Biotronik (b) Merck (b)	None	Medtronic (e) Biotronik (d) Boston Scientific (d) St. Jude Medical (c) Astra-Zeneca (c)	None	None	None
Craig January	University Of Wisconsin Hospital and Clinic, Madison, WI, USA	None	None	None	None	Cellular Dynamics International (d)	None
Gregory Lip	University of Birmingham, Birmingham, UNITED KINGDOM	Bayer (c) Astellas (c) Sanofi-Aventis (c) BMS/Pfizer (c) Boehringer Ingelheim (c) Merck (b) AstraZeneca (b) Biotronik (b) Portola (b)	Boehringer Ingelheim (d) Bayer (c) Sanofi-Aventis (c) BMS/Pfizer (c)	None	None	None	None

Continued

Writing group	Employment	Consultant/advisory board	Speakers' bureau/ honoraria	Research grant	Fellowship support	Board Mbs/ stock options/ partner	Others
Steven Markowitz	New York Presbyterian Hospital and Cornell Medical Center, New York, NY, USA	Medtronic (b) Boston Scientific (b) St. Jude Medical (b) Biotronik (b) Sanofi- Aventis (c)	None	None	None	None	None
Mohan Nair	Fortis Flt Lt Rajan Dhall Hospital, New Delhi, INDIA	None	None	None	None	None	None
I. Eli Ovsyshcher	Soroka Medical Center, BeerSheva, ISRAEL	None	None	None	None	None	None
Hui-Nam Pak	Korea Univ Cardiovascular Center, Seoul, KOREA	None	None	None	None	None	None
Takeshi Tsuchiya	MC Co., Ltd., Tokyo, JAPAN	St. Jude Medical (b) Nihon Kohden (b)	None	None	None	None	None
Dipen Shah	Hopital Cantonal De Geneve, Division of Cardiology, Geneva, SWITZERLAND	Biosense Webster (b) Medtronic (b) St. Jude Medical (b) Biotronik (b) Endosense (c)	Biosense Webster (b) Medtronic (b) Biotronik (b) Endosense (c)	Biosense Webster (e) St. Jude Medical (d)	None	Endosense (c)	None
Teo Wee Siong	Nat Heart Centre Singapore, SINGAPORE	Medtronic (b) St. Jude Medical (b) Biosense Webster (b) Boston Scientific (b)	None	None	None	None	None
Panos E. Vardas	Heraklion Univ Hospital, Stavrakia, GREECE	Servier (b) Boehringer Ingelheim (b) Medtronic (b) Bayer (b) Pfizer (b)	None	None	None	None	None

(a) = $0.
(b) = <$10,000.
(c) = >$10,000 to <$25,000.
(d) = >$25,000 to <$50,000.
(e) = >$50,000 to <$100,000.
(f) = >$100,000.

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